MALAYSIAN SOCIETY OF ANAESTHESIOLOGISTS

Year Book 2009/2010

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Foreword

The Malaysian Society of Anaesthesiologists (MSA) is once again proud to present to our members the third issue of our Year Book 2009/2010. It is a compilation of articles that review current and interesting topics in anaesthesia, intensive care and pain management. Unlike journals that collect original articles and studies, our yearbook refreshes us on updates and controversies on various important issues in our discipline. This is one way the MSA supports and promotes continuous professional development for its members.

I wish to thank our contributors, from the very senior knowledgeable members to those brilliant younger ones, for their effort and time spent in making this publication complete. The articles are peer reviewed, hence they were not simple submissions and acceptance. I hope MSA members will appreciate the hard work involved and for that I must thank Professor Dr Marzida Mansor, the editor, who did an excellent job. We appreciate your perseverance and patience but I am sure the end-product makes it all worthwhile!

I hope MSA members will benefit from our Year Book and look forward to our next issue. Congratulations once again to the team involved, from the contributors, the reviewers and the editor for producing articles of interest and quality.

Norsidah Abdul Manap
President, MSA
December 2010

Preface

I would like to thank the Malaysian Society of Anaesthesiologists (MSA) for giving me the honour to compile the MSA Year Book for 2009/2010. I have started compiling the articles since 2009 but only managed to publish it in 2010. A million thanks to those who have contributed their precious time and effort to either writing the articles or reviewing them.

The objective of the Year Book has been to publish some of the talks that were given in conferences by the anaesthesiologists to benefit members of the society who were not able to attend these conferences due to heavy teaching or clinical commitments.

In this third MSA Year Book publication, we have tried as much as possible to cover a range of topics in anaesthesia which include among others, updates on paediatric anaesthesia, intensive care, anaesthesia for neuroradiology, geriatric anaesthesia and current concepts of appropriate care in anaesthesia.

As you may have noticed we have also invited some young authors. The response has been encouraging and we can now be rest assured that our fraternity does not lack young talent.

Finally I would like to thank Dr Mary Cardosa for her support in helping to proofread the book and special acknowledgement to Ms Kong Yoon Moi whose professionalism and efficiency have greatly contributed to the completion of this book.

I hope that you enjoy reading this book as much as we have enjoyed compiling it.

Marzida Mansor

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Major Controversies in Perioperative Fluid Therapy in Children

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INTRODUCTION

A fluid management strategy for every child who is scheduled for surgery should address three key areas: fluid deficit, maintenance fluid requirement and on-going losses (blood loss and surgical losses). There are some debatable issues regarding fluids for maintenance therapy and this chapter hopes to highlight the major problems. Neonates and infants are not included in the discussion.

HISTORICAL BACKGROUND: WATER, ELECTROLYTES AND CALORIES IN MAINTENANCE THERAPY FOR CHILDREN

The infusion of hypotonic maintenance fluids has been practiced since the 1950s according to the protocol from Holliday and Segar.[1] The popular 4:2:1 formula describes the amount required to replace physiologic losses from insensible losses and urine output which respectively contribute 1/3 and 2/3 of maintenance volume.

While water needs have been shown to parallel energy metabolism (1 ml water required for the consumption of 1 calorie), the appropriate quantity of electrolytes (especially sodium) in the volume of water is less precise. The amount of electrolytes is based on the composition of electrolytes found in the same volume of human and cow's milk that is consumed: 3 mmol/kg/day of sodium and 2 mmol/kg/day of potassium. Glucose is added to support brain metabolism, reduce protein and fat catabolism and prevent ketosis. This is the physiological basis for the infusion of Dextrose 5% (D5) or D10 in 0.18% to 0.45% saline (potassium added as needed) in surgical paediatric patients in the perioperative period. These fluids are isotonic when administered but effectively hypotonic once the glucose component is metabolized.

Two major controversies arise in the intraoperative and postoperative periods from the implementation of the above traditional strategy of maintenance fluid therapy:

1) Is the sodium content appropriate (hypotonic)?
2) Is glucose useful or harmful?

1. Problem with sodium content

Maintenance fluid therapy that is practised widely today is based on physiological concepts that may differ from what should actually be applied to ill children who have various underlying pathophysiological processes that require surgery and anaesthesia. Questions have been raised regarding hypotonic solutions as a cause for the development of acute hyponatremia. Do hypotonic solutions maintain tonicity balance in the perioperative period?

Pathophysiology and presentation of acute hyponatremia

The concept that extracellular fluid (ECF) is the "internal environment for sustaining all life" remains unchanged and unchallenged in modern medicine.[2] Sodium is the principal cation in the ECF compartment. Regarding fluid-related complications in the perioperative period, no other electrolyte has attracted as much attention as sodium. It is a convenient marker of tonicity homeostasis and indicates the ratio between effective osmoles and total body water. It regulates water movement across cell membranes and the presence of hyponatremia favors the movement of water into cells.

The normal surgical stress response is an increased secretion of antidiuretic hormone (ADH), resulting in water retention and hyponatremia. Hyponatremia, Na <135 mmol/L, reflects an expanded ECF compartment that is rarely caused by actual sodium loss. Severe hyponatremia

occurs when Na < 130 mmol/L or any level of hyponatremia that is associated with symptoms.

Acute dilutional hyponatremia is a potential problem in probably every postoperative patient who has undergone surgery (minor to major) and who receives hypotonic fluids (either in the intraoperative or postoperative period). The most severe neurological sequelae and deaths in both children and adults have been reported in postoperative patients who are affected by many non-osmotic stimuli for ADH production, including volume depletion, pain, nausea and vomiting, stress and narcotics. Children under 16 years are more at risk for an additional two reasons: low threshold and larger brain-skull volume ratio than adults.

A source of electrolyte free water (EFW) and an inability to excrete free water in the kidney are central issues to the problem. Table 1 shows the % EFW in the commonly used crystalloid solutions. The clinical presentation is variable and may prove difficult to diagnose. The most consistent symptoms include headache, nausea, vomiting and weakness. A life-threatening situation occurs when hyponatremic encephalopathy occurs with brain herniation. Children who develop symptomatic hyponatremia are at substantially higher risk to brain damage and death than adults.[3] If the crisis is not rapidly managed, there is poor prognosis. Fatal cerebral oedema has occurred during surgery.[4]

TABLE 1: Sodium content, osmolality and % EFW in commonly used crystalloid solutions

Crystalloid	Sodium (mmol/L)	Osmolality (mosm/kg H2O)	% electrolyte free water (EFW)
Dextrose 5%	0	252	100
Saline 0.18%/dextrose4%	30	282	80
Saline 0.45%/dextrose2.5%	75	293	50
Hartmann's solution	131	278	16
Dextrose 5%/Ringer's sol	130	525	16
Saline 0.9%	150	308	0
Dextrose 5%/saline 0.9%	150	560	0

What is reported in the literature on acute hyponatremia in children?

The routine use of hypotonic solutions has been questioned due to concerns of hyponatremic encephalopathy.[5,6] As far back as in 1953, Talbot cautioned about the potential danger of giving hypotonic fluids in patients at risk of ADH excess.[7] Moritz reported that more than 50% of children who developed symptomatic hyponatremic encephalopathy had serum Na < 125 mmol/L, and there were at least 26 deaths in minor and major surgeries.[8]

Brazel measured serum sodium in the postoperative period after spine surgery in 12 children who received hypotonic saline or isotonic saline and found a significant decrease in sodium and osmolarity in the group that received hypotonic fluid.[9] Hoorn suggested avoiding hypotonic fluid if plasma Na < 138 mmol/L in hospitalized children.[10] Some authors believe that the ADH response makes it sensible to reduce the volume of postoperative fluids by approximately 33%-50% compared with normal maintenance amounts.[11, 12]

The popularity of hypotonic fluids for maintenance therapy was reported in a recent survey in United Kingdom.[13] In the intraoperative period 60.1% of anaesthetists prescribed hypotonic dextrose saline solutions while 75.2% used them postoperatively. D4 in 0.18% saline was the most widely administered. Two recent systematic reviews are cited below to illustrate the uncertainties

in expert opinions concerning the appropriate sodium content in maintenance fluid therapy for hospitalized children.

In a systematic review Choong concluded that there was potential harm with hypotonic fluids.[14] Four of the six studies reviewed involved surgical patients. Although no single fluid composition or rate was considered ideal for all children, an isotonic or near-isotonic solution was considered preferable, being more physiological and therefore a safer choice in the perioperative period and acute phase of illness.

In Beck's systematic review on hypotonic versus isotonic maintenance fluid therapy in hospitalized children, three studies were included.[15] All the studies were observational and it was difficult to justify any conclusion (only one involved surgical patients). Specific recommendations for perioperative maintenance fluid therapy were inconclusive because the author's analysis involved a broad range of medical and surgical patients and there were many confounding factors. The need for further research was stressed.

Is isotonic maintenance fluid the answer (0.9% NaCl or Ringer's lactate)?

It is still uncertain whether isotonic or near-isotonic solution is the ideal fluid for maintenance therapy. For example, while Moritz has brought forward a case for isotonic saline,[16] Holliday proposes that "isotonic saline expands extracellular fluid and is inappropriate for maintenance therapy".[17]

Although the arguments in favour of isotonic solutions are forceful, there are still concerns in promoting them as best practice to meet maintenance fluid requirements for children:

1) There are no trials that adequately compare hypotonic versus isotonic fluids.
2) The effectiveness in the prevention of acute hyponatremia is uncertain.
3) The safety aspect is questioned.
4) Why is hyponatremia still observed in the postoperative period despite the administration of isotonic fluids? (Steele suggested that isotonic fluid can result in hyponatremia, possibly due to acute volume expansion from isotonic fluid leading to excretion of hypertonic urine and hence a fall in plasma sodium.[18])
6) There is a potential risk of hypernatremia and fluid overload (especially in children with congestive heart failure, cirrhosis and nephrosis).

What can be concluded with regard to sodium content in maintenance fluids?

The last word on sodium content in maintenance therapy has yet to be heard.

It is uncertain whether the root of the problem lies with too much fluid or the wrong type of fluid infused. Measurement of plasma sodium and osmolality, as well as urine sodium and osmolality, may be the optimum guide to prescribe fluid needs in the perioperative period.

2. Problem with glucose content

Lately, concerns have arisen in pediatric anaesthetic literature regarding the need for glucose in surgery rather than consideration for sodium content. In the past, worries of intraoperative hypoglycemia have dictated the use of hypotonic dextrose saline in children. There are now many experts who believe that the issue of hypoglycemia has been over-emphasised. On the other hand, a blanket policy that avoids dextrose in perioperative fluid therapy for all surgical paedatric patients is unlikely to receive full support from anaesthesiologists. The risk of hypoglycemia needs to be balanced against hyperglycemia.[19]

Adverse effects of hypoglycemia and hyperglycemia

Glucose is an essential fuel for the normal brain. Without an adequate supply of glucose, alternative sources of energy are derived from substrates in the catabolism of muscle protein and circulating fatty acids, leading to ketosis. Hypoglycemia can be deadly when it presents with severe central

nervous system disturbances, such as coma and seizures. Sustained or repetitive hypoglycemic episodes have a major impact on normal brain development and function in children.

Hyperglycemia is also detrimental to the brain. Experimental results indicated worsening effects of brain ischemia/hypoxia if glucose was given prior to the insult.[20] However, the possible aggravation of neurological damage induced by ischemia/hypoxia is difficult to assess via clinical trials. Other problems of hyperglycemia include dehydration and electrolyte imbalance from osmotic diuresis. A controversial relationship exists between hyperglycemia and nosocomial infections.[21]

What happens to the blood glucose level in routine surgical paediatric patients?

Energy requirements during anaesthesia are close to basal metabolic rate and hyperglycemia is more likely to occur during surgery than hypoglycemia. In the intraoperative period, there is reduced uptake of glucose by the muscle. The sugar level is also elevated by the metabolic response to surgery and anaesthesia, together with anxiety and pain. This is further affected by impaired effectiveness of insulin during anaesthesia (stress-induced insulin resistance). Overall, these circumstances produce a situation of decreased tolerance to exogenous glucose and an increased endogenous glucose production.

It is important to realise that some children are prone to hypoglycemic episodes and they are likely to benefit from dextrose administration -

1) premature babies and neonates with limited glycogen stores and impaired gluconeogenesis.
2) children on beta-blockers (propranolol induced-hypoglycemia).
3) children with regional anaesthesia, a technique that reduces hyperglycemic response to surgery.
4) children with conditions at risk of hypoglycemia (hyperalimentation, infants of diabetic mothers, hypopituitary, large hepatoma/fibroma/sarcoma).

Prolonged fasting periods are no longer recommended for children who are waiting for surgery. The use of new guidelines in fasting prior to surgery improves hydration and contributes to euglycemic levels.[22] Welborn found that if children were allowed to drink clear fluids 2-3 hours before surgery, their blood sugar levels were within normal limits compared with those allowed clear fluids up to 6 hours before surgery.[23] Hence, the vast majority of children do not need glucose in the perioperative period or blood glucose monitoring. A blood glucose value of 2.4 mmol/L is often quoted as the acceptable level in infants and children.

Is there an appropriate glucose content in maintenance fluid therapy?

Early studies from 1970s to 1980s showed that there was a risk of hypoglycemia from preoperative starvation in children. Watson suggested a 10% incidence of hypoglycemia.[24] There has been a change in focus from the danger of hypoglycemia to a more relevant clinical issue, that of hyperglycemia. A re-evaluation of the role of glucose has resulted in a dramatic decrease in dextrose administration in the perioperative period.

One study showed that if D5 was used, up to 30% children had hyperglycemia with blood glucose level >11mmol/L[25] while another reported that the value of glucose could vary up to 28 mmol/L in the postoperative period.[26]

Hongnat evaluated two hydrating solutions during surgery, D5 or D2.5 in 0.3% or 0.4% saline, and concluded that the use of the former was more likely to result in hyperglycemia and hyponatremia than the latter, particularly in children less than 4 years old.[27] To prevent lipid mobilization leading to ketosis, a dextrose infusion rate of 120mg/kg/hour has been found to be acceptable.[28]

Although D2 or D2.5 solution is associated with less blood glucose rise during surgery, favorable results have been reported with the administration of low dextrose concentrations, such as D1 or D0.9.

Three randomized studies evaluated the effects of D1 or D0.9 in lactated Ringer's and reported that hypoglycemia was prevented and blood sugar levels were maintained in the normal range.[29, 30, 31]

It appears convincing that D0.9 or D1 may be the compromise as it is sufficient to prevent hypoglycemia and ketosis in children whereas D4 or D5 has a high risk of hyperglycemia. It has been suggested that a solution of D0.9 in Ringer's lactate known as Polyionique B66 (available in France) should be considered appropriate for routine infusion in paediatric patients in the perioperative period.[19]

CONCLUSION

There is no ready-to-use safe and optimal fluid for maintenance therapy in the perioperative period in children, particularly with respect to sodium and dextrose amounts. At the present moment, anaesthesiologists have not much choice but to depend on the type of crystalloids that are available in their place of practice. While awaiting prospective randomized trials and consensus guidelines from a panel of experts, it is perhaps timely to reflect on the advice of Holliday and Segar: "Even after all the questions are answered, it should be acknowledged that no hydration or laboratory method will ever replace the presence of a physician with good clinical judgement and the careful follow-up, that each critically ill patient deserves".[32]

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Emergence Agitation in Children

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INTRODUCTION

Emergence agitation is a common & significant postanaesthetic problem in children. It is not a new phenomenon in clinical practice. In early 1960's, Eckenhoff et al reported signs of postoperative hyperexcitation in patients who had ether, cyclopropane or ketamine anaesthesia for tonsillectomy, thyroidectomy and circumcision.[1] They also observed that children experienced postoperative agitation more often than adults (12-13% vs 5.3%). When the use of halothane became more common and with the recognition and better management of postoperative pain, the incidence of emergence agitation declined considerably. However with the introduction of new, low solubility inhalational anaesthetic agents like sevoflurane & desflurane, the problem of emergence agitation reemerged.

DEFINITION OF EMERGENCE AGITATION

There is a variety of behavioral disturbances which a child may experience when he emerges from anaesthesia. These behavioural disturbances have been interchangeably described in the literature as postanaesthetic excitement, delirium, and agitation. Most of the literature on this subject does not differentiate between these terms.

Emergence agitation has been defined as a state of nonpurposeful restlessness and inconsolability that is often accompanied by thrashing, screaming, prolonged crying and disorientation upon recovery from anaesthesia. Often the child appears to be unaware of his surroundings, and does not recognize or identify familiar objects or people. Sometimes the child also exhibits combative behaviour. Although emergence agitation is self-limiting, it can be very frightening for the parents or caregivers. It makes nursing and monitoring difficult and may result in physical harm to the child and dislodge intravenous access, drains, catheters, dressings etc. It is therefore important to prevent or control it.

INCIDENCE OF EMERGENCE AGITATION

The incidence of emergence agitation varies, depending on definition of "emergence agitation" and the assessment tools used. Reported incidence varies, ranging between 10-67% (Table 1). Greatest incidence has been observed with the use of low solubility agents e.g. sevoflurane and desflurane and in pre-school, preverbal children.

ASSESSMENT TOOLS FOR MEASURING EMERGENCE AGITATION

There is no standardized tool to measure emergence agitation. More than 15 different rating scales have been used but none are sufficiently specific and sensitive to assess children's behaviour upon

TABLE 1: Incidence of Postoperative Emergence Agitation

Authors	Agent	Incidence %
Lerman et al.[2]	Sevoflurane	8
Picard et al.[3]	Sevoflurane	46
Voepel-Lewis et al.[4]	Sevoflurane	20
Cohen et al.[5]	Sevoflurane/Desflurane	18/24
Lapin et al.[6]	Sevoflurane	67
Welborn et al.[7]	Sevoflurane/Halothane/Desflurane	10/25/55

emergence. It is difficult to interpret behaviour in small children who are not able to verbalize pain, anxiety, hunger or thirst. There is no agreement as to the point where behaviours are considered not 'normal'. Pain is a confounding factor and behavioral signs of emergence agitation often mimic those of postoperative pain and moreover agitation is also part of assessment of postoperative pain.

Most authors used self-developed unvalidated 3 to 5 point scores that used either crying or thrashing requiring restraint as their threshold for agitation. Recently Sikich and Lerman developed a new scale, the Paediatric anaesthesia emergence delirium (PAED) scale (Table 2), incorporating cognitive-related assessment items in addition to agitation behaviors.[8] Studies have shown reliability and validity of this scale.[8,9] Unfortunately,

TABLE 2: Pediatric Anesthesia Emergence Delirium (PAED) Scale

	Score
1. The child makes eye contact with Caregiver	4 = not at all
	3 = just a little
2. The child's actions are purposeful	2 = quite a bit
3. The child is aware of his/her surroundings	1 = very much
	0 = extremely
4. The child is restless	0 = not at all
	1 = just a little
5. The child is inconsolable	2 = quite a little
	3 = very much
	4 = extremely
Maximum score is 20	
The higher the score, the higher degree of emergence delirium	

the authors did not define the threshold for emergence agitation/delirium.

Aetiology

No single aetiology has been determined to explain emergence agitation. When an increased incidence of emergence agitation was noticed in the early trials of sevoflurane it was thought to be due to pain in the presence of a rapid recovery. In several studies, the preemptive analgesic approach successfully reduced the incidence of emergence agitation, suggesting that pain may be its major source.[10] On the other hand, postanesthesia agitation has been observed even when pain has been efficiently treated.[11,12,13] In a recently study, Cravero et al compared recovery after sevoflurane and halothane in children during magnetic resonance imaging, a non-painful intervention.[14] They found that the incidence of emergence delirium after sevoflurane was substantively greater than that after halothane.

The rapid recovery from sevoflurane has been speculated to cause emergence agitation. Studies comparing the emergence from sevoflurane and propofol, showed that although emergence was rapid from both agents, the incidence of emergence agitation after sevoflurane anesthesia was higher, while emergence from propofol was associated with a calm and euphoric state.[15] Oh et al have shown in a recent study that rapid awakening is not the cause of emergence agitation following sevoflurane.[16] Controlling the speed of emergence by gradually decreasing the sevoflurane concentration only prolonged recovery without decreasing the incidence of emergence agitation.

Factors Affecting Emergence Agitation

Age

The highest incidence of emergence agitation has been observed in children between 2-5 years of age. A study by Aono et al show that a higher incidence of postoperative agitation in preschool boys anaesthetized with sevoflurane when compared to older children.[11] Viitanen et al reported an incidence of 55% in children 1–3 years of age.[17] The authors speculated that the psychological immaturity of preschool children, coupled with the rapid awakening in a strange environment, may have been the main cause.

Pre-operative Anxiety

The correlation between preoperative anxiety and postoperative agitation has been studied by a number of authors. A number of studies have shown that higher levels of preoperative anxiety were associated with an increased risk of emergence agitation.[18,19] However, no cause-effect relationship has been established.

Anaesthesia-related factors

Anaesthetic Agents

The more insoluble agents like desflurane and sevoflurane are associated with a higher level of postoperative emergence agitation when compared with halothane and propofol. Propofol has been shown to have a very low incidence of emergence agitation. Lapin SL et al found that the incidence of emergence agitation was 67% with sevoflurane and 29% with halothane.[6] Picard et al studied quality of recovery of children aged 3–10 years undergoing elective tonsillectomy, who received propofol as induction and maintenance compared with children who received sevoflurane anaesthesia for induction and maintenance.[3] There was a significantly greater incidence of postoperative agitation in the sevoflurane group (46%) compared with the propofol group (9%) (p=0.008). Desflurane has also been found to have a higher incidence ranging between 50-80% when compared with halothane.[5]

Premedication

Midazolam has been shown to decrease emergence agitation following sevoflurane anesthesia in some studies.[6,20] In contrast, other studies showed no effect following sevoflurane or halothane anesthesia.[21,22] Kararmaz et al found that oral ketamine premedication reduced the incidence of postanaesthesia emergence agitation in children without delaying recovery after desflurane.[23]

Parental Presence upon Awakening

Although there have been studies done on the effect of parental presence on the quality of induction of anesthesia in children, no randomized controlled studies have evaluated the effect of parental presence on the quality of emergence from anesthesia. Demirbilek et al observed that some children are calmed simply by the presence of a parent despite the presence of pain at the surgical site.[24] Weldon et al showed that the incidence of emergence agitation was further decreased after parents rejoined their children in the postanesthesia care unit (PACU).[13] Many believe that the presence of a parent with the child following emergence from anesthesia might contribute to a smoother recovery by making the PACU a less hostile environment.

Types of Surgery

Surgical procedures that involve the tonsils, thyroid, middle ear, and eye have been reported to have higher incidences of postoperative agitation and restlessness.[2,4] Eckenhoff et al speculated that a "sense of suffocation" during emergence from anaesthesia may contribute to emergence agitation in patients undergoing head and neck surgery.[1] For ophthalmology procedures, it is possible that when vision is disturbed following surgery and eye patching, the reactivity of the child to a hostile environment upon awakening from anesthesia may be distorted, thus the increased incidence of emergence agitation.

Long Term Effects

There is no evidence that emergence agitation has any impact on long term outcome. Keaney

et al found no relationship between sevoflurane and development of long term maladaptive behavioral changes although children who had sevoflurane exhibited more immediate post-operative distress.[25] Kain et al found no increased incidence of maladaptive postoperative behavior changes or sleep disturbances in children undergoing anaesthesia with sevoflurane compared with halothane.[26]

Prevention & Treatment

Since the aetiology of emergence agitation is unclear, no clear cut strategy for its prevention has been developed. Many measures have been used. These include use of benzodiazepine as premedication,[6] oral ketamine,[23] intraoperative opioids[27,28] and recently the use of intravenous clonidine[29] and dexmedetomidine.[30] There are two studies in which the authors hypothesized that switching from sevoflurane to either isoflurane[31] or desflurane[9] might attenuate the incidence of emergence delirium in children.[9] In the first study, Bortone et al compared the incidence of emergence delirium in preschool age children with regional blocks after inguinal surgery with sevoflurane or isoflurane.[31] Using a self-styled scale to evaluate emergence delirium and a large cohort of children (n=128), they concluded that switching from sevoflurane to isoflurane for maintenance reduced the incidence of emergence delirium by 66%. Because the authors used a non-validated scale to evaluate emergence delirium this limits the universality of the results and precludes verification by other authors. In the second study, Mayer et al randomized children to receive either sevoflurane or desflurane for maintenance of anesthesia during tonsillectomy and adenoidectomy surgery and measured emergence delirium during recovery with the PAED scale.[9] They determined that the incidence of emergence delirium after sevoflurane was twice that after desflurane. However their sample size was small and pain may have been a confounding variable. At the moment no effective drugs or methods have been identified to prevent emergence agitation. However it is recognized that prevention of pain is indispensable to prevent emergence agitation but not sufficient as sole method.

Management of Emergence Agitation

Emergence agitation usually occurs within the first 30 minutes after anaesthesia and is time limited. However it carries the risk of injury, bleeding and dislodging drains, dressing or intravenous lines. It also causes parental distress and requires increased nursing care and thus delays discharge from PACU. Therefore there is a need to adopt preventive and therapeutic strategies. It is important that there must be adequate pain relief and physical comfort provided to the child. As the child may be upset by environmental stimuli, it is important to provide a quiet recovery room with minimal disturbances. Parental presence will be a great help. Steps must be taken to protect the child from physical self-injury when the child exhibits combative behaviours. Rescue medications that have been used IV include fentanyl 1-2 μg/kg[7], propofol 0.5-1.0mg/kg[32] and midazolam 0.02-0.10 mg/kg.[5] A single bolus dose of dexmedetomidine 0.5 μg/kg has also shown to be efficient in the PACU for emergence agitation.[33]

CONCLUSION

Emergence agitation is a distinct entity which has been observed in sevoflurane, desflurane and isoflurane anaesthesia. At the present moment, aetiology is unclear and there is no clear-cut preventive strategy for it. There are still many unanswered questions and further trials are necessary to discover the underlying causes and to determine which factors might help to predict and prevent it.

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Intraoperative Tight Glycaemic Control, What is the Evidence?

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Perioperative glycaemic control is related to patient outcome. Surgery, critical illness and trauma are all associated with an increase in the secretion of catabolic hormones in the presence of a relative insulin deficiency. Even non-diabetic patients will become hyperglycaemic perioperatively due to a combination of decreased insulin secretion and tissue insulin resistance.

Hyperglycaemia has been identified as an independent risk factor for perioperative surgical complication including death. Factors that influence blood glucose values in the perioperative period are the diabetes itself, starvation (both preoperative and postoperative), hormonal and metabolic response to the stress of surgery and anaesthetic drugs. Insulin administration in the perioperative period to control blood glucose has been advocated for many years, for its potential therapeutic benefits. However, to date there is no universal application in the use of insulin to control intraoperative blood glucose.

TIGHT GLYCAEMIC CONTROL

Van den Berghe et al first introduced the term tight glycaemic control in the critically ill patients.[6] In a randomized controlled trial (RCT), 1548 adults patients admitted to surgical ICU receiving mechanical ventilation, were randomly assigned to either intensive insulin therapy or conventional therapy. In the intensive insulin therapy group, blood glucose was maintained between 4.4 - 6.1 mmol/l. In the conventional therapy group, infusion of insulin was started when blood glucose was 11.0 mmol/l and then maintained between 10.0 to 11.0 mmol/l.

This study concludes that blood glucose levels of **4.4-6.1 mmol/l** improved morbidity and mortality in surgical ICU patients. Mortality was reduced from 11% to 7% in the entire study population. Futhermore, patients who stayed in the ICU for more than three days had reduction in mortality from 21% to 14% and among those treated for at least five days, mortality reduced from 26% to 17%. Complications, such as severe infections and organ failure, were also reduced.

EVIDENCE TO SUPPORT TIGHT GLYCAEMIC CONTROL INTRAOPERATIVELY

This landmark study by Van den Berghe et al advocated for glycaemic control in critically ill patients. It is tempting to extrapolate the conclusions of this large study to routine surgical practice but the generalisability of the data has not yet been established. Hence, following the publication of this trial in 2001, many attempts have been made to achieve strict glycaemic control in ICU patients and patients undergoing surgery, with varying and sometimes disappointing results. So, what is the evidence to support tight glycaemic control intraoperatively?

Ingels C et al assessed the long term outcome in 970 patients admitted to the cardiac intensive care unit after high-risk cardiac surgery with regards to the effects of intensive insulin therapy during critical illness.[7] A hospital mortality of 7.5% was noted in the conventional insulin therapy group. The blood glucose in these patients was more than 12mmol/l. The observed mortality in the intensive insulin therapy group whose blood glucose levels were maintained between 4.4 to 6.1 mmol/l was 3.4%. Hence, blood glucose levels of **4.4 to 6.1 mmol/l** was found to improve morbidity and mortality in cardiac surgical ICU patients.

Lazar HL et al reported on a prospective study of 141 diabetic patients undergoing coronary artery bypass graft (CABG).[8] They had either received Glucose-Potassium-Insulin (GKI) infusion targeting blood glucose of **6.9 to 11.1**

mmol/l or a standard therapy of intermittent subcutaneous insulin targeting blood glucose of less than 13.9 mmol/l. The treatment was started before anesthesia and continued for 12 hours after surgery. The GKI infusion was initiated just before anaesthetic induction and continued for 12 hrs after surgery. Patients who received GKI infusion had a substantially lower incidence of atrial fibrillation (17% vs 42%, *p*=0.0017) and a shorter postoperative length of hospital stay (6.5 vs 9.2 days, p=0.003). They also had reduced episodes of recurrent ischaemia and wound infections over the subsequent 2 years.

Patrick Le Comte et al retrospectively analyzed two groups of consecutive patients undergoing cardiac surgery with cardiopulmonary bypass between August 2004 and June 2006.[9] In the first group, no tight glycemic control was implemented (Control, n = 305). Insulin therapy was initiated at blood glucose levels of more than 150 mg/dL. In the group with tight glycemic control (n = 745), intra- and postoperative blood glucose levels were targeted between **80 to 110 mg/dL**. Postoperative renal impairment or failure was evaluated with the RIFLE score, based on serum creatinine, glomerular filtration rate and/or urinary output. In non-diabetic patients, tight perioperative blood glucose control was associated with a significant reduction in postoperative renal impairment and failure after cardiac surgery according to the RIFLE criteria. In non-diabetics, tight blood glucose control was associated with a decreased need for postoperative dialysis, as well as decreased 30-day mortality, despite a relatively short ICU stay.

Many studies have reported the benefits of tight glycaemic control. However, recently Gandhi GY et al reported that tight glycaemic control during cardiac surgery does not reduce perioperatve death, morbidity and length of stay in the ICU hospital. In fact, it leads to an increase in death and stoke in the intensive treatment group.[10]

ROLE OF INSULIN

Insulin has important effects on carbohydrate, fat and protein metabolism. It lowers the blood levels of glucose, fatty acids and amino acids and promotes their storage into glycogen, triglycerides and protein. Effectiveness of insulin therapy at preventing hyperglycemia has been shown by many studies. However the effect of insulin administration on plasma levels of free fatty acids and triglycerides has largely been ignored.

Perioperative hyperinsulinaemic normoglycaemic (HING) clamp causes hypolipidaemia after coronary artery surgery. Hyperinsulinaemic normoglycaemic clamp is a method in which insulin is administered at high dose (supra-physiological). Soluble insulin is infused at a fixed rate of 0.1 IU/kg/hr. This will predictably cause hypoglycaemia and hypokalaemia. To counteract this effect, glucose and potassium are concomitantly administered - a separate mixture of glucose 30%, KCl 80mmol/l and phosphate 60 mmol/l is infused at a variable rate adjusted to maintain blood glucose at **4.0-6.0 mmol/l**.

Apart from changes in plasma concentration of glucose, HING clamp is also associated with significant changes in the plasma concentration of free fatty acids (FFA), triglycerides, lipoprotein TG, ketone bodies and lactate. Cardiac function is critically dependent on utilization of these substrates and their availability. The heart can oxidize carbohydrates, lipids such as fatty acids, triacylglycerols (TAG), very low density lipoprotein (VLDL) and ketone bodies. The healthy heart generates about 70% of its energy requirement from fatty acid oxidation and the remaining ATP synthesis is derived from carbohydrates. Plasma concentration of FFA is increased in stress response and in diabetes due to an increase in adipose tissue lipolysis and fatty acid release by lipolytic hormones such as catecholamines. Hence, both availability and myocardial utilisation of FFA increase at this time. Insulin lowers the plasma concentration of FFA by inhibiting adipose tissue lipolysis. Plasma concentration of FFA may be lowered to a very low level, probably too low to allow uptake by the heart. This includes lowering of TAG, VLDL, ketone bodies but not lactate. The heart may be negatively affected by the acute withdrawal of the substrate that normally provides 70% of its energy requirement. Therefore, we need

to distinguish between tight glycaemic control and hyperinsulinaemic therapy as hyperinsulinaemic normoglycaemic clamp is associated with significant changes in the plasma concentration of a number of substrates other than glucose that is potentially hazardous for the heart.

SO, HOW TIGHT SHOULD THE PATIENT'S BLOOD GLUCOSE BE REGULATED INTRA OPERATIVELY?

The ideal range of blood glucose in the perioperative period has only been established in cardiac surgical patients. Futher studies need to be done to establish the ideal range of blood glucose in patients, especially diabetic patients under going non cardiac surgery. However, there is good evidence showing that controlling the blood glucose to less than 10 mmol/l in the perioperative period for diabetic patients improves outcome. It is also shown that continuous insulin infusions provide better glycaemic control than intermittent regimens and combined glucose-insulin-potassium regimens have the advantage of inherent safety. However, blood glucose must be monitored frequently and controlled carefully, and this is the key to successful perioperative management. Shall tight glycaemic control be applied to patients under going surgery? Futher studies need to be done. If tight glycaemic control is applied in any intraoperative patients, it is prudent that blood fatty acid concentrations be monitored with the same frequency as blood glucose levels.

The current guideline on goals for glycaemic control of hospitalized patients produced by the America College of Endocrinology in conjunction with the American Society of Anaesthesiologist recommends that:

1. Always maintain blood glucose below 180 mg/dl. There is biochemical evidence suggesting a favorable alterations in myocardial and skeletal metabolism, immune function, inflammation, endothelial cell and platelet function with normoglycaemia.
2. Maintain blood glucose between 80-110 mg/dl in ICU patients.
3. Avoid oral hypoglycaemic drugs unless patients are on a regular diet. Oral hypoglycaemic drugs do not maintain tight glycaemic control. The long half-life of these drugs make titration in the perioperative period difficult. Futhermore, many of the oral drugs do not decrease serum glucose but rather increase tissue sensitivity to insulin.
4. Provide basal insulin in patients who are insulin deficient.
5. Create and implement a hypoglycaemia prevention and management protocol.

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Updates on Enteral Nutrition in ICU

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Adequate nutrition support is essential in the management of the critically ill intensive care unit (ICU) patient. In these patients, malnutrition is associated with impaired immune function, impaired ventilatory drive and weakened respiratory muscles, leading to prolonged ventilator dependence and increased infectious morbidity and mortality.[1] Malnutrition is prevalent in ICU patients, and has been reported as being as high as 40%, and is associated with increased morbidity and mortality.[2]

The benefits of nutrition support in the critically ill include improved wound healing, a decreased catabolic response to injury, improved gastrointestinal structure and function and improved clinical outcomes including a reduction in complication rates and length of stay, with accompanying cost savings. Despite its widespread use in ICU, many areas in clinical practice remain controversial. This article addresses some of the many issues that are commonly encountered in daily practice.

SHOULD THE INITIAL NUTRITIONAL RISK IMPACT THE DECISION TO START EARLY NUTRITION SUPPORT?

It is rational and imperative, though not evidence based, that a formal initial assessment of nutrition risk on ICU day 0 guides the decision-making for early nutrition support. Malnutrition is a disorder of body composition in which macronutrient and/or micronutrient deficiencies occur when nutrient intake is less than required, and is associated with less optimal clinical outcomes. Assessment of malnutrition in critically ill patients includes evaluation of clinical, anthropometric, chemical, and immunologic parameters reflecting altered body composition.[3] Loss of body weight, which is universally coincident with protein caloric malnutrition, provides a readily accessible indication of altered nutritional status. Weight loss in excess of 10% whether in obese or normal-weight individuals in the past 6 months is important and suggestive of nutritional risk.[4]

Hepatic secretory proteins such as albumin, transferrin, retinol binding protein and prealbumin are markers of visceral protein stores and are used as indicators of nutritional status. As these proteins have various half-lives, they have variable sensitivity as predictors of nutritional status. Hepatic protein production is also influenced by numerous factors in addition to the nutritional status, including disorders of hepatic function, protein losing states, and acute infection or inflammation. The frequent presence of these conditions in ICU patients limits the effectiveness of these proteins as markers of nutritional deficiency or the effectiveness of nutrition support. Anthropometry measurements, creatine height index and other measurements are also not validated and reliable in ICU patients. No simple recommendation can be given regarding the "best" test for nutritional assessment in ICU. Use of any of these methods can be appropriate, providing the limitations are clearly understood.

DOES ENTERAL NUTRITION (EN) COMPARED WITH PARENTERAL NUTRITION (PN) RESULT IN BETTER OUTCOMES IN THE CRITICALLY ILL ADULT PATIENT?

Compared with PN, EN is associated with a significant reduction in infectious complications in numerous prospective randomised controlled trials.[5,6,7] This is not attributed to the higher blood sugar levels and calorie intake in the parenteral receiving patients as previously postulated. There is no apparent difference in mortality rates across groups receiving EN or PN. Safety, cost, and feasibility considerations also favor the use of EN over PN. ASPEN guidelines 2009, recommends EN over PN with a grade B level of evidence.[8]

EN support also favorably modulates the inflammatory cascade and subsequent hypermetabolic / hypercatabolic response. Early enteral feeding preserves intestinal mucosal function, which becomes the 'motor' of the inflammatory cascade during the stress response. EN maintains structural integrity by maintaining villous height and supporting the mass of secretory IgA-producing immunocytes which comprise the gut-associated lymphoid tissue (GALT) and in turn contribute to mucosal-associated lymphoid tissue (MALT) at distant sites such as the lungs, liver, and kidneys.[9-11]

In addition to having a large number of immune cells, the gastrointestinal system is also responsible for preventing bacterial translocation or translocation of bacterial antigen. During starvation, this barrier may become leaky allowing bacteria or their antigens to access the circulation or lymphatics and then reach other end organs. Thus it makes sense that EN is to maintain gut integrity, modulate stress and the systemic immune response, and attenuate disease severity.[12] Small feeds of 10-30ml/h is enough to prevent mucosal atrophy.

DOES EARLY EN COMPARED WITH DELAYED NUTRIENT INTAKE RESULT IN BETTER OUTCOMES IN THE CRITICALLY ILL ADULT PATIENT?

Early EN can be defined as "within 24 to 48 hours after admission to ICU". Canadian clinical practice guidelines for nutrition support conclude that early EN is associated with a trend toward a reduction in mortality, reduction in infectious complications but no difference in length of hospital stay.[14] Nutritional endpoints shows a significant improvement in the groups receiving early EN (calorie intake, protein intake, percentage goal achieved, better nitrogen balance achieved). In contrast, ESPEN (European Society of Parenteral and Enteral Nutrition) guidelines concludes that there is no data showing improvements using early EN in critically ill patients. Despite this, they recommed with a level C evidence that early EN be intiatied.[15]

Despite advocating early enteral nutrition, initiation of feeding is delayed in the critically ill, injured and postoperative patients who develop gastroparesis, which limits the ability to tolerate gastric feeding. Furthermore, these patients frequently have diminished or absent bowel sounds that are incorrectly interpreted to indicate that the small bowel is "not working". However, it is now recognized that small bowel function and the ability to absorb nutrients remains intact despite critical illness, the presence of gastroparesis, and absent bowel sounds.

HOW MUCH EN SHOULD CRITICALLY ILL PATIENTS RECEIVE?

The existing body cell mass is a major determinant of the total caloric requirement. The total caloric requirement can either be estimated or directly measured. Whether precisely matching energy input with expenditure improves patient outcomes remains controversial. Whereas in the obese patient, the estimate equations are even more problematic without availability of direct measurements such as indirect calorimetry. It is also important to note that calories provided via infusion of propofol should be considered when calculating the nutrition regimen.

ESPEN guidelines suggest that during the acute and initial phase of critical illness an exogenous energy supply in excess of 20–25 kcal/kg BW/day may be associated with a less favourable outcome (Grade C evidence). During recovery (anabolic flow phase) the aim should be to provide 25–30 total kcal/kg BW/day (C). Patients with a severe undernutrition should receive EN up 25–30 total kcal/kg BW/day.[15] Interestingly the Canadian guidelines do not have any recommedations on total caloric requirements.

In subsets of obese patients (BMI >30), hypocaloric enteral feeding of 60% to 70% of target energy requirements is recommended. Achieving some weight loss may reduce the risks of comorbities of obese patients in ICU. These comorbidities are insulin resistance, sepsis, infections, deep venous thrombosis and organ failure.[16,17] It is now recognised that there is a relationship between growing energy

deficit and the number of complications. There seems to be a cut off of cumulated energy deficit (10,000 kcal) beyond which the complications increase (infections, wound healing).[18]

WHAT ROUTE OF EN IS PREFERRED?

ASPEN guidelines recommendations state that either gastric or small bowel feeding is acceptable.[8] Canadian and ESPEN guidelines suggest that while gastric feeds is acceptable, in cases or institutions where obtaining small bowel ascess is feasible, this is the preferred route of choice.[14,15] Whether jejunal feeding reduces nosocomial pneumonia is still controversial as studies performed thus far reveal conflicting results. Jejunal feeding is of greater value in patients at high risk for intolerance to EN (on inotropes, continuous infusion of sedatives, or paralytic agents, or patients with high nasogastric drainage) or at high risk for regurgitation and aspiration (nursed in supine position).

MONITORING TOLERANCE TO EN

Monitoring of tolerance to feeds should be done in a holistic manner incorporating patients' symptoms of abdominal discomfort/distention, clinical examination, passage of stool/flatus and abdominal X-Rays. ASPEN guidelines discourage withholding EN feeding for gastric residual volume (GRV) <500 mls in the absence of other signs of intolerance.[8] Previously the cut off value for cessation of EN feeding was a GRV of 50-150 mls, varying between institutions. Studies have now demonstrated a higher GRV of 500 mls does not increase the risk of regurgitation, aspiration or pneumonia.[19,20] In fact GRVs do not correlate with incidences of pneumonia or aspiration. Frequent cessation of feeds for diagnostic tests and procedures will eventually lead to a negative calorie balance. Withholding of feeding occurs in more than 85% of ICU patients for an average of 20% feeding time (more than 65% of times due to avoidable reasons).[21] Intubated patients with postpyloric feeding tubes in combination with a nasogastric (NG) tube (for concurrent gastric decompression) or patients who have a large bore NG tube that allows for gastric decompression need not be fasted unless in high risk of aspiration (i.e. tracheostomy, prone positioning). If fasted, 4 hours is usually adequate.

STRATERGIES TO OPTIMIZE EN AND MINIMIZE RISK OF EN

While it is often difficult to provide 100% of goal calories by the enteral route, studies in which a protocol was used to increase delivery of EN have shown that delivering a volume of EN where the level of calories and protein provided is closer to goal improves outcome.[22,23] Studies have shown that the incidences of nosocomial pneumonia are more closely associated with aspiration of contaminated oropharyngeal secretions than regurgitation and aspiration of contaminated gastric contents.[24,25]

Among the measures to reduce risk of aspiration during EN feeding are:

a) Intubated patients should be nursed with a head of bed elevation of 30-45 degrees.
b) Continous infusion is prefered compared to bolus feeding in high risk patients.
c) Chlorhexidine mouthwash used twice a day to reduce risk of ventilator associated pneumonia.

ASPEN guidelines also recommends with a Grade E level of evidence to withhold enteral feeding in settings of hemodynamic compromise requiring a high dose of catecholamine agents or large volume fluid resusitation to maintain cellular integrity. These patients are at risk of subclinical ischemia and reperfusion injury involving the intestinal microcirculation. Although bowel ischemia is a rare complication of EN, occuring in less than 1% of cases,[26,27] EN should be witheld in hypotensive patients (mean arterial blood pressure <60 mm Hg).

IMMUNONUTRITION

A large body of data suggest that adding pharmaconutrients to enteral formulations provides even further benefits on patient

outcome than use of standard formulations alone. Glutamine, considered a conditionally essential amino acid, exerts a myriad of beneficial effects on antioxidant defenses, immune function, production of heat shock proteins, and nitrogen retention. Addition of agents such as selenium, ascorbic acid (vitamin C), and vitamin E provides further antioxidant protection. Currently, supplemetal of enteral glutamine in standard enteral feeding is recommended by APEN, ESPEN and the Canadian Guidelines in a subset of patients with burns and trauma. The suggested dose is 0.3-0.5 g/kg/day. There is a shorter hospital stay and reduced infectious complications in these subgroup of patients. One study in burns patient also showed a reduction in mortality with enteral glutamine supplementation.[28]

The role of specialized immune (myeloid suppressor) cells, whose role is to regulate the availability of arginine, necessary for normal T lymphocyte function, is now well recognised. These myeloid suppressor cells are capable of causing states of severe arginine deficiency which impact production of nitric oxide and negatively affect microcirculation. Immune-modulating diets containing arginine and ω-3 fatty acids appear to overcome the regulatory effect of myeloid suppressor cells. Agents such as RNA nucleotides increase total lymphocyte count, lymphocyte proliferation, and thymus function. In a dynamic fashion, the ω-3 fatty acids eicosapentaenoic acid (EPA) and docosohexaenoic acid (DHA) displace ω-6 fatty acids from the cell membranes of immune cells. This effect reduces systemic inflammation through the production of alternative biologically less active prostaglandins and leukotrienes.

Currently these immune modulating diets are recommended for use in patients undergoing elective upper GI surgeries. It can also be used in patients with mild to moderate sepsis (APACHE <15).[15] In severe sepsis, use of arginine may worsen outcome. It is said that in severe sepsis, arginine may be converted to nitric oxide contributing to hemodynamic instability. EPA and DHA help to stabilize the myocardium and lower the incidence of cardiac arrhythmias and decrease incidence of acute respiratory distress syndrome (ARDS).[29] In those patients with ARDS or Acute Lung Injury, enteral nutrition containing anti-inflammatory lipid profile (omega-3 fish oil, borage oil) with antioxidants is advocated in the Canadian, ESPEN and ASPEN guidelines.

CONCLUSIONS

Nutritional therapy in ICU should be based on guidelines using the latest evidence as there have been many studies done in recent times. EN via tube feeding is the preferred way of feeding in the critically ill ICU patient. Patients should be fed sooner than later. EN should be titrated based on a protocol to maximize benefits and improve outcome. Monitoring of tolerance to feeds should be done in a holistic manner and a GRV up to 500mls can be accepted to continue feeds with caution. Interruption to feeding for procedures should also be minimized. As nutrition is now considered therapuetic rather than just supportive, clinicians should carefully consider the composition of the nutrition with regard to lipid content, glutamine, antioxidants and other micronutrients depending on the individual patient's clinical condition and needs.

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Sedation and Analgesia in Critically Ill Adults

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Critically ill patients in ICU frequently require invasive monitoring and other support that can lead to pain and anxiety.[1] Inadequate relief of pain and discomfort cause inadequate sleep and agitation. This can provoke a stress response in the patient characterized by tachycardia, increased myocardial oxygen consumption, hypercoagulability, immunosupression and persistent catabolism.[2] However the combined use of analgesics and sedatives may ameliorate the stress response in critically ill patients.[3,4] Pain may also contribute to pulmonary dysfunction through guarding of respiratory muscles, thus causing restricted movement of the chest wall and diaphragm.[5]

PAIN ASSESSMENT

The most reliable and valid indicator of pain is the patient's self report.[6] Assessment of pain intensity may be performed with unidimensional tools such as verbal rating scale (VRS), visual analogue scale (VAS) and numeric rating scale (NRS). However this may not be relevant in critically ill patients. Pain assessment and response to therapy should be performed regularly by using an appropriate scale and systematically documented. Patients who cannot communicate should be assessed through subjective observation of pain-related behaviour and physiological indicators as well as changes in these parameters following analgesic therapy.

ANALGESIA THERAPY

Analgesia therapy includes non-pharmacological interventions such as attention to proper positioning, stabilization of fractures and elimination of irritating physical stimulation. Pharmacological therapies include opioids, NSAIDs, paracetamol and dexmedetomidine. Desirable attributes of an opioid include rapid onset, ease of titration and low cost. However hypotension may result from vasodilatation and active metabolites may cause prolonged sedation in renal insufficiency. Of the opioids, fentanyl has rapid onset and short duration of action but repeated dosing may cause accumulation and prolonged effects. Fentanyl may be administered via a transdermal patch in haemodynamically stable patients with more chronic analgesic needs. The patch provides consistent drug delivery but the extent of absorption varies depending on many factors. Fentanyl patches are not a recommended modality for acute analgesia because of their 12-24 hour delay to peak effect and similar lag time to complete offset once the patch is removed. Pethidine has an active metabolite that causes neuroexcitation and may interact with antidepressants (contraindicated in MAOI and best avoided with SSRIs), thus making it unsuitable for repetitive use. Remifentanil requires continuous infusion because of its very short duration of action, which could be beneficial in selected patients requiring interruptions for neurologic examination.[7] Its use can precipitate severe pain if infusion is stopped suddenly. Significant bradycardia can be encountered if bolus is given. Preventing pain is more effective than treating established pain; therefore analgesics should be administered on a continuous or scheduled intermittent basis, with supplemental bolus doses as required.[6] When a continuous infusion is used, a protocol incorporating daily awakening allowed more effective analgesic titration and a lower total dose of morphine.[8] Daily awakening is also associated with a shorter duration of ventilation and ICU stay.[8] In non-critically ill patients, patient controlled analgesia (PCA) has been reported to result in stable drug concentration, a good quality of analgesia, less sedation, less

opioid consumption and fewer adverse effects.[9,10] Patient selection is important when PCA is used and particular attention should be paid to the patient's cognition, haemodynamic reserve and previous opioid exposure. The use of an opioid reversal agent such as naloxone is not recommended after prolonged analgesia because it can induce withdrawal and may cause nausea, cardiac stress and arrhythmias. Analgesics with agonist-antagonist action such as buprenorphine can also elicit withdrawal symptoms and should be avoided during prolonged opioid use. It is recommended that a plan and goal of analgesia should be established for each patient and communicated to all caregivers to ensure consistent analgesic therapy.[11]

Nonopioid Analgesics

Nonsteroidal anti-inflammatory drugs (NSAIDs) provide analgesia via the nonselective, competitive inhibition of cyclooxygenase, a critical enzyme in the inflammatory cascade. NSAIDs have the potential to cause significant adverse effects including gastrointestinal bleeding, bleeding from platelet inhibition and development of renal insufficiency. Patients with hypovolaemia, the elderly and those with preexisting renal impairment may be more susceptible to NSAID-induced renal injury.[12,13] Administration of NSAIDs reduce opioid requirement. Paracetamol can be used to treat mild to moderate pain and in combination with an opioid, it produces a greater

TABLE 1: Pharmacology of selected analgesics (1, 17, 30-32)

Agent	Equianalgesic Dose (i.v.)	Half-life	Metabolic Pathway	Active Metabolites (Effect)	Adverse Effects
Fentanyl	200 µg	1.5-6 hr	Oxidation	No metabolite, parent accumulates	Rigidity with high doses
Hydromorphone	1.5 mg	2-3 hr	Glucuronidation	None	. . .
Morphine	10 mg	3-7 hr	Glucuronidation	Yes (sedation, especially in renal insufficiency)	Histamine release
Meperidine	75-100 mg	3-4 hr	Demethylation and hydroxylation	Yes (neuroexcitation, especially in renal insufficiency or high doses)	Avoid with MAOIs[c] and SSRIs[d]
Codeine	120 mg	3 hr	Demethylation and glucuronidation	Yes (analgesia, sedation)	Lacks potency, histamine release
Remifentanil	. . .	3-10 min	Plasma esterase	None	. . .
Ketorolac	. . .	2.4-8.6 hr	Renal	None	Risk of bleeding, GI and renal adverse effects
Ibuprofen	. . .	1.8-2.5 hr	Oxidation	None	Risk of bleeding, GI and renal adverse effects
Acetaminophen	. . .	2 hr	Conjugation	. . .	. . .

[a]More frequent doses may be needed for acute pain management in mechanically ventilated patients.
[b]Cost based on 2001 average wholesale price.
[c]MAOIs = monoamine oxidase inhibitors.
[d]SSRIs = selective serotonin-reuptake inhibitors.

TABLE 1: (Continued)

Agent	Intermittent Dose[a]	Infusion Dose Range (Usual)	Infusion Cost per day 70 kg[b]
Fentanyl	0.35-1.5 µg/kg i.v. q 0.5-1 hr	0.7-10 µg/kg/hr	100 µg/h: $26.00
Hydromorphone	10-30 µg/kg i.v. q 1-2 hr	7-15 µg/kg/hr	0.75 mg/hr: $5.00-11.00
Morphine	0.01-0.15 mg/kg i.v. q 1-2 hr	0.07-0.5 mg/kg/hr	5 mg/hr: $3.50-12.00
Meperidine	Not recommended	Not recommended	. . .
Codeine	Not recommended	Not recommended	. . .
Remifentanil	. . .	0.6-15 µg/kg/hr	10 µg/kg/hr: $170.00
Ketorolac	15-30 mg i.v. q 6h, decrease if age > 65 yr or wt < 50 kg or renal impairment, avoid > 5 days use.		. . .
Ibuprofen	400 mg p.o. q 4-6 hr	. . .	. . .
Acetaminophen	325-650 mg p.o. q 4-6 hr, avoid > 4 g/day	. . .	. . .

analgesic effect than higher doses of morphine alone.[14] Paracetamol should be maintained at less than 2 grams per day for patients with a significant history of alcohol intake or poor nutritional status and less than 4 grams per day for others.[16] Dexmedetomedine is a novel highly selective α_2-agonist, which has been shown to provide safe analgesia as well as sedation in the ICU when given as a single agent by intravenous infusion.[17] The characteristics of commonly used opioids and nonopioids are reviewed in Table 1.[11,15]

SEDATION

Sedatives are common adjuncts for the treatment of anxiety and agitation in ICU. The causes of anxiety are multifactorial and are likely secondary to inability to communicate amid continuous noise, ambient lighting and excessive stimulation. Sleep deprivation and the circumstances that lead to an ICU admission may increase patient anxiety, affecting up to 50% of ICU patients.[18,19] Effort ought to be made to reduce anxiety, which includes frequent reorientation, maintenance of patient comfort, provision of adequate analgesia and optimization of the environment. The use of sedation with medication is needed most of the time in ICU. Agitation is common in ICU, occurring at least once in 71% of patients.[18] It can be caused by multiple factors such as extreme anxiety, delirium, adverse drug effects and pain.[18] When patients exhibit signs of anxiety or agitation, the first priority is to identify and treat any underlying physiological disturbances such as hypoxaemia, hypoglycaemia, hypotension, pain and withdrawal from alcohol and drugs. Agitation can have deleterious effects on patients

by contributing to ventilator dysynchrony, increase in oxygen consumption and inadvertent removal of devices and catheters.[20]

Sedative medication reduces the stress response and improves the tolerance of routine ICU procedures.[21] Sedative-amnestic therapy is required to reliably attain amnesia.[22,23] Without amnesia, many patients who recall their ICU stay report unpleasant or frightening memories, which may contribute to post-traumatic stress disorder (PTSD).[24] Amnestic sedatives may paradoxically contribute to agitation and disorientation because patients may not remember where they are or why they are in ICU.

SEDATION ASSESSMENT

A defined sedation goal has been shown to reduce the duration of mechanical ventilation and length of stay in ICU.[25] The appropriate target level of sedation will primarily depend on the patient's disease process and any therapeutic or supportive interventions required. A sedation goal or endpoint should be established and regularly redefined for each patient.[11] Regular assessment and response to therapy should be systematically documented.[11] The use of a validated sedation assessment scale is recommended.[11] Some of the important reasons to use sedation assessment scales include the ability to accurately document patient status, ability to

TABLE 2: Revised Riker Sedation Agitation Scale

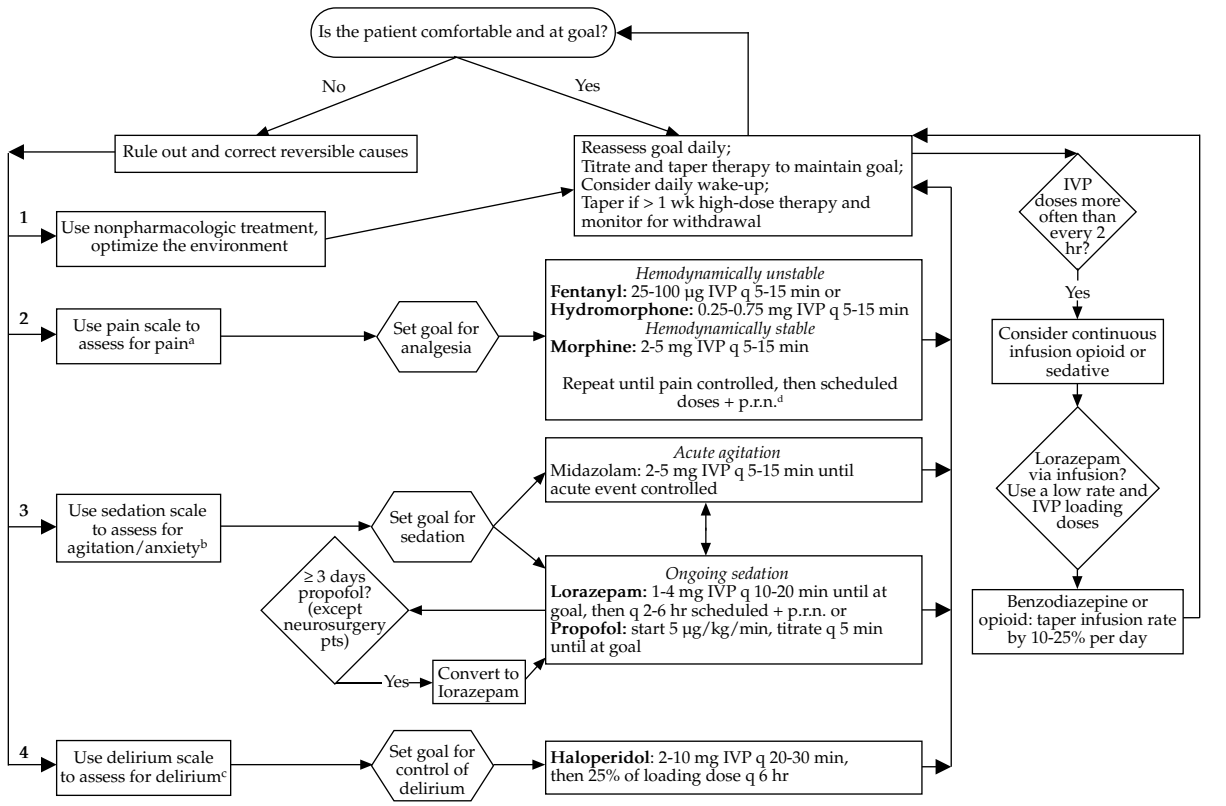
Scale	Description	Defintion
+3	Agitated and restless	When awaken or otherwise, pulling at ETT, trying to remove catheters or requires physical restraints
+2	Awake but mildly agitated	Anxious but mildly agitated. Attempts to sit up but calms down with verbal instructions
+1	Awake and calm	Awake, calm and easily follows commands
0	Aroused by voice and remains calm	Awakens easily to verbal stimuli. Remains awake, calm and easily follows command
-1	Aroused by movement	Awakens to loud verbal stimuli or gentle shaking. Has eye contact for at least 10 seconds but drifts off to sleep OR Awakens to loud verbal stimuli or gentle shaking and follows simple commands
-2	Aroused by painful stimuli	Localising or flexion to pain. Does not communicate or follow commands
-3	Unarousable	Extension, minimal or no response to painful stimuli

TABLE 3: Richmond Agitation Sedation Scale (RASS)

+4	Combative, violent
+3	Very agitated
+2	Agitated, fights ventilator
+1	Restless
0	Alert and calm
-1	Drowsy, >10s eye opening to voice
-2	Light sedation, <10s
-3	Moderate sedation, movement to voice
-4	Deep sedation, movement to touch
-5	Unarousable, no movement to touch

TABLE 4: Ramsay Scale

1	Awake and anxious
2	Awake, cooperative, accepting ventilation, oriented and tranquil
3	Awake, responds only command
4	Asleep, brisk response to light glabella tap or loud noise
5	Asleep, sluggish response to light glabella tap or loud noise stimulus but does not respond to painful stimulus
6	Asleep, no response to light glabella tap or loud noise



[a]Numeric rating scale or other pain scale.[18]
[b]Riker Sedation-Agitation Scale or other sedation scale.[82]
[c]Confusion Assessment Method for the ICU.[185]
[d]See Table 1 for intermittent dosing for specific agents.

Algorithm for the sedation and analgesia of mechanically ventilated patients.[11] Doses are approximate for a 70-kg adult.

accurately communicate between ICU caregivers, ability to titrate sedation therapy to established clinical goals, ability to optimize patient comfort and safety, potentially able to minimize days of mechanical ventilation as well as decrease length of ICU stay. Although there are numerous published and validated sedation assessment scales, it is the familiarity and routine use of any one scale which is more important, as long as it is performed in a standardized and consistent fashion. Objective measures of sedation such as Bispectral Index (BIS) have not been completely evaluated and are not yet proven useful in the ICU although preliminary data suggest a good correlation between BIS and Sedation Agitation Scale.[33] Table 2 illustrates the Revised Riker

Sedation Agitation Scale which has both sedation and agitation components incorporated.[26] Table 3 is the Richmond Agitation Sedation Scale (RASS)[27] and Table 4 is the Ramsay scale.[28]

SEDATION THERAPY

Benzodiazepines

Benzodiazapines block acquisition and encoding of new information and potentially unpleasant experiences (anterograde amnesia) but do not induce retrograde amnesia. As a class they are particularly good at relieving anxiety and producing amnesia and hypnosis. Their effects are mediated by depressing the excitability of the limbic system through reversible binding at the gamma aminobutyric acid (GABA)-benzodiazepine receptor complex. They have minor muscle relaxant effects that are mediated by the glycine receptors in spinal and supraspinal sites. All produce some degree of cardiovascular and respiratory depression. Paradoxical agitation has been observed during light sedation with benzodiazepines and may be the result of drug-induced amnesia or disorientation. Diazepam, a relatively old benzodiazepine, has fallen into disrepute because of concern about its long-acting metabolites. One in particular (nor desmethyl diazepam) has a longer elimination half-life than the parent drug. Being lipid soluble, it requires to be administered in a special solvent (e.g. propylene glycol), which is a tissue irritant. Lorazepam has a relatively clean metabolic pathway and a short duration of action with prolonged administration. Its metabolites are glucuronides, which are inactive. Glucuronidation pathways are spared in liver disease, unlike other metabolic pathways, and this drug may be useful in such conditions. However, lorazepam solvents, polyethylene glycol and propylene glycol have been implicated as the cause of reversible acute tubular necrosis, lactic acidosis and hyperosmolar states after prolonged high-dose infusions. The dosing threshold for this effect has not been prospectively defined but these case reports described doses that exceeded 18mg/hour and continued for longer than 4 weeks and higher doses (>25mg/hour) continuing for hours to days.[29] Midazolam is a commonly used benzodiazepine which has a rapid onset and short duration of action and it is water soluble at pH 4 and fat soluble at pH 7. This avoids unnecessary solvents. However, prolonged sedative effects have been reported in critically ill patients who are obese, have a low albumin level or with renal failure after receiving midazolam infusion as sedation.[30]

Propofol

Propofol is a short acting GABA agonist that offers easily titratable sedation. Like benzodiazepines, it acts on the GABA receptor, but at a different part – the A sub-unit. Metabolised mostly by the liver, its metabolites are inactive. There are probably significant extra hepatic sites of metabolism. Long term or high dose infusions may result in hypertriglyceridaemia. Other adverse effects commonly seen include hypotension, bradycardia and pain upon peripheral venous injection. The hypotension is dose related and more frequent after bolus dose administration. Prolonged use of more than 48 hours of high doses of propofol (>66 mcg/kg/min infusion) has been associated with lactic acidosis, bradycardia and lipidaemia in paediatric patients.[31] Doses of more than 83 mcg/kg/min have been associated with an increased risk of cardiac arrest in adults.[32] The US Food and Drug Administration (US FDA) has specifically recommended against the use of propofol for the prolonged sedation of paediatric patients. Patients receiving propofol should be monitored for unexplained metabolic acidosis or arrhythmias. While propofol appears to possess anticonvulsant activity, excitatory phenomena such as myoclonus have been observed. There are several case reports and small uncontrolled studies describing the efficacy of propofol in refractory status epilepticus and electroconvulsive therapy.

Ketamine

This is an anaesthetic agent similar in structure to phencyclidine. Its effects are mediated by N-methyl-D-aspartate (NMDA) receptor

stimulation. Ketamine possesses dissociative hypnotic, amnestic and analgesic properties. However ketamine causes an increase in heart rate and blood pressure in normal patients through the release of cathecolamines. This may not occur in critically ill patients though. It is also a bronchodilator and has been used to treat severe acute asthma. One of its major adverse effects is producing nightmares. Due to this, if it is used as sedation, it should be combined with a benzodiazepine. The suggested dose is 25-50mg as an intravenous bolus with an infusion rate of 10-30 mg/hour. When given as an infusion it may be mixed with midazolam in a 10:1 mixture (ketamine: midazolam)

Dexmedetomidine

Dexmedetomidine is a relatively new selective, full alpha-2 agonist. Compared to clonidine,

Pharmacology of selected sedative agents:

Agent	Onset After i.v. Dose	Half-life of Parent Compound	Metabolic Patway	Active Metabolite	Unique Adverse Effects
Diazepam	2-5 min	20-120 hr	Desmethylation and hydroxylation	Yes (prolonged sedation)	Phlebitis
Lorazepam	5-20 min	8-15 hr	Glucuronidation	None	Solvent-related acidosis/ renal failure in high doses
Midazolam	2-5 min	3-11 hr	Oxidation	Yes (prolonged sedation, especially with renal failure)	
Propofol	1-2 min	26-32 hr	Oxidation	None	Elevated triglycerides, pain on injection
Haloperidol	3-20 min	18-54 hr	Oxidation	Yes (EPS)[c]	QT interval prolongation

[a] More frequent doses may be needed for management of acute agitation in mechanically ventilated patients.
[b] Cost based on 2001 average wholesale price.
[c] EPS = extrapyramidal symptoms.

Agent	Intermittent i.v. Dose[a]	Infusion Dose Range (Usual)	Cost per day 70 kg patient[b]
Diazepam	0.03-0.1 mg/kg q 0.5-6 hr	. . .	20 mg q 4 hr: $5.00-20.50
Lorazepam	0.02-0.06 mg/kg q 2-6 hr	0.01-0.1 mg/kg/hr	48 mg/day: $55.00
Midazolam	0.02-0.08 mg/kg q 0.5-2 hr	0.04-0.2 mg/kg/hr	6 mg/hr: $65.00-309.00
Propofol	. . .	5-80 µg/kg/min	50 µg/kg/min: $235.00-375.00
Haloperidol	0.03-0.15 mg/kg q 0.5-6 hr	0.04-0.15 mg/kg/hr	10 mg q 6 h: $62.00-65.00

dexmedetomidine is 8 times more potent. As a sedative, it is notable for its lack of suppression of the respiratory drive and for its potential to provide some analgesia and anxiolysis. By comparison with other drugs, dexmedetomidine results in sedation from which patients can be more easily aroused, without them being startled. Although approved by the US FDA for infusion rates of up to 0.7 mcg/kg/min for 24 hours or less in mechanically ventilated patients, recent reports have identified safe use of higher doses for longer periods of time (up until 1 week).[34] Dexmedetomidine reduces need for analgesics by 50-70% compared to propofol. However it is not reliably amnesic and it increases systemic vascular resistance and pulmonary vascular resistance at all dose ranges. Other effects of dexmedetomidine includes dry mouth, decreased bowel motility and decreased oxygen consumption. It has no effect on intracranial and intraocular pressures. Dexmedetomidine decreases activity of the sympathetic nervous system and this can lead to unopposed vagal activity. Due to this problem, it should be given as an infusion rather than as a bolus dose.

SEDATIVE AND ANALGESIC WITHDRAWAL

The potential for opioid, benzodiazepine and propofol withdrawal should be considered after high doses or more than approximately 7 days of continuous therapy. Doses should be tapered systematically to prevent withdrawal symptoms. Opioid withdrawal signs and symptoms include dilation of the pupils, sweating, lacrimation, rhinorrhea, piloerection, tachycardia, vomiting, diarrhea, hypertension, yawning, fever, tachypnea, restlessness, irritability, increased sensitivity to pain, cramps, muscle aches and anxiety. Benzodiazepine withdrawal signs and symptoms include dysphoria, tremor, headache, nausea, sweating, fatigue, anxiety, agitation, increased sensitivity to light and sound, paresthesias, muscle cramps, myoclonus, sleep disturbances, delirium, and seizures. Propofol withdrawal has not been well described but appears to resemble benzodiazepine withdrawal.

DELIRIUM

As many as 80% of ICU patients have delirium, characterized by an acutely changing or fluctuating mental status, inattention, disorganized thinking and an altered level of consciousness that may or may not be accompanied by agitation.[11] Delirium may be associated with confusion and different motoric subtypes: hypoactive, hyperactive or mixed. Hypoactive delirium, which is associated with the worst prognosis, is characterized by psychomotor retardation manifested by a calm appearance, inattention, decreased mobility and obtundation in extreme cases. Hyperactive delirium is easily recognised by agitation, combative behaviours, lack of orientation and progressive confusion after sedative therapy. Diagnosis of delirium is guided by the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)*. In ICU patients who are often non-verbal, the Confusion Assessment Method for the ICU (CAM-ICU) can be used. The method is shown in Table 5. Routine assessment for the presence of delirium is recommended.

Treatment of Delirium

Psychotic or delirious patients may become more obtunded and confused when treated with sedatives, causing paradoxical increase in agitation. Neuroleptic agents are the most common drugs used to treat delirium. They are thought to exert a stabilizing effect on cerebral function by antagonizing dopamine-mediated neurotransmission at cerebral synapses and basal ganglia. Abnormal symptomatology is inhibited but the patient's interest in the environment is diminished. Haloperidol is the commonest agent used in the treatment of delirium, commonly given as intermittent intravenous injection, starting with a 2 mg bolus followed by repeated doses every 15 to 20 minutes. High doses of haloperidol of more than 400mg per day have been reported but QT prolongation may result. Once delirium is controlled, regular scheduled doses every 4 to 6 hours may be continued for a few days followed by tapering over several days. Extrapyramidal symptoms can occur, less frequently after intravenous compared to oral administration. Concurrent benzodiazepine use may mask this.

TABLE 5: The confusion assessment method for the diagnosis of delirium in the ICU (CAM-ICU)

Feature	Assessment Variables
1. Acute Onset of mental status changes or Fluctuating Course	Is there evidence of an acute change in mental status from the baseline? Did the (abnormal) behavior fluctuate during the past 24 hours, i.e., tend to come and go or increase and decrease in severity? Did the sedation scale (e.g., SAS or MAAS) or coma scale (GCS) fluctuate in the past 24 hours?
2. Inattention	Did the patient have difficulty focusing attention? Is there a reduced ability to maintain and shift attention? How does the patient score on the Attention Screening Examination (ASE)? (i.e., Visual Component ASE tests the patient's ability to pay attention via recall of 10 pictures; auditory component ASE tests attention via having patient squeeze hands or nod whenever the letter "A" is called in a random letter sequence)
3. Disorganized thinking	If the patient is already extubated from the ventilator, determine whether or not the patient's thinking is disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject. For those still on the ventilator, can the patient answer the following 4 questions correctly? 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does one pound weigh more than two pounds? 4. Can you use a hammer to pound a mail? Was the patient able to follow questions and commands throughout the assessment? 1. "Are you having any unclear thinking?" 2. "Hold up this many fingers." (examiner holds two fingers in front of patient)? 3. "Now do the same thing with the other hand." (not repeating the number of fingers)
4. Altered level of consciousness (any level of consciousness other than alert (e.g., vigilant, lethargic, stupor, or coma)	Alert: normal, spontaneously fully aware of environment, interacts appropriately Vigilant: hyperalert Lethargic: drowsy but easily around, unaware of some elements in the environment, or not spontaneously interacting appropriately with the interviewer; becomes fully aware and appropriately interactive when prodded minimally Stupor: difficult to arouse, unaware of some or all elements in the environment, or not spontaneously interacting with the interviewer; becomes incompletely aware and inappropriately interactive when prodded strongly; can be aroused only by vigorous and repeated stimuli and as soon as the stimulus ceases, stuporous subjects lapse back into the unresponsive state. Coma: unarousable, unaware of all elements in the environment, with no spontaneous interaction or awareness of the interviewer, so that the interview is impossible even with maximal prodding

Patients are diagnosed with delirium if they have both Features 1 and 2 and either Feature 3 or 4.

"SAS = Sedation-Analgesia Scale, MAAS = Motor Activity Assessment Scale, GCS = Glasgow Coma Scale.

SLEEP

Sleep is believed to be important to recover from an illness. Sleep deprivation may impair tissue repair and overall cellular immune function.[35] Sleeplessness induces additional stress in critical care patients. Sleep in ICU has been characterized by few complete sleep cycles, numerous awakenings and infrequent REM sleep. Atypical sleep patterns were demonstrated in critically ill patients receiving high doses of sedatives.[36] Nonpharmacological interventions to promote sleep include environmental modification, relaxation, back massage and music therapy. Light mimicking the 24 hour day helps patients achieve normal sleep patterns. Pharmacological therapy includes the use of sedative-hypnotics like benzodiazepines and zolpidem. It is recommended that sleep promotion should include optimization of the environment and nonpharmacological methods to promote relaxation with adjunctive use of hypnotics.[11]

CONCLUSION

Sedation is an important component of the treatment of mechanically ventilated critically ill patients. There are currently a wide range of pharmacological agents available for the diverse needs of this heterogenous group of patients. It is important that the goals of sedation in the critically ill patients be defined and communicated to every ICU care provider. All currently available sedatives have limitations. Rather than seeking the ideal drug, strategies of drug administration that focus on principles of sedative pharmacology in critical illness should be utilized. Administration of sedative agents should be titrated to effect and arousability should be frequently assessed. ICU physicians should look out for side effects specific to the drug used and early weaning off sedation should be instituted if the patient's condition allows it. A sedation protocol incorporating daily awakening is associated with shorter duration of ventilation and ICU stay.[8]

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Perioperative Mortality – A Review

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INTRODUCTION

The field of anesthesiology has always emphasized the importance of patient safety, and has often been taken as a model for patient safety. Indeed, in the early 1980s, rapid improvements in anesthesia safety were made over a very short period of time, primarily through the implementation of new clinical practice guidelines and improvements in vital signs monitoring technology. In 2002, Lagasse, reviewed the literature to determine whether the claim that anesthesia remains safe today is based on valid published data, as estimates on the incidence of anesthesia-related perioperative mortality are few and inconsistent. He suggested large international data pools to provide strong evidence for developing risk adjustment models and identify best practices.[1]

A commonly cited report from 1989 indicated that the rate of perioperative death directly attributable to anesthesia management is approximately 1 per 100,000 for generally healthy persons.[2] In 1995, perioperative deaths in Finland was reported to be 1.5 / 1000 cases.[3] In 1999 the Institute of Medicine (IOM) via its Committee on Quality of Health Care asserted, "Anesthesia is an area in which very impressive improvements in safety have been made." In support of this assertion the Committee stated that anesthesia mortality rates have decreased from 2 deaths per 10,000 anesthetics administered in the 1980s to about 1 death per 200,000 to 300,000 anesthetics administered[4]. The Confidential Enquiry into Perioperative Deaths in the United Kingdom is a systematic analysis of a large population which has contributed much to anaesthesia safety.[5] The perceived safety of anesthesia has encouraged more complex surgeries to be performed on patients who might have been considered too unhealthy for surgery in the recent past, and yet even proponents for the safety of anesthesia admit that further progress is needed to improve anesthesia safety for less healthy persons.[6] The increased safety of anaesthesia, coupled with economic pressures, also have contributed to the rise in the number of outpatient surgeries being conducted, perhaps a testament to the safety of anaesthesia by surgeons and patients.

The potential risk factors for anaesthetic morbidity and mortality are well known and include patient's age and American Society of Anesthesiologists (ASA) physical status (PS), type of anesthesia (monitored anesthesia care [MAC], general, regional or combined), time under anesthesia care, emergency or trauma status, the occurrence of a perioperative adverse event, perioperative hypothermia, deliberate intraoperative hypotension, the need for invasive monitoring (via arterial line, cardiovascular catheter or pulmonary artery), and postoperative intensive care unit (ICU) admission. Several of these factors have been implicated in earlier studies on anesthesia-related perioperative adverse events[7] but have not been fully evaluated in recent years, and so the contribution of these factors to postoperative mortality in today's operating room environment remains unknown.

Anaesthetic mortality authorities often use the peer review process to analyse and interpret data in order to identify adverse outcomes as a result of "error," either human or system.[8] Nominal definitions for subcategorizing these two types of errors were used to add structure and increase the objectivity of the peer review process.[9,10,11] Error here was defined as an act that through ignorance, deficiency, or accident departs from or fails to achieve a desired outcome.[11] Human errors included failing to perform a technique properly, misuse of equipment, disregarding available data, failing to seek appropriate data, and responding incorrectly to available data due to a lack of knowledge. These human errors were considered deviations from the standard

of care. System errors, on the other hand, result in adverse outcomes that might otherwise be considered unavoidable and ordinarily dropped from the peer review process.[12,13] System errors included accidental occurrences resulting from performing a technique properly, equipment failure despite proper use, missed communication while following established protocol, inability to diagnose a disease process due to limitations of currently available screening and monitoring standards, inability to treat a disease process due to limitations in current standards of care, and inability to meet the demands for resources of equipment or personnel.

Morbidity and mortality studies done in Japan between 1999 and 2002, which involved 3,855,384 anesthetics, reported 2,443 cardiac arrests (6.34 per 10,000 anesthetics) and 2,638 deaths (6.85 per 10,000 anesthetics) due to life-threatening events in the operating room of which anaesthesia-related death accounted for 1.5% of total deaths.[14] The major preoperative causes of deaths were preoperative hemorrhagic shock, followed by cardiovascular diseases such as myocardial ischemia and congestive heart failure. Excessive surgical bleeding comprised 70.2% of surgery-related deaths. The major recorded intraoperative adverse events were myocardial ischemia, pulmonary embolism, and severe arrhythmias. The incidence of cardiac arrest and death totally attributable to anaesthesia was 1/100,000 anesthetics. Half of anaesthesia-related deaths were caused by airway or ventilatory problems. Other causes of anaesthesia-related death were medication accidents and infusion/transfusion accidents. It was recognized that considerable effort is required to reduce intraoperative life-threatening events caused by human error.

An audit of the incidence, causes and outcome of perioperative cardiac arrest was conducted in a university hospital in Pakistan.[15] All perioperative cardiac arrests from induction of anaesthesia to post anaesthesia care unit discharge or intensive care unit admission during non-cardiac surgery, from January 1992 to December 2006 were included. Outcome variables were noted as immediate survival and survival to discharge. Forty-two anaesthesia-related cardiac arrests occurred among 140,384 patients. Overall frequency was 2.99 per 10,000 (95% confidence interval: 2.90 to 3.08). Twenty-four (3.77/10,000) were females. Thirty-four (13.59/10,000) patients were ASA physical status III to V, 10 (4.95/10,000) were children and 14 (4.28/10,000) above 60 years. Sixteen patients (6.48/10,000) were undergoing emergency surgery. Anaesthesia was deemed primarily responsible in nine cases (0.64/10,000). The causes of anaesthesia-related arrests were medication related (4), airway related (3), massive air embolism (1) and under-replacement of fluids (1). The event was considered to be avoidable in 26 cases. Seventeen patients died during the arrest, 15 survived more than one hour and 10 were discharged home. The number of perioperative cardiac arrests and their mortality was higher in patients with poor physical status and in emergency surgery. The number was also higher in infants, patients above 60 and females. The majority of the cases were considered avoidable, indicating the importance of prevention strategies.

The Thai Anaesthetic Incident Study (THAI), which involved a total of 163403 consecutive anaesthetics, reported the following adverse events: oxygen desaturation (31.9:10,000), cardiac arrest (30.8:10,000), death within 24 hours (28.3:10,000), difficult intubation (22.5:10,000), re-intubation (19.4:10,000), unplanned ICU admission (7.2:10,000), neurological complications (4.8:10,000), equipment malfunction/failure (3.4:10,000), suspected myocardial ischemia or infarction (2.7:10,000), awareness during anesthesia (3.8:10,000), late detected esophageal intubation (4.1:10,000), failed intubation (3.1:10,000), anaphylaxis or anaphylactoid reaction (2.1:10,000), nerve injury (2:10,000), pulmonary aspiration (2.7:10,000), drug error (1.3:10,000), hazard to anesthesia personnel (1.5:10,000), unplanned hospital admission (0.1:10,000), total spinal block (1.3:10,000) and mismatch blood transfusion (0.18:10,000). Respiratory adverse events were common direct anesthesia related events. The high incidence of cardiac arrest and death within 24 hours of an anaesthetic highlighted concerns for prevention strategies.16

The perioperative mortality review committee in the Ministry of Health Malaysia was established in 1992.[17] The main shortfalls in delivery of care as mentioned in its most recent biennial report included poor preoperative optimization and inadequate management of intraoperative problems, which still feature as anaesthetic causes of mortality. Poor fluid management was of particular concern. The inappropriate use of local anaesthetic drugs emerged as a significant cause of mortality in that report. Several recommendations have been made in that report, which included: All anaesthetic staff should be reminded about adequate preoperative optimization. In particular, patients with hypovolaemia and cardiovascular instability need careful assessment and adequate fluid resuscitation. There should be appropriate fluid replacement and accurate assessment of circulatory volume during anaesthesia. Central venous monitoring is safe and should be encouraged when indicated. A high level of care and vigilance is needed during administration of local anaesthetic drugs for regional anaesthesia and pain management. Adequate care and monitoring in the intensive care unit postoperatively is necessary to avoid unnecessary mortality and morbidity. In general there should be early and active involvement by specialists throughout the perioperative period.

Outcome studies of perioperative cardiac arrests in a Brazilian tertiary general teaching hospital between April 1996 and March 2005 reported 186 cardiac arrests (34.6:10,000) and 118 deaths (21.97:10,000) were found.[18] Major risk factors for cardiac arrest were neonates, children under 1 yr and the elderly ($p<0.05$), male patients with ASA III or poorer physical status ($p<0.05$), emergency surgery ($p<0.05$) and general anaesthesia ($p<0.05$). Patient disease/condition was the major cause of cardiac arrest or death ($p<0.05$). There were 18 anaesthesia-related cardiac arrests (3.35:10,000); 10 were totally attributed (1.86:10,000) and 8 partially related to anaesthesia (1.49:10,000). There were 6 anaesthesia-related deaths (1.12:10,000); 3 were totally attributable and 3 partially related to anaesthesia (0.56:10,000 for both). The main causes of anaesthesia-related cardiac arrest were respiratory events (55.5%) and medication-related events (44.5%).

Medical simulation has been introduced into anaesthesiology to enhance professional competence. It can be used to improve team performance and can be used for team training, based on crisis resource management principles[19]. Virtual reality (VR) simulation can address problems anaesthetists may face in very uncommon but critical moments e.g. unexpected intraoperative cardiac arrest. Integrating standardized patients into simulation is an innovation called hybrid simulation, in which task trainers and standardized patients are used together to provide a high-fidelity simulation environment. Several issues of interest to those just entering the field include the basic techniques of post-simulation "debriefing with good judgment". Suitable scenarios designed to individual needs would be useful to those trying to create their own curricula and materials. Good audiovisual technologies associated with simulation are helpful to those faced with the challenge of setting up a robust simulation program.

Current data suggests that the overall perioperative mortality rate for patients having ASA Physical Status 1–5 is approximately 1 per 500 anesthetics. The literature suggests a wide range of perioperative mortality rates, which are probably caused by differences in operational definitions and reporting sources, as well as a lack of appropriate risk stratification. Anesthesia-related mortality rate, as determined by peer review, has been stable over the last decade at approximately 1 death per 13,000 anesthetics. The theory of organizational safety teaches that "safety" is a never-ending process whose success may not be measured strictly by epidemiologic methods. The profession of anesthesiology itself is a model concerning patient safety processes.[20] Anesthesiologists have played important leadership roles in addressing organizational safety in all of healthcare. Anesthesiology was the first medical profession to treat patient safety as an independent problem. Anesthesiology has implemented widely accepted guidelines on basic monitoring, conducted long-term analyses of closed malpractice claims, addressed fatigue of residents serving in-house call, developed patient simulators as meaningful training tools, and

tackled problems of human error. Most importantly the profession has institutionalized safety in its scientific and governing bodies, creating the ASA's Patient Safety and Risk Management Committee and the Anesthesia Patient Safety Foundation. Anaesthetists must accept this challenge and begin efforts to standardize methodology of data collection and analysis so that data can be shared worldwide. Large international data pools will allow anaesthetists to develop risk adjustment models and identify best practices. Only then can anesthesia become a model of safety based on scientific evidence.

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Geriatric Anaesthesia

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The elderly are a growing segment of the population in many parts of the world and there is an increasing need for surgical procedures in them.[1] 12% of those aged 45 to 60 years may undergo surgery annually, and this number increases to 21% in those who are 65 years and older. The elderly present a challenge to the anaesthetist, as they have a decrease in their functional physiological reserves and a diminished ability to withstand the stress of illness, surgery and anaesthesia.[2] The elderly with co-existing disease are even more vulnerable and advanced age in conjunction with co-morbidity is a significant risk factor for increased perioperative morbidity and mortality.

PHYSIOLOGICAL CHANGES IN THE ELDERLY

CARDIOVASCULAR CHANGES

At the cellular level, there is an isomyosin shift, expression of fibrosis-related genes, altered growth-controlling factors, impaired excitation-contraction coupling, impaired calcium homeostasis, increased myocyte apoptosis and increased antinatriuretic peptide secretion. Age-related changes seen in cardiac morphology include decrease in myocyte number with an increase in myocyte size, leading to an increase in ventricular wall thickness. Age related fibrosis of the conduction system leads to a decrease in conduction fibre density and decrease in sinus node cell number. There is increased tissue stiffness, as seen in decreased intrinsic contractility, increased myocardial contraction time and decreased myocardial contraction velocity. There is an associated increased ventricular filling pressure, leading to increased left atrial pressure and size. There is also increased action potential time and decreased coronary flow reserve.

Ageing is accompanied by neurohumoral changes. There is increased sympathetic nerve activity while the parasympathetic system activity decreases. Though plasma cathecolamine concentration increases, β adrenoceptor mediated modulation of inotropy and chronotropy decreases. α1 adrenoceptor responsiveness increases. Baroreceptor reflex activity decreases. Table 1

TABLE 1

LV end diastolic volume	**increased**
LV end systolic volume	**increased**
Ejection fraction	**no change**
Stroke volume	**increased**
Heart rate	**decreased**
Cardiac output	**no change (males) / decreased (females)**
Stroke work	**increased**
Early diastolic filling rate	**decreased**
Systolic arterial pressure	**increased**
Systemic vascular resistance	**no change (males) / increased (females)**

is a summary of the changes in cardiovascular physiology seen in healthy individuals aged 20 to 80 at rest.[3]

RESPIRATORY SYSTEM

Changes in respiratory mechanics

Musculoskeletal changes leads to rigidity of the thoracic cage. This is due to narrowing of the intervertebral spaces, stiffening of the cartilages and replacement of elastic tissues of the ribs and sternum, progressive kyphoscoliosis causing an upward anterior rotation of the ribs and sternum causing an increase in the anteroposterior diameter of the thoracic cage. There is also atrophy of the diaphragm and the intercostal muscles. Table 2 gives a summary of the changes in respiratory mechanics.

TABLE 2

Total lung capacity	**reduced**
Vital capacity	**reduced**
Inspiratory reserve capacity	**reduced**
Expiratory reserve capacity	**reduced**
Closing volume	**increased**
Residual volume	**increased**
Functional residual capacity	**no change**
Forced vital capacity	**reduced**
Forced expiratory volume in 1 second	**reduced**
The reduction in lung and chest wall compliance	**increases the work of breathing**

Changes in gas exchange

There is reduced functional surface area for gas exchange due to loss of alveolar septa and reduced expansion of alveolar spaces. Capillary membrane thickness is increased causing decreased permeability and therefore a reduction in efficiency of gas exchange.

The increase in closing volume increases air trapping and V/Q mismatch; therefore the elderly have a lower resting PaO2. (**PaO2= 100 - 0.4 x [age in years] mmHg**).

Response to hypoxia and hypercarbia

Response to hypoxia and hypercarbia is markedly reduced (by 50%) compared to younger patients, making the elderly more sensitive to the respiratory depressant effects of anaesthesia.

Airway reflexes

Upper airway reflexes are blunted, making aspiration more likely. Cough reflex is less efficient in terms of volume, force and flow rate. Ciliary action is also decreased, making post-operative atelectasis and pneumonia more likely in the elderly.[5]

NEUROLOGICAL SYSTEM

Age universally reduces total nervous system tissue mass, neuronal density, production and concentration of neurotransmitters and receptors. There is also a reduction in complexity of neuronal connections and a decreased ability to integrate multiple neuronal inputs. Two major central nervous system disorders associated with surgery and anaesthesia are **postoperative delirium** and **postoperative cognitive dysfunction**.[11]

RENAL SYSTEM

Age-related loss of renal parenchyma is associated with a decrease in renal blood flow and a reduction in the renal vascular bed. Renal functional reserve is reduced with an associated reduction in glomerular filtration rate and tubular function. Therefore the aged kidney has difficulty in maintaining fluid, electrolyte and acid-base homeostasis.

Creatinine clearance (ml/min) = (140 - age) x weight (kg) x Constant / serum creatinine (mmol/L)

Constant for males = 1.23

Constant for females = 1.04

HEPATIC SYSTEM

There is a reduction in hepatic mass and hepatic and splanchnic blood flow. There is also reduction in the microsomal demethylation pathways and hepatic cholinesterase activity.

ENDOCRINE/METABOLIC

Basal metabolic rate is reduced by 1% per year after the age of 30. Impaired thermoregulatory control, associated with the fall in metabolic rate and reduced muscle mass, can lead to perioperative hypothermia. This is increased metabolic stress causing increased oxygen consumption, vasoconstriction and catecholamine release.

The elderly patient also has increased risk of thyroid disorders, osteoporosis, nutritional disorders, impaired glucose tolerance and non-insulin dependant diabetes mellitus.

MUSCULOSKELETAL SYSTEM

Arthritis is common, leading to pain and reduced mobility. Osteoporosis may occur. Patients are at risk of fractures, dislocations and deformities.

SKIN

Skin and subcutaneous tissue are thin and fragile. The elderly patients bruise easily, and are at risk of developing pressure sores and skin abrasions. Venous access may be difficult. Extravasation of drugs may occur if infused with high pressure.

PHARMACOKINETICS & DYNAMICS

Drug metabolism often relates to the organ system functions and their reserve. Due to the decreased CNS, hepatic, renal, gastric and lung function and decreased cardiovascular reserve, as well as decreased lean body mass, decreased body fluid volume and increased fatty tissue, the elderly often metabolize drugs differently from the younger age group. In general, drug metabolism may be significantly reduced due to the failing function of the systems previously mentioned.

Due to the increase in fatty tissue, the decrease in total body water, the distribution of the medication either from oral, intravenous or intramuscular routes and increases in volume of drug distribution, the elderly often have a change in uptake, and thus reduced clearance. Decrease in the metabolism and excretion is also due to decreased hepatic and renal functions. The elderly group should be treated differently when administering medications, and more attention should be paid in particular to drug interaction. Further study definitely needs to be done for drug metabolism in the aged group so that drugs can be prescribed intelligently to avoid adverse reactions.

ANAESTHETIC MANAGEMENT

The anaesthetic management will be discussed preoperatively, intraoperatively and postoperatively. It is important to include multidisciplinary teams in the management. This team should include the primary surgical team, the anaesthetist, geriatrician, nurses, nutritionists and therapists.

PREOPERATIVE MANAGEMENT

The aim of preoperative management is to establish rapport, conduct a thorough assessment and optimization of the patient, obtain informed consent and formulate an anaesthetic plan.

In the elderly it is also important to establish rapport with the caregivers and include them in the discussion for patient management. At the same time, it is important to recognize the patient's autonomy during decision making, i.e. the patient's wishes and dignity is to be respected. Assessment should be done in a private and comfortable environment, with the presence of a caregiver, if the patient wishes.

A thorough assessment of the patient will require cooperation from the caregivers, as they may be required to provide history of the patient's premorbid functional status.[5] Assessment should include the patient's current morbidity, presence of co-morbidities and their complications, medications history and compliance, patient's premorbid functional status, e.g. mini mental state examination, METS, nutritional assessment. The functional status assessment is very important as any changes observed serves as the most important perioperative outcome. A social assessment is also necessary, as it helps the anaesthetist gauge the support patient may have postoperatively. After a careful assessment, it is important to risk stratify the patient, so a management plan can be formulated.

Only patients with the adequate capacity and competency should provide consent for surgery and anaesthesia. Any doubts regarding the patient's ability to do so would require further assessment from qualified staff. If the patient is unable to provide consent, the patient's will, advanced directives and power of attorney should be checked. If such are unavailable, consent is obtained from patient's relatives with the assumption that their decision is in the patient's best interest.

A management plan is then formulated. This includes optimization, period of fasting, fluid therapy, premedications, monitoring, anaesthetic technique, analgesia and postoperative care.

INTRAOPERATIVE MANAGEMENT

A quick but thorough assessment should be done and documented just before patient is pushed to the operation theatre. Particular attention should be paid to patient's general condition and mental status, and whether the preoperative plans were carried out.

Monitoring should be tailored to the patient's physical status rather than the procedure being done. For example, a patient with ASA 4 may need invasive monitoring for a minor surgical procedure.

Positioning may be difficult due to restriction of joint movement secondary to arthritis. Not only this will cause problems to obtain optimal position for anaesthesia and surgery, but it may also cause severe joint pains postoperatively. It is also important to care for pressure points to prevent pressure sores.

Venous access should be free flowing, easily accessible and fixed appropriately. They may not be easy to obtain, yet rapidly lost due to the fragile vessel wall.

Maintenance of ***normothermia*** is essential. Patients should be prewarmed, wrapped and active warming devices should be used, when available. Fluids should be prewarmed and warming devices should be available.

Fluids should be managed carefully as over- and underhydration are not well tolerated. Hydration status should be assessed continuously and fluids replaced based on documented and estimated loss. Parameters that are helpful are mental status, pulse rate and volume, blood pressure trends, central venous pressure and urine output.

Anaesthetic technique

The choices available are local, regional and general anaesthesia. Technique should be tailored to the patient's physical status and type of surgery. Attention to detail, availability of trained and supervised staff and communication

between the surgical and anaesthetic teams are vital. Regardless of the technique, supplemental oxygen should be administered to all patients. It is important to remember that meticulous control of physiological parameters is more important than the anaesthetic technique.

Whenever possible, local anaesthesia is preferred, as it produces less physiological disturbances and allows patients to return to normal function promptly.

Regional anaesthesia can be used effectively in a cooperative patient. The advantages are reduced thromboembolic events, reduced confusion, reduced postoperative respiratory disorder, reduced endocrine stress response to surgery, reduced blood loss and the ability to monitor mental status during surgery. However, in the uncooperative patient, the anaesthetist may be tempted to administer sedatives which may lead to altered mental status, hypoventilation and cardiorespiratory complications

The disadvantages of regional anaesthesia include sympathetic blockade causing peripheral vasodilation[6] and, if blockade is above T4, the SA and AV nodes and myocardial contractility are also affected. It is important to remember sympathetic blockade extends above the level of sensory blockade. Regional anaesthesia is also potentially more difficult in the elderly due to difficulty in positioning the patient, presence of spondylosis and osteoarthritis.[6]

General anaesthesia may be administered if regional techniques are contraindicated or if it is indicated by the surgery. The advantages include the anaesthetist being in control of the patient's airway, oxygenation and ventilation, and it does not require the patient to be cooperative, compared to regional anaesthesia.

The disadvantages include difficulty in managing the airway due to osteoporotic mandible, loose teeth, temporomandibular joint stiffness, lax oropharyngeal tone, edentulous jaws, cervical spondylosis and arthritis of the atlanto-occipital joint.[6]

As arm-brain circulation time is often increased, doses and rate of administration of intravenous induction agents should be reduced. There would also be increased sensitivity to volatile anaesthetics, opioids and benzodiazepines but decreased sensitivity to inotropes and vasopressors. Whenever possible, short acting drugs like desflurane, sevoflurane, alfentanil and fentanyl should be used.[6]

Analgesia is very important. Drugs given should be titrated. Short acting agents are preferable. Multimodal analgesia with paracetamol, local anaesthetic wound infiltration, regional blocks and opioids should be used.

POSTOPERATIVE MANAGEMENT

It is important to return patients to the baseline functional status. It is therefore important to prevent complications. Proper nutrition aids healing and recovery. Glycaemic control and fluid management should be continued from the preoperative period. It is also important to commence DVT prophylaxis until patients are fully mobile.

Patients should be monitored for cardiovascular complications e.g. hypertension, hypotension, acute cardiac event, arrythmias; respiratory complications e.g. respiratory failure, pneumonia; neurological complications e.g. stroke, postoperative cognitive dysfunction; renal failure and sepsis. Presence of complications should be detected early and treatment instituted.

Oxygen therapy should be continued up to three days postoperatively, as muscle fatigue may not be apparent till then. Early mobilisation facilitates recovery. Physiotherapy and occupational therapy should begin early.

Analgesia is extremely important.[10] The aims of postoperative analgesia are to provide patient comfort and satisfaction, encourage early mobilisation, reduce postoperative morbidity and reduce length of hospital stay. Continuous assessment of pain is important. Family members may be able to assist in assessment e.g. changes in

posture, facial expression. Drugs used should be titrated to the patient's response and side effects should be monitored. Pain control is usually substandard, due to the mistaken perception that the elderly patient has a higher pain threshold, is unable to tolerate opioids and may not be able to use the PCA machine.

Paracetamol is a good and safe analgesic. NSAIDs should be avoided in patients with renal impairment and previous peptic ulcers. They should not be used in high doses over a long period of time. Opioids may be administered orally or IV, via PCA. Intramuscular administration is painful and unreliable. Patients should be monitored for respiratory depression, sedation, confusion, nausea, vomiting, ileus and pruritus.

CONCLUSION

Elderly patients are vulnerable to the stresses of trauma, surgery and anaesthesia. They require a thoughtful preoperative assessment of organ function and reserve, meticulous intraoperative management of coexisting disorders, maintenance of normothermia and vigilant postoperative monitoring and pain control.

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Anaesthetic Considerations for Interventional Neuroradiology

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Interventional Neuroradiology (INR) has proven its role in the management of many diseases of the central nervous system. In the past decade with recent advances in various diagnostic and interventional procedures, the variety and complexity of procedures being performed by this route is increasing and this creates challenges for the anaesthetist.

The advantages of the minimally invasive surgery include: reduced trauma to normal tissue, preservation of function, more rapid recovery, reduced morbidity, and shorter hospital stay. There is also increasing evidence to suggest that there are less complications associated with endovascular procedures for certain conditions compared to the open technique.[1] The anaesthetist plays a crucial role in facilitating neuroradiological procedures and this requires an understanding of the specific procedure, their potential complications and their management.

GENERAL PRINCIPLES

Adherence to the basic principle of neuroanaesthesia should be continued in the management of patients in the neuro-radiology unit with special considerations for remote anaesthesia. Good communication between the anaesthetic team, neuroradiologist and the radiographer is important during the procedure. Detailed patient evaluation, understanding of underlying neuropathology and the procedure being performed are essential for a successful outcome. The need for general anesthesia or sedation should be decided after discussion with the neuro-radiologist considering the nature of the procedure and the patient's condition. Anaesthetists in the neuro radiology suite should be able to optimize the cerebral blood flow (CBF), cerebral perfusion pressure (CPP) and control the intracranial pressure (ICP) as the procedure and its complications can affect the cerebral flow and pressure. Essential monitoring includes blood pressure, fluid status and temperature as large volumes of fluids are used for flushing the endovascular catheter and the temperature of the radiology suite is usually low.

ANAESTHETIC CONSIDERATIONS

Anaesthetic considerations include:

- Provision of anaesthesia away from the main operating suite (Remote anaesthesia)
- Working in reduced light
- Poor access to the patient
- Concerns of ionizing radiation
- Transport of critically ill patients to and from the INR room
- Maintaining patient immobility and physiological stability
- Manipulating systemic and regional blood flow
- Managing anticoagulation
- Treating sudden unexpected complications
- Rapid and smooth recovery from anaesthesia to facilitate neurological assessment

PRE-ANAESTHETIC ASSESSMENT

In addition to the normal per–anaesthetic evaluation one should pay special attention to neurological assessment to identify any pre-existing deficit.[2] Special attention should also be given to the patient's Glasgow Coma Score, baseline blood pressure, cardiac reserve, renal function (hypotension, contrast) and coagulation profile as anticoagulation is often needed.

GENERAL ANAESTHESIA

General anaesthesia (GA) is preferred by most neuroradiologists as it provides an immobile patient with improved image quality, patient comfort and better control of respiratory and haemodynamic profiles. Other factors which favor general anaesthesia will be peadiatric patients, uncooperative patients, and preparation for potential catastrophic complications. The GA machine is best located at the patient's feet to allow imaging equipment to move freely around the patient's head. A secure intravenous (IV) access should be available with extension tubing and infusion of drugs such as anticoagulants should be given through a separate canula.

Standard monitoring is required. An arterial line will facilitate blood pressure monitoring and arterial blood gas sampling to maintain the PaCO2 at optimum levels for intracranial procedures. Deliberate hypertension (for occlusion and vasospasm) or hypotension (to slow the blood flow in the feeding artery of arterio-venous malformation (AVM) may be needed and all the necessary drugs should be available. Bladder catheterization is required as significant volumes of heparinized flush solutions and contrast are often used and administration of diuretics (mannitol and frusemide) may be required. Hypothermia can occur in INR suites, so special attention is needed to monitor and maintain the body temperature.

The disadvantage of GA is the inability to perform neurological assessment intra operatively and manipulation of the airway at intubation and extubation may cause hypertension, coughing and increase in intracranial pressure (ICP). A LMA can be used as an alternative to endotrachel intubation. With most of the new anesthetic agents, the induction and emergence can be smooth and rapid and depth can be rapidly controlled with minimum haemodynamic changes. The ideal anaesthetic agent should not impair cerebral auto regulation, carbon dioxide reactivity or cerebral metabolism. Short acting anaesthetic agents are preferred, because it is possible to blunt any painful manipulation without delaying the recovery time. Propofol might have the beneficial effect by reducing the cerebral metabolic rate and CBF while still maintaining the auto regulation.[3] The superiority of sevoflurane over desflurane in neuroanaesthesia is still debatable. Sponheim et al did not find significant increases in intracranial pressure in 36 children between the use of sevoflurane or desflurane.[4] In two different studies in healthy patients, isoflurane was found to impair autoregulation, although this was reversible with hyperventilation, while autoregulation was virtually intact with sevoflurane1–1.2% at normocapnia.[5,6] Although further large-scale studies are needed, sevoflurane appears to be the most suitable volatile agent for nueroanaesthesia.

Interventional neuroradiological procedures are less painful. Even though any of the opioids can be used, a continuous infusion of remifentanil may be superior to fentanyl or alfentanyl. The rapid onset of action, short half-time elimination as well as the haemodynamic properties of remifentanil enables the anaesthetist to control analgesia and achieve rapid emergence of the patient.[7] The α-2 agonist dexmedetomidine has been shown to provide good haemodynamic stability during intracranial tumor surgery, attenuating the response to intubation and emergence.[8] Nitrous oxide is preferably avoided, due to the risk of enlargement of micro air bubbles during the injection of contrast or fluids. It also produces cerebral vasodilatation and impairs cerebral auto regulation.[9]

SEDATION AND MONITORED ANAESTHESIA CARE

Sedation and monitored anaesthesia care (MAC) have been used in patients undergoing awake-craniotomy. Dexmedetomidine provides sedation and analgesia without respiratory depression and has been used as a sole agent, an adjunct, and a rescue drug for awake-craniotomy.[10,11,12] Patients sedated with dexmedetomidine are arousable and co-operative when stimulated and the lack of respiratory depressant effect is an added advantage.

The benefits include intraoperative neurological assessment and avoidance of heamodynamic changes associated with intubation and extubation.

The selection of sedation regime should be based on the procedure being done, experience of the anaesthetist and availability of the drugs. Most importantly the patient should be co-operative.

When used for sedation during embolization of cerebral arteriovenous malformations, dexmedetomidine 0.2–0.7μg kg^{-1} h^{-1} significantly impaired cognitive testing.[13] These patients had also received fentanyl and midazolam, and significant sedative synergism has been reported between midazolam and dexmedetomidine.[14] Dexmedetomidine 0.3–0.6 μg kg^{-1} h^{-1} was used successfully as a sole agent during implantation of deep brain stimulators. It provided satisfactory sedation, did not mask clinical signs of Parkinson's disease and reduced the need for antihypertensives.[12]

Propofol is the most frequently used drug for both sedation and general anaesthesia. It provides titratable sedation and a rapid smooth recovery when used as target-controlled infusion. In a recent study of 50 patients comparing propofol and remifentanil with propofol and fentanyl for conscious sedation, there was no difference in conditions among groups and most patients were completely satisfied.[3]

Airway management is generally uneventful during sedation. However, any sedation inevitably runs the risk of hypoventilation or airway obstruction and there must always be a plan for securing the airway if necessary. In addition, patient positioning may limit access and further contribute to airway compromise.

ANTICOAGULATION

Anticoagulation is almost always needed as the catheters and coils can promote thrombus formation. Anaesthetists are responsible for maintaining anticoagulation and reversing it in the event of bleeding. Heparin is still commonly used as its effect can be easily monitored with activated clotting time and rapidly reversed with protamine. An initial loading dose followed by intermittent doses according to ACT (to maintain 2-2.5 times the baseline) may be needed.[15]

COMMON PROCEDURES:

Closing or occluding procedures include embolization of aneurysms, A-V Malformations and arterio-venous fistulae (AVF) of the brain and spinal cord, pre operative embolization of vascular tumors such as menigiomas, temporary or permanent occlusion of arteries intra or extra cranially. Other procedures include treatment of vasospasm or stenosis by angioplasty and stenting, chemical and mechanical thrombolysis in stroke.

Cerebral angiography

Cerebral angiography makes up the majority of work, although it has recently been superseded by the by noninvasive technique such as magnetic resonance angiography (MRI) and computed tomography angiography (CTA). Most of these patients are awake but some patients may need sedation or GA (for airway control or to keep them immobile) depending on their neurological status. Patients should understand the importance of lying still during the procedure and they should be warned about the dark room, hot sensation over neck and face during injection, and headache due to the traction by the catheter or guide wire during manipulation.

Endovascular treatment for cerebral aneurysm

The incidence of cerebral aneurysm in the general population is 1.5-8%.[16] Cerebral aneurysms are responsible for 77% of acute spontaneous subarachnoid haemorrhage (SAH). The morbidity and mortality (3%) rates related to embolization of an acute aneurysm are lower than those associated with an untreated acute ruptured aneurysm.[1] Endovascular coiling can be safely done within hours of aneurysm rupture. The size and the configuration of the aneurysm are the key factors with regards to the success of coiling. Aneurysms can be classified into small, <12mm in diameter; large, 12-24mm and giant, >24mm. Total occlusion can be achieved in 57-85% of aneurysm with neck diameter 4mm whereas it is only 15-35% for >4mm.[17]

General anaesthesia is preferred for coiling as the lack of movement and physiological stability during the interventional procedure reduces the incidence of perforation. Perforation of aneurysm with an already ruptured aneurysm is 2.3-3% and unruptured aneurysm is <0.5%.[18] Thromboembolic complications are 2.5-5%. Parent artery compromise due to coil displacement occurs in 2.5%. Patients with SAH, WFNS Grades 1 and 2, with small aneurysms in the anterior circulation, have a better clinical outcome after coiling than clipping. One-year follow-up in 1594 patients has shown that there is 22.6% relative risk reduction and 6.9% absolute risk reduction in morbidity and mortality in patients who underwent coiling.[1] In posterior circulation aneurysms' coiling is preferred After the ISAT trial, coiling is generally considered as the first option in most of the centers in UK.[19]

Embolization of AVM & AVF

AVM is a vascular convolute with a nidus that is fed by one or more arteries and drained by one or more veins. The prevalence of AVM in the population is 0.5% and embolization is curative in 20 %.[20] It is often performed to reduce the size of the nidus before surgery. General anaesthesia is preferred for embolization of AVM, as it facilitates visualization of structures and prevents patient movement. Temporary apnea and a Valsalva menoeuvre can be applied to improve visualization. Controlled hypotension and flow arrest are also be easily achieved with GA, which may be required to reduce the flow across the AVM. AVF consists of a direct connection between an artery and vein and coiling is successful in 85-95% of patients.[21]

COMPLICATIONS

Complications can be rapid and catastrophic and it is important to know whether it is an occlusive or haemorrhagic crisis as these two require a different approach for management. Haemorrhagic complications are often accompanied by an abrupt rise in mean arterial pressure (MAP). Immediate reversal of heparin may be required and lowering of blood pressure is needed.[22] Mannitol may be given to reduce cerebral oedema. Patients may need emergency craniotomy and clipping of the aneurysm and need to be transferred to the operation theater immediately.

Occlusive complication: In the event of occlusion the blood pressure should be raised to improve the blood flow in collaterals and maintain normocarbia. Thrombolytic agents are commonly used. Local intra arterial tissue plasminogen activator has shown to achieve a recanalization rate of 44% Anti platelet drugs such as abciximab have shown promising results.[23]

Treatment of vasospasm:

The Triple–H therapy of hypertension, hypervolemia and haemodilution is often instituted. The associated risks with this therapy are pulmonary oedema, myocardial ischemia, electrolyte imbalance and cerebral oedema.[24,25] Intra-arterial papavarine has been shown to have clinical improvement in 25 to 50% but its potential associated side effects are monocular blindness, mydriasis, transient increase in ICP, hypertension and tachycardia.[26] Intra arterial nimodipine and nicardipine to treat vasospasm has been shown to be successful in small groups of patients.[27,28]

Contrast Reaction

The newer non-ionic contrast such as iohexol has a lower incidence of mild and moderate reactions whereas fatal reactions have occurred with ionic agents. Reactions can be caused by hypertonicty, direct cardiac depression or idiosyncratic anaphylactoid reaction. For patients with previous reaction to contrast, pretreatment with steroids and antihistamines is recommended.[29] Contrast nephropathy is the third most common cause of hospital-acquired renal failure and accounts for 12% of patients.[30] Risk factors include diabetes mellitus, volume depletion, high dose of contrast, use of nephrotoxic drugs and pre-existing renal disease. To prevent renal complications, perioperative fluid management should be aimed at normovolaemia. N- Acetyl cysteine, 600-1200mg twice a day for two days before and after the procedure has shown significant reduction

in the incidence.[31] Isotonic bicarbonate infusion may also reduce the incidence of contrast induced nephropathy by alkanizing tubular fluid and thereby minimizing tubular damage.[32]

Post operative care

All patients should be cared for in the high dependency unit (HDU) or in the intensive care unit (ICU) if necessary and all patients should remain supine until the femoral sheath is removed. The MAP should be kept 15-20% below the baseline for 24hrs for post AVM embolization to prevent cerebral oedema and haemorrhage. A MAP 20-30% above normal may be required in patients with occlusive condition or vasospasm to maintain CPP. Maintenance of heparinization is recommended in the post operative period if a large surface area of coil is exposed in the parent vessel, or if an embolic complication was encountered.[22] Post operative nausea and vomiting can be a problem due to anaesthetic agents and contrast. It is important to maintain adequate hydration, as there can be significant diuresis due to the hyperosmolar contrast. Continuous neurological observation should be made to identify any new deficit and appropriate intervention should be carried out. Continuous neurophysiological monitoring during the procedure may reduce ischaemic complications.

Radiation Hazard

Personnel working in neurointerventional rooms run the risk of exposure to ionizing radiation. The sources include direct radiation from the x-ray tubes, leakage radiation through collimators and protective shielding, and scatter radiation that is reflected from the patient and the surrounding area. The radiation exposure drops off proportional to the square of the distance from the source, therefore the activity near the head of the patient should be kept to a minimum during fluoroscopy. All the personnel in the room should wear protective lead aprons and thyroid shields throughout the procedure. Venous access should have extension tubing connected to it for infusion of fluids and drugs. If there is no facility for the anaesthetist to monitor the patient from a distance (adjoining console area), they should sit away from the patient. Clear lead screens can be used to reduce the exposure further.

CONCLUSION

With rapid advancement in endovascular interventions, we can expect more complex procedures as well as more complications in INR suites. In the near future, the neurosurgical operation theaters will be equipped with fluoroscopy and other imaging techniques so that these interventions are done in theaters. Basic understandings of neurophysiology, complexity of the procedure, awareness of the complications that may occur and being prepared to manage problems are key points for the success of anaesthesia. It is also important for Anaesthetists to keep abreast of recent advances in interventional neuroradiology and neuroanaesthesia.

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Appropriate Care

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WHAT KIND OF CARE DO PATIENTS NEED FROM DOCTORS?

In 1999, there was an outcry in the United States when the American public learnt for the first time that 1 in 6 patients were mismanaged in the hands of health care-providers. This was embodied in the report "To Err is Human: Building a Safer Health System[1]". A commission was very rapidly set up to soothe these frayed nerves. In 2001 this commission produced a report "Crossing the Quality Chasm: A New Health System for the 21st Century[2]" which describes appropriate care as envisioned by providers as well as patients. This should include 6 elements and they emphasize on the care being Safe, Timely, Effective, Efficient, Equitable and Patient-centered. While these elements are important in most health care provision, it is particularly important in the provision of acute care where effective, safe and timely intervention can determine the outcome of a patient's life.

A similar debate seems to be swirling in our midst and our public has the right to demand that our health care system delivers the 6 elements needed. The question now is how we should move in that direction by learning how others have done so.

LEVEL OF CARE[3]

Doctors are taught not only to make a diagnosis but to categorize patients into different levels of de-compensation from their disease condition. These different categories not only allow doctors to prognosticate their patients' condition but more importantly to allow them to push for the correct level of care to be instituted for the sicker patients. In the acute care situation, this categorization allows the timely focus of the correct provision of care for these patients. Correct provision needs the presence of the correct expertise with appropriate facilities and equipment. Absence of one or the other may detract from the provision of correct or appropriate care especially as the elements of good care are fairly stringent.

MATCHED CARE[3]

In an ideal situation, where the level of care is generally high, all patients can potentially have the correct level of care. Even in the most developed of countries this is never achievable as it is very expensive to maintain at that level. The alternative arrangement is for care of patients to be appropriately matched with their needs so that they get the appropriate level of care. This requires a high level of organization even in the hospital setting, more so in the public domain.

MAL-DISTRIBUTION OF CARE[4]

Just as wealth is not distributed evenly in most areas, facilities and care -providers are equally mal-distributed and this adds to the burden of providing appropriate care. The rich are more likely to seek care much earlier when the level of care is much lower; they are also more likely to have better access to good care. This mal-distribution and differential access constitutes non-equitable care and is one of the most difficult issues to overcome in the provision of appropriate care especially when health care costs escalate.

APPROPRIATE CARE[5]

In the light of what has been highlighted thus far, appropriate care would be care provided so that the disease condition is reversed or comes under control. The obstacles to provide appropriate care can thus be plentiful and in the acute care setting it can even be a race against time. It behooves a care-provider to recognize the level of de

compensation, to determine if he knows what should be appropriately done or has the facilities in addition to reverse the life-threat or alternatively to get the correct provider either in the form of correct facility/expertise for the care of the patient. All 3 of these steps in provision of care take a certain amount of time, maturity and honesty if it is to be appropriately delivered.

In the United Kingdom, hospitals are classified into 3 different levels, Level 1, 2 and 3 with the last being able to provide the highest level of care with the appropriate expertise and facilities. The public is educated to choose the correct hospital for the correct level of care so that precious time is not wasted especially in the event of acute de-compensation. Our public should equally be exposed to this kind of education. The main issue however before we do so should be to determine how we should honestly classify our various public and private health facilities into its different levels of provision so that matched care is achievable

APPROPRIATE CARE MEASURE (ACM)[6]

All care provision should be audited. Various parameters have been developed to measure care, Appropriate Care Measure (ACM) being one of them. It was defined by the Medicare Modernization Act in the United States and used by the Hospital Quality Alliance to allow CARE in participating hospitals to be compared against each other focusing on the care each is providing for patients in 3 disease conditions i.e. acute myocardial infarct [AMI], heart failure[HF] and pneumonia [PN]. (5 measures for AMI, 2 for HF, and 3 for PN) The composite measure captures whether or not a patient received all the care he or she was eligible to receive based on the 10 measures with the number of patients who are admitted with the condition as the denominator and the number of patients who received the appropriate care in the category they were admitted into as the numerator.

COORDINATING CARE

Whatever the measured parameter, the database should be utilized objectively for improvement of care with the correct initiation of changes that the database dictates. Implementing the changes required to improve care calls for good coordination of care[7,8] – an element of care which has hitherto not being a central focus. Just improving the doctor or nurse patient ratio or allotting budget to improving equipping of facilities is simply not enough. In the complex health system that most patients find themselves in, the care must be coordinated especially now that most patients are likely to meet many different providers all with different expertise to offer. In the acute care setting this is an even more difficult issue to deliver as timely coordinated care requires even more knowhow in the ergonomics of provision. Whether we are policy makers, administrators, care-provider, health care educationist or patient advocates, we must work together to deliver the appropriate care that a patient needs.

WHAT CAN WE DELIVER IN TERMS OF CARE?

We should narrow the gap between what is considered proper in the advanced countries and what we can deliver. We should also narrow the gap between what our patients need and what is possible for us to deliver. It is important to remember that the failure of appropriate care in most instances would be patient suffering and in the worst of circumstances it could be the untimely DEATH of another patient.

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Do Not Resuscitate : Are We Clear About It?

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INTRODUCTION

As anaesthesiologists and intensive care physicians, we are often involved with the "Do Not Resuscitate" order. Eventhough this end point objective should be decided by the primary team caring for the patient, often anaesthesiologists are in a dilemma when in acute settings patients with poor prognosis or terminal illness are referred for intubation and mechanical ventilation.[1]

It is a common scenario for doctors initiating resuscitation in terminally ill patients. Difficulties in making further decisions may arise especially in patients for whom it may be possible to "jack-up" the heart after cardiorespiratory arrest as their admission to ICU for continued organ support would be clinically futile because they would be unlikely to survive due to their premorbid conditions.[2,3]

Patients who suffer hypoxic brain damage would result in permanent disability, especially if there is a delay between the cardiorespiratory arrest and the initiation of CPR.[2] Some CPR attempts can be traumatic as death can occur in an unexpected and chaotic manner which is not in line with personal, cultural and religious beliefs of the unprepared family members.[4]

DEFINITIONS AND POSITION STATEMENTS

Do Not Resuscitate (DNR) orders are abbreviated in many forms. They appear as Do Not Attempt Resuscitation (DNAR), Not For Resuscitation (NFR), Do Not Intubate (DNI) but eventually they all mean the same. There are recent efforts to rebrand it as Allow Natural Death (AND) as this has a positive psychological resonance.[5] Having a negative prefix to DNR order may not go well with the patient's relatives who may conclude that the health care providers are not doing anything or giving up without trying.

DNR order is strictly about not performing CPR and should not be confused with withdrawal of treatment. Withdrawal of treatment involves a multidisciplinary approach where good communication between the health care providers as well as the next of kin regarding coming to the end of life treatment.[6] However, DNR and withdrawal of treatment has a thin line separating them, thus the simultaneous discussion about it always happens in the end of life setting. DNR should also be differenciated from the practice of euthanasia which is legalized in countries like the Netherlands, Belgium and even our neighbour Thailand.[7]

CPR is performed in an attempt to restore spontaneous breathing and circulation in patients with cardiac and/or respiratory arrest. It was first described in the 1960s by Kouwenhoven.[8] CPR is an invasive medical therapy which includes chest compressions, defibrillation with electric shocks, injection of drugs and ventilation of the lungs.

It is a fact that the survival rates after cardiorespiratory arrest and CPR are relatively low. If a cardiac arrest occurs in hospital setting, the chances of surviving to hospital discharge is found to be 15-20%. If it occurs out of hospital, the survival rate is lower, at 5-10% (2,3). Immediate intervention upon witnessing the arrest contributes to a higher probability of successful outcome. Prognosis also depends on factors such as the cause of the arrest, how soon CPR is started after the arrest and the equipment and trained staff available to deliver it. CPR can also cause adverse effects such as rib or sternal fractures and hepatic or splenic rupture. It can lead to prolonged treatment in an intensive care unit (ICU).

Prolonging a patient's life should provide benefit and improve the quality of life. Often doctors forget this and consider intervention near the end of life as purposeful for the patient. Is it in fact just an excuse?. We wonder, was the decision made for

the patient's or doctor's comfort. Viewing death as a failure to treat should be abolished. Health care providers must treat death as a natural progression of life. It is never acceptable to prolong life at all costs with no regard to the potential burdens of treatment. The decision to advocate advanced care should be based on the balance of burdens, risks and benefits to the individual as well as the people around them at that time.

RESPONSIBILITY

Decisions on not to resuscitate were first legalized in the mid-1970s. In the USA the American Medical Association was the first to suggest that decisions regarding withholding resuscitation be documented formally. It was emphasized that CPR was intended for the prevention of a sudden, unexpected death, not the treatment of a terminal, irreversible condition.[9] Detailed DNR policies were produced. Patient's right to self-determination was promoted hence the concept of "advance directive", where the patient can request that CPR be not instituted if he suffers a cardirespiratory arrest.

We do not practice advance directives in Malaysia. It is done in small isolated cases. It is an informal acknowledgement which is not legally binding between the primary carer and the patient. The facilities for care of chronic terminal patients in our country is not as well organised as developed countries; hence it is more difficult for patients and their relatives to know and decide upon care at the end of life. Discussing topics related to "end of life" is a taboo rather than an obligation of our physicians and surgeons.[10,11] Patients and their families may be unaware or in denial about the stage of their disease. This is the main problem for other acute carers when these patients appear in the emergency department for an acute problem which maybe totally futile despite medical intervention.[12,13]

Who would make the DNR order for patients who are in coma and unable to decide for themselves. In the UK, the leading clinical consultant who takes care of the patient would ultimately decide, based on factors which favor patient's quality of life.[14,15] It should be noted that the provisions of the Human Rights as well as the core medical ethics are referred to in justifying such act. In USA, the surrogate decision maker who is usually the next of kin can make the decision with a comprehensive advice from the clinical consultant in charge. It should be emphasized that communication between the health providers and family is vital. it is the clinical outcome upon which the decision is based, rather than an emotional non-clinical reasoning by family members.[13]

The reasons for the differences of emphasis on decision makers are due to the different healthcare system they are in (National Health Service vs Mutual Health Organisations Insurance). It is obvious that optimal usage of resources becomes the main principle behind DNR decisions. Healthcare is expensive and unnecessary spending on futile outcomes is questioned all the time. Non-economic prolonged care may reflect the clinical consultant's competency. Expenditure burdens that the next of kin might bear in maintaining vegetative patients become a major factor in surrogative decisions.[12] This concept of not burdening family members, may increase the application of advanced directive orders in the future.

OBJECTIVE SCORING

How do the physicians decide on who lives and who dies? As mentioned earlier it is the balance between burden and benefit to the patient with concordance of ethical considerations (Table 1,2,3).[28]

Is there any clinical scoring that we can use which may predict the most likely outcome for the ill patient?

The ideal scoring system which predicts mortality, would be one that identifies a population of patients who had a near 100% mortality (positive predictive value) and is also able to detect the 50-90% of ICU deaths in whom clinicians decide to withdraw full ICU treatment (sensitivity). ICU

TABLE 1: Guiding principles in DNR policy

- Open communication/discussion/sensitivity.
- Sufficient information given about benefits/risks/likely outcomes.
- Patients' right to refuse or withdraw consent.
- Equal rights for patients unable to make own decisions.
- No obligation to offer futile/non-beneficial treatment.

TABLE 2: CPR outcomes

Benefit likely

- There is a good chance that CPR will restore cardiac and respiratory function and that the restored function will be maintained. The likelihood of the person's returning to his or her pre-arrest condition is high.

Benefit uncertain

- The person's condition or prognosis or both may not have been assessed before the loss of cardiac and respiratory function. It is unknown or uncertain whether CPR will restore functioning. The subsequent prognosis or the likelihood of adverse consequence is also unknown or uncertain.

Benefit unlikely

- There is little chance that CPR will restore cardiac and respiratory function; even if the function is restored, it is unlikely to be maintained. The likelihood of the patient's returning to his or her pre-arrest condition is low.

Benefit absent

- There is almost certainly no chance that the person will benefit from CPR, either because the underlying illness or disease makes recovery from arrest virtually unprecendented or because the person will be permanently unable to experience any benefit.

TABLE 3: Situations where CPR should/should not be performed

Should

- People likely to benefit from CPR should be given this treatment if the need arises, unless they have specifically rejected it.
- People for whom the benefit of CPR is uncertain or unlikely should be given this treatment if the need arises, unless they have specifically rejected it. CPR should be initiated until the person's condition has been assessed.

Should not

- People who have rejected CPR and those who almost certainly will not benefit from it should not be given this treatment if an arrest occurs.

admission scoring systems eg. APACHE (Acute Physiology and Chronic Health Evaluation) I-IV, Mortality Prediction Model (MPM), Simplified Acute Physiology Score (SAPS II), organ system failures (OSF), Organ Dysfunction and Infection score (ODIN), Multiple Organ Dysfunction Score (MODS), Sequential Organ Failure Assessment (SOFA) are used in various countries around the world to quantify DNR decisions.[16,17,18,19,20,21]

These scores were designed to determine the rate of survival in the ICU population and were not designed to predict outcome for individual patients. They stratify patients and allow for comparison. They may be accurate to estimate the mortality of the whole ICU population but they are less accurate to discriminate which patient will live and which one would die.[17] This can be seen on Table 4 on how most of the scores are poor in predicting mortality (sensitivity).[29]

TABLE 4: Positive predictive value and Sensitivity of Scoring models

scoring system	positive predictive value	sensitivity	sample	reference
MPM_0 >90% mortality	69%	13%	8724 28% mortality	Rowan 1994 (20)
APACHE II >90% mortality	83%	7%	8724 28% mortality	Rowan 1994 (20)
MPM_0 >90% mortality	75%	7.8%	10027 20% mortality	Moreno 1998 (21)
SAPS II >90% mortality	85%	11%	10027 20% mortality	Moreno 1998 (21)
critical care fellow >90% mortality	71%	31%	366 40% mortality	Kruse 1988 (22)
critical care nurses >90% mortality	68%	22%	366 40% mortality	Kruse 1988 (22)
APACHE II >90% mortality	71%	26%	366 40% mortality	Kruse 1988 (22)
critical care fellows in training >90% mortality	76%	27%	215 33% mortality	Brannen 1989 (23)
APACHE II >90% mortality	71%	5.9%	215 33% mortality	Brannen 1989 (23)
Riyadh programme predicted to die	100%	38%	831 35% mortality	Chang 1989 (24)
modified APACHE II predicted to die	95%	23%	3600 16% mortality	Atkinson 1994 (25)
modified APACHE II predicted to die	59%	23%	3350 21% mortality	Rogers 1994 (26)
APACHE III > 90% mortality at first day	93%	13%	17440 17% mortality	Knaus 1991 (27)
APACHE III > 90% mortality on any day	90%	31%	17440 17% mortality	Wagner 1994 (28)
physician (SUPPORT) >85% mortality	85%	34%	4028 47% mortality	Knaus 1995 (30)
SUPPORT model >85% mortality	88%	22%	4028 47% mortality	Knaus 1995 (30)
SUPPORT model + physician >85% mortality	89%	31%	4028 47% mortality	Knaus 1995 (30)

There is no absolute clinical predictive model that can be used to justify one's decision if questioned in court. However, decisions made while maintaining the principals of patient autonomy as well as justice holds a major factor in justifying the order.

PENDING ISSUES

Communication breakdown between the treating physician, patient and patient's family is often the main reason why DNR order can be controversial.[11,13] We tend to focus on the disease and not the quality of life of the patient. In patients with terminal illness or chronic disease with organ failures, the main doctor in charge rarely paint a realistic picture of the patient's condition. Discussions to allow natural death when cardiorespiratory failure happens is not thought through together at the follow up clinic level, or before discharge following an admission for acute care. Often family members are not involved thus bringing the dying patient back to the hospital again.

For patients who are severely ill with little or no chance of survival, a proper family conference should be carried out to inform the family about the situation and prognosis and to discuss what is the best for the patient. Family members may initially resistant to the idea of "DNR", but if it is communicated clearly, the family would definitely agree to allow their loved one to die in dignity. The family may have an unrealistic expectations on success of CPR based on television and movies.[22] Physicians should consider not just the patient but whoever are affected as well. The end of life care guidelines published by NHS UK and Australia clearly emphasize continuous communication between doctors and relatives from the day the patient is impaired by his disease.[23,24]

The number of ICU beds in Malaysian hospitals are very limited.[25] Those found not to fulfill the ICU entry criteria or when the ICUs are full, patients are ventilated in the wards. Patients with futile prognosis continue to be mechanically ventilated and supported while waiting for the inevitable. This causes anxiety among the family members who may not have been given adequate explanation about the progression of the disease which is coming to the end of life. The mortality of patients being ventilated in the ward is high and this is usually expected with the level of care that we are able to provide to these locations.[26] Unfortunately unlike ICU, ward management is very territorial. Multiple teams partition themselves on care with nobody really looking after the patient as a whole. Often unnecessary prolonged suffering occurs, resulting in an unpleasant experience for the family members and denying the patient the right to die in dignity.

CONCLUSION

There is a start and an end of life cycle for every organism. Doctors should be aware that death is imminent in severely ill patients especially in the aged. Patients with terminal illness or chronic illness with severe multiple organ dysfunction are the primary candidate for not intervening when they become severely ill.

Hospitals should have a clear documentation on resuscitation and withholding/withdrawal of treatment as a requirement for accreditation. We should take up this exercise not just for the sake of accreditation but because it is a good practice to ensure optimal care from health to death. The resources issues may not be obvious now but the overall escalating healthcare cost will definitely push policies such as this forward.

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