SASM: Leading the Anesthesia and Sleep Medicine March into the Future

The Society of Anesthesia and Sleep Medicine (SASM) is acclaimed as the premiere organization that has contributed to improved patient care and influenced patient safety through education, research and scientific progress. I believe that SASM has made tremendous strides and responded to the dynamic changes in the perioperative care of patients with sleep-disordered breathing (SDB). One such effort is development of evidence-based recommendations that should guide anesthesia practitioners with regards to preoperative screening and assessment of adult patients with obstructive sleep apnea published in the August 2016 issue of Anesthesia & Analgesia journal. The next project is on the way. A task force is currently conferring to critically assess the available evidence that would allow development of the best practices for the intraoperative management of patients with SDB. We believe that the implementation of these recommendations should improve perioperative management of this challenging patient population.

The multidisciplinary membership with expertise in anesthesia and sleep medicine is in the forefront of research addressing optimal management of patients with SDB. I consider SASM as a “think tank” with focus on perioperative care of patients with SDB. The education committee of SASM has undertaken several educational efforts including preparation of white papers related to challenging and controversial aspects of care of OSA patients requiring procedural sedation/analgesia or continued on page 3
Individuals with sleep breathing disorders can suffer from long-term consequences of their disease, however, more evidence is emerging that these individuals are also at risk for serious complications during and following surgery. This issue of the newsletter features a wide range of topics that are timely and relevant to clinicians caring for patients with various sleep breathing disorders during the perioperative period.

In this issue, Dennis Auckley, MD, discusses the considerations associated with caring for patients with chronic insomnia during the perioperative period. He reviews some of the pharmacological agents for chronic insomnia, the side effects associated with these agents, and provides summary recommendations for management of patients with chronic insomnia.

The perioperative considerations for management of patients with Congenital Central Hypoventilation Syndrome (CCHS) are reviewed by Saptashree Melissa Basu, MB BCHir, FRCA. Technological advances in management of these individuals have led to improved survival so that perioperative clinicians will be more likely to encounter patients with CCHS undergoing surgical procedures in the future.

Toby Weingarten, MD, presents a comprehensive review of recent evidence, including experience at Mayo Clinic, on postoperative respiratory arrests, who is at risk, and when these events are most likely to occur.

David Samuels, MD, and Enrico Camporesi, MD, provide a thought-provoking opinion piece on the use of perioperative opioids and the current opioid crisis. They challenge the current practice of prescribing opioids for postoperative pain and describe the changes they have made in their practice that may lead to improved safety.

This issue also features a report from Bhakti Patel, MD, on the use of helmet ventilation for acute respiratory distress syndrome – a promising new form of noninvasive ventilation.

Lastly, Lee Si Jia, MD, Ong Thun How, MD, and Hairil Rizal Abdullah, MD describe some of the differences in the epidemiology and screening of OSA in Singapore, and the challenges and future directions for perioperative management of sleep apnea in Singapore.

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general anesthesia as well as pain management. Another area of potential expansion is international outreach. SASM could provide education and professional guidance to our international colleagues that are attempting to improve perioperative outcome in patients with SDB. We can provide advice not only with respect to clinical practice but also in the matters concerning quality of care and research. I believe that such efforts will help cultivate relationships between SASM and International Professional Societies. The first step towards this objective is to develop communications with interested groups that would organize combined lecture panels during their scientific conferences. The liaison committee under the leadership of David Hillman, MD, PhD, and Frances Chung, MBBS, FRCP has plans to expand the activities of SASM to Asia and Europe.

Along with the numerous opportunities that will allow SASM to grow and remain a vibrant organization, SASM also faces challenges. One of these is to increase the membership numbers. SASM’s officers and its Board are always mindful of the need to attract new members and therefore are always looking for ways of providing value to our members. There are numerous efforts to add membership value. Meltem Yilmaz, MD, Ellen Soffin, MD, PhD, and Stavros Memtsoudis MD, PhD, and the membership committee have responded to this challenge.

Another challenge faced by SASM is to maintain, if not increase, the support from corporate sponsors, which is necessary to advance our educational mission and support research. With changes in market forces, this corporate support is shrinking. I am lucky to have an excellent group of Board Members, Committee Chairs and members who are working hard to advance SASM. If our organization has to continue growing, it is necessary that members continue to share their ideas for improvement as well as participate on committees. I look forward to all of your help and support in these interesting times. I am sure that together we are embarking on an exciting, productive and rewarding journey.

As mentioned in my report published in the January 2017 issue of our newsletter, we have made significant changes in the organizational structure of SASM. This has required changes in our bylaws. David Hillman, MD, PhD, has assumed the responsibility to summarize the proposed revisions and circulate it to the membership for comment and approval. Two-thirds of the membership will be required to approve the revisions at the Annual General Meeting in Boston in October.

As with previous annual meetings, this year’s annual meeting will be held on October 19-20, 2017, in Boston, Massachusetts. The theme of this conference is “Perioperative and Sleep Medicine: Controversies and Challenges.” As you will notice from the program on SASM website (www.sasmhq.org), Stavros Memtsoudis, MD, PhD, Program Chair and Babak Mokhlesi MD, MSc, Program Co-Chair have identified several clinical as well as research topics that will be presented by the experts in their fields. As with previous annual meetings, this year’s meeting will be educational. Please make plans to attend our next conference. I look forward to meeting you in Boston at our annual meeting held just prior to the American Society of Anesthesiologists’ Annual meeting in October.

Best wishes!
Many of us will experience insomnia (difficulty falling and/or staying asleep) at some point during our lifetime. In the overwhelming majority, insomnia resolves, often within weeks to a few months (acute insomnia), and usually without any long-term sequelae. However, in approximately 10-20% of the general population, insomnia may become a persistent problem (chronic insomnia), affecting psychological health (i.e. depression and anxiety), physical health (i.e. hypertension, diabetes, cardiovascular mortality) and occupational health (i.e. disability). The prevalence of chronic insomnia in primary care populations may be substantially higher.

The causes of insomnia are quite varied and significant clinical detective work is warranted to seek reversible and treatable etiologies. Even with the best sleuthing, a reversible underlying cause may not be found and specific therapies are often utilized. There is mounting evidence for non-pharmaceutical approaches to managing insomnia, particularly with cognitive behavioral therapy (CBT), though limited access to this therapy, and lack of patient willingness to consider CBT, often lead to pharmacologic attempts at managing insomnia. The use of all types of sleep aids have been on the rise, making it likely that perioperative providers will encounter patients utilizing these treatments on a somewhat regular basis. These medications may pose certain challenges for patients undergoing anesthesia and surgery due to potential drug-drug interactions, additive effects with anesthetics and opioids, changes in metabolism in the perioperative environment, and possible withdrawal symptoms with abrupt cessation.

Standard preoperative evaluation should include asking patients about any OTC medications or herbal supplements. The majority of the OTC sleep aids contain antihistamines, mostly diphenhydramine and doxylamine, which have mild sedation as a side effect and thus are thought of as “safe” to use as chronic sleep aids. However, this class of medications has been increasingly associated with cognitive impairment with long-term use, particularly in the elderly, and their role in insomnia management has been questioned. In addition, antihistamines have potential anticholinergic side effects, leading to constipation, urinary retention in men, and drying of secretions, all of which may be relevant in the perioperative setting. Confusion and delirium are also possible side effects that are more common in the elderly. Antihistamines are generally not advised to be combined with opioids due to concerns about enhanced risk of respiratory and central nervous system depression.

Of interest, the American Academy of Sleep Medicine (AASM) recently published practice guidelines for the pharmacologic treatment of chronic insomnia and recommended against using antihistamine as sleep aids, though the strength of the recommendation was “weak.”

Other common OTC sleep aids often include melatonin or valerian root, both of which are considered herbal supplements and thus not regulated by the Federal Drug Administration (FDA). Both melatonin and valerian root are generally considered safe with minor side effects (e.g. headaches, sedation), though caution is recommended when combining these sleep aids with other sedatives, which may be relevant to the postoperative setting. Valerian root may also potentiate some of the effects of certain anesthetics agents (benzodiazepines, barbiturates, opioids), so tapering the dosage preoperatively might need to be considered. Like antihistamines, the AASM recently recommended against the use either melatonin or valerian for the treatment of chronic insomnia (“weak”).

There has been significant expansion in the types of prescription sleep aids available over the last two decades due to a better understanding of the mechanisms of sleep-induction. The traditional classes of sleep aids include benzodiazepines and...
sedating antidepressants, with the newer categories including nonbenzodiazepine benzodiazepine receptor agonists, melatonin receptor agonists and orexin receptor antagonists.

The benzodiazepines bind to several gamma-aminobutyric acid (GABA) type A receptor subtypes resulting in sedation. Typical drugs used as sleep aids in this class include triazolam, temezepam, flurazepam and lorazepam. While the recent AASM guideline approved of the use of triazolam and temezepam for chronic insomnia (both “weak” recommendations), there is growing concern about long-term use of these medications due to dependency, cognitive impairment and, in the elderly, motor incoordination that may increase the risk of falls. In addition, this class of medications has the potential to worsen underlying obstructive sleep apnea (OSA) and could be a contributor to respiratory depression. On the other hand, the abrupt cessation of benzodiazepines may lead to rebound insomnia, agitation and delirium. In the perioperative arena, there should be careful consideration of dosing of these medications, as well as the need for enhanced cardiopulmonary monitoring, particularly in patients with underlying OSA or hypoventilation syndromes.

The only FDA-approved antidepressant for the treatment of insomnia is doxepin, a tricyclic antidepressant (TCA), that is given a “weak” recommendation for its use in insomnia management by the AASM. Doxepin is prescribed in relatively low doses for insomnia (3-6 mg compared to 25-50 mg for other indications) and thus is fairly well tolerated with low risk for significant side effects. However, it does have the potential for anticholinergic and central nervous depression (CNS) depression effects, and has a long list of drug-drug interactions, so thoughtful use is warranted in the inpatient setting. Other antidepressants sometimes used for insomnia management, though not endorsed by the AASM, include other TCA medications, such as amitriptyline, and serotonin modulators, such as trazodone. In general, these medications have low risk side effect profiles at the doses used in treating insomnia. In the perioperative setting, confusion, orthostatic hypotension and increased risk for tachycardia and arrhythmias are uncommon, but notable potential side effects. And again, withdrawal syndromes can occur with abrupt cessation.

Nonbenzodiazepine benzodiazepine receptor agonists target single GABA type A receptor to induce somnolence. There has been a dramatic rise in recent years in the prescription of this class of medications, which includes zaleplon, zolpidem and eszopiclone, due to their reasonable efficacy and improved safety profile as compared to traditional benzodiazepines. The side effects attributable to these medications are similar to benzodiazepines, though generally less frequent and less severe. However, recent work has associated these medications with higher rates of falls and delirium in the inpatient setting, suggesting careful consideration when using them in postoperative patients. For chronic users, rebound insomnia may occur with sudden discontinuation.

Melatonin receptor agonists were recently developed as sleep medications with ramelteon being specifically approved for the treatment of insomnia. This medication is generally well-tolerated with a good safety profile, though it's overall efficacy as a sleep aid is more limited than some of the others already discussed. It appears safe to use in patients with OSA and no significant withdrawal or rebound insomnia has been noted with stopping this medication.

The newest class of sleep-inducing medications, the orexin receptor antagonists, was developed from work based on better understanding of the mechanisms leading to sleepiness in patients with narcolepsy. Suvorexant is the first commercially available FDA-approved drug in this class and appears to be have limited side effects (headaches and sleepiness) at present. CNS depression and narcolepsy-like symptoms (cataplexy, sleep-related paralysis and hallucinations) are potential concerns but appear uncommon. Minor effects on OSA have been noted with no documented withdrawal symptoms noted to date.

Summary recommendations

Due to the high prevalence of insomnia in the general population, perioperative providers will regularly encounter patients who are taking medications for the treatment of insomnia, either self-prescribed or physician-prescribed. Questions may arise as to whether or not to continue these medications in the perioperative setting, particularly given their potential for side effects in the inpatient environment as well as the risk of drug-drug interactions. While multiple factors need to be considered for any individual case (i.e. which medication, co-morbidities,
anesthesia/opioid plan, surgery type), some general guidelines include;

1. It's probably safe to continue most outpatient sleep aids perioperatively, though dose reduction or closer monitoring (oximetry and/or end-tidal carbon dioxide monitoring) after surgery may be warranted in some situations. Examples might include;
   a. Tapering valerian preoperatively in a patient planned to undergo anesthesia involving benzodiazepines or barbituates.
   b. Enhanced monitoring in a patient on benzodiazepines for insomnia who is expected to need postoperative opioids, particularly if they have a diagnosis of, or are at-risk for, OSA or hypoventilation, or are elderly.

2. If considering stopping a sleep aid preoperatively, consultation with the patient’s primary care provider and/or sleep specialist may help to avoid unwanted withdrawal syndromes.

3. Almost all of the sleep-inducing medications are metabolized via the liver, so this needs to be factored in dose considerations if changes in liver function occur following surgery.

4. All sleep aids run the risk of enhanced CNS depression in the inpatient setting, so these medications should be stopped if this problem arises.

5. Insomnia and OSA often coexist and thus screening for OSA preoperatively should be considered even in patients with insomnia as their primary sleep diagnosis.

If questions remain about how best to manage a given patient, consultation with the local sleep medicine service is recommended. ✤

**References:**


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**Table 1. Common Insomnia medications and potential risk in the inpatient setting**

<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
<th>Condition</th>
<th>Relevant Potential Side Effects</th>
<th>Risk for Withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>OTC Antihistamines</td>
<td>Melatonin</td>
<td>SOI</td>
<td>Enhanced sedation</td>
<td>No</td>
</tr>
<tr>
<td>OTC Valerian</td>
<td>SOI</td>
<td>Anesthetic interaction (V)</td>
<td>Yes (V)</td>
<td></td>
</tr>
<tr>
<td>Benzodiazepines Temazepam Triazolam</td>
<td>SOI/SMI</td>
<td>SOI</td>
<td>CNS depression</td>
<td>Yes</td>
</tr>
<tr>
<td>Antidepressants Doxepin Trazodone</td>
<td>SM</td>
<td>SOI/SMI</td>
<td>Confusion / sedation</td>
<td>Yes</td>
</tr>
<tr>
<td>aning pain</td>
<td></td>
<td></td>
<td>Drug-drug interactions</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Arrhythmias (uncommon)</td>
<td></td>
</tr>
<tr>
<td>BZD receptor agonists Zaleplon</td>
<td>SOI</td>
<td>SOI/SMI</td>
<td>CNS depression</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Zolpidem</td>
<td>SOI</td>
<td>Confusion / delirium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eszopiclone</td>
<td>SM</td>
<td>Fall risk</td>
<td></td>
</tr>
<tr>
<td>Melatonin receptor agonists Ramelteon</td>
<td>SOI</td>
<td>Sedation</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Orexin receptor antagonist Suvorexant</td>
<td>SM</td>
<td>Sedation</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>a. Side effects most concerning for inpatients. Other side effects can occur.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OTC = over-the-counter; SOI = sleep onset insomnia; SMI = sleep maintenance insomnia; CNS = central nervous system; BZD = benzodiazepines; V = valerian</td>
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</table>
Congenital central hypoventilation syndrome (CCHS) is a type of sleep disordered breathing characterized by a decreased drive to breathe during sleep despite progressive hypercapnia and hypoxia. The individual usually possesses adequate ventilation when awake, but hypoventilates when asleep. In the more severe forms, diminished ventilation occurs during both sleep and wakefulness. Diagnosis is made by genetic testing.

CCHS is a multi-system disorder that causes autonomic dysregulation and signs such as bradycardia and transient asystole. It is sometimes referred to as congenital central alveolar hypoventilation syndrome, and was first reported in 1970. It was often also referred to as Ondine’s curse and this term appeared in anesthetic literature as early as 1987. When CCHS occurs in association with Hirschsprung’s disease it is called Haddad syndrome.

Ondine (or Undine) was a mythological water nymph whose unfaithful mortal husband was cursed to remember all automatic bodily functions. He died when he fell asleep because he forgot to breathe. In the literature, Ondine’s curse was first reported in 1970. It was often also referred to as Ondine’s curse and this term appeared in anesthetic literature as early as 1987. When CCHS occurs in association with Hirschsprung’s disease it is called Haddad syndrome.

In 2003, the discovery of the gene causing CCHS occurred. The condition results from polyalanine repeat expansion mutations (PARM) in the paired like homeobox 2B (PHOX2B) gene in more than 90 percent of cases, and alternative PHOX2B mutations in the remaining cases. CCHS can occur as an isolated feature or in association with a number of neurocristopathies (neural crest cell pathologies). Most notably Hirschsprung disease (Haddad syndrome) 20% of the time and tumors of the sympathetic nervous system particularly neuroblastoma, ganglioneuroblastoma, and ganglioneuroma found in 5%-10% of CCHS patients.

The condition was originally reported at an incidence of approximately 1 in 50,000 – 200,000 live births. This number has been on the rise since the introduction of genetic testing. Laboratories from the United States, France, Italy, Japan, Germany, Taiwan, China, The Netherlands, Chile, the UK, and Australia combined have now diagnosed nearly 1,000 cases with PHOX2B mutation-confirmed CCHS dating to 2009. The milder phenotype is likely to be underdiagnosed.

In 2009 the American Thoracic Society produced a policy statement on CCHS. The aim of the committee was to conduct independent literature reviews and then come to a consensus on the diagnosis and treatment of CCHS. The seven main summary findings are listed in table 1.

Currently, literature regarding the perioperative evaluation and management of CCHS in adults is limited. Anesthesiologists and other perioperative clinicians need to be aware of possible late presentations of the condition, to have a clinical suspicion and understand how CCHS is diagnosed and managed. Mortality has improved due to advancements in management of children with CCHS so anesthesiologists may be more likely to encounter adults with this condition presenting for surgical procedures.

A previous review of the literature revealed there were no randomized controlled trials relevant to the

Perioperative Concerns for Congenital Central Hypoventilation Syndrome

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question of anesthesia for patients with CCHS.17 This was not likely to be feasible in such a rare condition. There were 15 relevant case reports. These were categorised as pertaining to the following: novel presentations of the condition following sedation or anesthesia, anesthetic techniques used in patients with established CCHS and patients with CCHS who experienced anesthetic complications.

Review of the anesthetic case reports showed that patients presented from all populations for surgical procedures with ages that ranged from neonates up to age 59 years. Where the diagnosis was known, anesthetic techniques usually involved gaseous induction with sevoflurane (often via tracheostomies if present), avoidance of long acting sedatives, opioids and muscle relaxants. There appeared to be few post-operative complications.8-11 Regional techniques were used where possible with close monitoring postoperatively.12

A number of cases related to novel presentations of the disease following sedation or anesthesia which in fact led to diagnosis.13-15 Patients often presented for minor procedures such as dental extraction, tonsillectomy or adenoidectomy and then did not breathe adequately at the end of surgery or in the post-anesthesia recovery room. The sequelae of undiagnosed CCHS resulted in postoperative complications such as hypoxia, desaturations, apneas, seizures, unplanned intensive care admissions, prolonged hospital stays and long-term tracheostomies.

In summary a PHOX2B mutation is required to make the diagnosis of CCHS.12 A blood test looking for the specific PHOX2B mutations leads to diagnosis and gives valuable information into the severity of the disease. Late onset congenital central hypoventilation syndrome (LO-CCHS) is the term applied to individuals who are diagnosed with CCHS after 28 days of age. LO-CCHS is considered to be a milder form of CCHS and presents later in life often in the second decade.13 LO-CCHS which is typically the 20/25 phenotype can be unmasked by administration of sedation or anesthetic agents or a recent respiratory infection or diagnosis and treatment of obstructive sleep apnea with persisting apneas.

The mainstay of CCHS treatment is ventilatory support which can be invasive or non-invasive, primarily during sleep. Mobile patients can be treated by diaphragmatic pacing. Anesthesiologists and other perioperative clinicians should be aware of undiagnosed LO-CCHS, and include this condition in the differential diagnosis of patients with unexplained respiratory depression after surgery. Anesthetic techniques should minimize use of agents that further depress respiration post-procedure and ensure adequate monitoring to detect apneas in the postoperative period.14

References:

Table 1. Summary Findings of the American Thoracic Society Policy statement on CCHS (2009)

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<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A PHOX2B mutation is needed for a diagnosis of CCHS. Information on the specific PHOX2B mutation suggests the likely phenotype e.g. need for ventilation, risk of sudden cardiac death, and the risk of associated disorders, such as Hirschsprung disease or neural crest tumors.</td>
</tr>
<tr>
<td>2</td>
<td>Parents of patients with CCHS should be screened for the PHOX2B mutation to assess their own risk of requiring medical intervention and to determine the risk of passing the PHOX2B mutation and CCHS on to their other children.</td>
</tr>
<tr>
<td>3</td>
<td>A high index of suspicion should be maintained for cases of unexplained alveolar hypoventilation, delayed recovery of spontaneous breathing after sedation or anesthesia or severe respiratory infection, seizures or neurocognitive delay.</td>
</tr>
<tr>
<td>4</td>
<td>Patients with CCHS require mechanical assisted ventilation for life. They will not outgrow the disorder or the need for support with ventilation.</td>
</tr>
<tr>
<td>5</td>
<td>As patients with CCHS have minimal lung disease, they have the greatest range of options for ventilatory support. Positive pressure ventilation via tracheostomy is recommended in the early years of life when brain growth and development requires optimal oxygenation.</td>
</tr>
<tr>
<td>6</td>
<td>Although specific PHOX2B mutations dictate the severity of the disease, more research is needed to understand how the PHOX2B genotype/mutation determines and correlates with the CCHS phenotype.</td>
</tr>
<tr>
<td>7</td>
<td>Consent should be obtained from patients with CCHS to perform autopsies after death to further identify and delineate biological abnormalities.</td>
</tr>
</tbody>
</table>

Adapted from American Thoracic society policy statement 2009

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As a member of the Society of Anesthesia and Sleep Medicine, I am keenly aware of the consequences of hypercapnic respiratory arrests following surgery. These events can result in devastating permanent injuries, such as anoxic brain injury, or even death, and the median payout when such cases go to litigation was over $200,000.1 Recent evidence has found that our previous estimate that only 1% of patients have substantial opioid-induced respiratory depression is a gross underestimate. A study at Cleveland Clinic found that more than 20% of subjects experienced prolonged episodes of hypoxemia as detected by continuous pulse oximetry compared to intermittent vital sign checks which missed 90% of cases.2 Continuous postoperative monitoring has been shown to reduce the impact of respiratory depression,3 and is considered to be superior to intermittent vital sign checks.4 The Anesthesia Closed Claims Project analysis found that in 78% of claims related to postoperative respiratory arrests the patient had a nursing check within 2 hours of the event.1 It has also been demonstrated that oxyhemoglobin saturations actually increase during intermittent vital sign checks,5 which could give the healthcare provider a false sense of security. Unfortunately, numerous barriers exist in today’s healthcare environment which preclude universal continuous monitoring of all postoperative patients. Faced with this reality, one option is to triage higher levels of postoperative monitoring to those patients at greatest risk. Fortunately, the literature is beginning to coalesce to allow us to identify which patients are at high risk and when these patients are at highest risk. An understanding of these factors will allow us to better tailor postoperative monitoring strategies.

The most widely appreciated factors that increase a surgical patient’s risk for hypercarbic arrest are obstructive sleep apnea (OSA) and the administration of sedating medications, especially opioids. A study from the Mayo Clinic found that a patient with diagnosis of or a positive screen for OSA had a 2.4 increased risk for being administered naloxone to reverse opioid-induced respiratory depression or over sedation during the first 48 hours after surgery.6 Even though OSA is common, 90% of cases are undiagnosed,7 and it is estimated 20% of adult surgical patients are at high risk for OSA.8 This is why practice guidelines call for OSA assessment routinely in surgical patients by obtaining both a detailed history and the use of an OSA assessment tool such as STOP-BANG.9,10 In addition to OSA, cardiovascular disease and central nervous system disorders including stroke and dementia have been shown to have increased risk for hypercarbic respiratory arrests, and in one study were four times more likely to be administered naloxone during Phase II anesthesia recovery compared to matched controls.6 Not surprisingly, perioperative administration of higher doses of opioids and the use of longer-acting (e.g., morphine, hydromorphone) vs. shorter-acting (e.g., fentanyl) opioids have also been found to be associated with increased risk.6 Events that occur in the postanesthesia recovery unit (PACU) can also alert the clinician that a patient may be at increased risk for later hypercarbic respiratory arrest. The Mayo Clinic has a unique system where recovery room nurses continually assess patients for four different types of respiratory depressive events: apnea, bradypnea, hypoxemia, and “pain/sedation mismatch” (Richmond Agitation-Sedation Scale11) score ≤ -2 with a numeric pain scale rating > 5 of 10.12,13 Patients who experience these events have their PACU discharge delayed for at least 2 additional 30-minute assessment periods, and those who have repeated events are placed on pulse-oximetry.
with telemetry and the use of non-invasive ventilation considered.12,13 Patients who experience repeated events were found to have higher rates of postoperative respiratory complications, and in the subset of patients who had both a positive OSA screen and repeated events this rate was 33%!13 Subsequently another study from Mayo Clinic found that patients who have a single adverse respiratory event are at 5 times the risk for needing emergent naloxone administration following PACU discharge.6 Not surprising, patients who require naloxone while in the PACU, are at higher risk for adverse postoperative complications.14 Based on these observations, our practice considers the clinical course in the PACU as an important assessment tool to determine the appropriate level of postoperative monitoring.

Understanding when patients are at highest risk is helpful in determining how long advanced postoperative monitoring is required. The Anesthesia Closed Claims Project database found 88% of postoperative opioid-induced respiratory depressive events occurring within the first 24 hours of surgery and 12% within the first 2 postoperative hours.1 The Mayo Clinic audit of postoperative naloxone administrations found 38% of administrations occurred in the first 4 hours of PACU dismissal, 58% within 12 hours, and 88% within 24 hours (Figure 1).6 Older reports have made similar observations that about 80% of events happen within the first postoperative day and the first few postoperative hours have the highest risk.15,16 The afternoon and early evening is the time when most respiratory arrests occur, and this is primarily driven by peak number of admissions from the PACU to the postoperative wards.15,17 The tendency for many events to occur in the first few hours of PACU dismissal probably reflects residual perioperative anesthetic and analgesic agents as well as lower levels of monitoring and stimulation on the ward compared to the PACU. It is interesting that there is not a circadian pattern for respiratory arrests because it is in contrast with known postoperative changes in sleep architecture.18 It should be noted that these patterns are not applicable to patients who have had neuroaxial administration of opioids, and monitoring practices should follow the 2009 guidelines from the American Society of Anesthesiologists Task Force on Neuraxial Opioids.19

These recent additions to the literature are helpful in providing better guidance as to when to use advance monitoring of patients in order to avoid hypercarbic respiratory failure. Patient features that suggest greater sensitivity to anesthesia and analgesia include central neurologic diseases such as dementia, cardiac conditions, and obstructive sleep apnea. Not surprisingly, greater opioid analgesic requirements also increase risk. Lastly, patients seem to be in the biggest danger the first few hours of PACU dismissal.

References
4. Weinger MB, Lee LA. No Patient Shall Be

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**SASM 7TH ANNUAL MEETING**

**OCTOBER 19-20, 2017**

**HILTON BOSTON LOGAN AIRPORT • BOSTON, MA**

**SAVE THE DATE!**

**PERIOPERATIVE & SLEEP MEDICINE: CONTROVERSIES & CHALLENGES**

#SASM17Boston
For more than two decades, we have seen the ravages of liberally prescribed opioids from the medical community.1 During the same time frame, we have also seen an increasing rate of obstructive sleep apnea in the population. Despite the public health community’s best efforts, most cases of obstructive sleep apnea remain undiagnosed.2 These two unfettered epidemics create the ‘perfect storm’, the rise in opioid induced respiratory depression, colloquially known as “dead in bed” syndrome.3,4 Many of the anesthesiologists who joined SASM had hoped to understand how to best treat our patients who are inevitably exposed to opioids in the perioperative period. We have become frustrated by the ever-increasing complexity of the decision tree analysis to determine which patients should be monitored for which surgeries and for how long. There is a never-ending search in our various organizations for the best setting and most appropriate monitor that will allow us to avoid this catastrophic event. Moreover, practice guidelines in these cases are difficult to enact as protocols, since there are no definitive suggestions.5

It has been more than ten years since the Anesthesia Patient Safety Foundation pointed out the dangers of opioids in the perioperative period.6 And it has been more than five years since they pronounced “no patient shall be harmed by opioid induced respiratory depression”.7 Despite these declarations, the problems with and complications of perioperative opioid use remain.

Simultaneously, we are in the midst of a prescription opioid addiction crisis, leading to an epidemic of overdose deaths. The Surgeon General has recently sent a letter to all U.S. physicians asking for us to be an agent of change in this escalating epidemic.8 Recent literature points to the perioperative period as a source of iatrogenic opioid dependence.9 Overprescribing opioid pills postoperatively has the dual effect of increased risk of addiction, and increased leftover pills in the medicine cabinet that are diverted for abuse.10 Can anesthesiologists become this agent of change the Surgeon General is looking for?

One solution is to cease utilization of toxic opioids as a first line agent. Adapting a multimodal technique both intraoperatively and postoperatively will remove the culprit. No opioids administered; no opioid-induced toxicities. By attacking the potentiation of pain at multiple non-mu receptors we can provide analgesia at the various sites responsible for the central sensitization of pain. Recent recommendations from the American Pain Society ask us to make use of multimodal agents prior to utilizing opioids. They state that systemic opioids may be eliminated.11

Since hearing the lecture by Jan Mulier on opioid free anesthesia at the 2015 SASM meeting, I (DS) have ceased to administer any intraoperative opioids. Replacing intraoperative fentanyl with sub-anesthetic ketamine, lidocaine, and magnesium in addition to other non-mu receptor agents has led to less opioid side effects such as nausea and vomiting and respiratory depression. This technique should become standard of care for all those with (or at risk of) obstructive sleep apnea. The rapid recovery with no opioids on board allows for early home readiness after outpatient surgery. The elimination of fentanyl also removes the possibility of opioid induced hyperalgesia that has recently been suggested12 and allowed us recently to document more rapid and convenient turn-around times for several surgical procedures.13 With the continuation of non-opioid oral agents postoperatively, three surgeons at our institution have decreased their postoperative hydrocodone prescription from 50 pills to 15 pills thus eliminating the number of pills available for diversion. By pursuing this technique further we can make

continued on next page
a profound difference in the opioid crisis.

First, do no harm.

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Noninvasive ventilation (NIV) has revolutionized the management of respiratory failure by supporting the work of breathing and improving gas exchange without an artificial airway. While the benefits of NIV have been most compelling in patients with COPD exacerbations and cardiogenic pulmonary edema, its failure rate approaches 60% in patients with acute respiratory distress syndrome (ARDS). Patients with ARDS often require positive end-expiratory pressure (PEEP) to recruit collapsed alveoli, decrease the shunt fraction, and thus improve hypoxemia. Often the levels of PEEP required for adequate lung recruitment are associated with substantial air leak and discomfort if delivered noninvasively by a standard facemask. Therefore, providers often rely on invasive mechanical ventilation for the high-fidelity delivery of PEEP in patients with ARDS. Unfortunately, this choice comes at the cost of increased risk of pneumonia, excessive sedation, delirium, and neuromuscular weakness in invasively mechanically ventilated patients.

We wondered whether an alternative interface—the helmet—might improve the efficacy of noninvasive ventilation in ARDS patients. The helmet is a pressurized transparent hood that encompasses the entire head and has a soft collar neck seal, which can accommodate high pressures without substantial leak (Fig 1). We hypothesized that the enhanced titration of PEEP and patient tolerability with the helmet would reduce the NIV failure rates in patients with ARDS.

We conducted a single center clinical trial comparing the endotracheal intubation rates in patients with ARDS who were randomized to helmet versus facemask NIV. We found that patients with helmet NIV had similar oxygen saturations as the facemask group, but were able to achieve those saturations with higher PEEP and less supplemental oxygen. Successful PEEP titration to 10 cm H₂O or higher was doubled with helmet NIV. Presumably as a result of this enhanced PEEP titration, endotracheal intubation rates were reduced from 61.5% to 18.2% with helmet NIV. In addition, the 90-day survival improved by 22% with helmet NIV. The clinical trial was stopped early for efficacy and safety given the results from parallel work by Frat and colleagues which demonstrated increased harm with facemask NIV in hypoxemic respiratory failure.

Adoption of helmet NIV like any new technology has a learning curve. Noninvasive ventilation settings have to be adjusted to improve patient-ventilator synchrony and to prevent carbon dioxide rebreathing. Nursing, respiratory, and physiotherapy staff require training to customize care plans for patients on helmet NIV. For instance oral care required helmet removal; however enteral feeds and medications could be given through a port that accommodated a straw for enteral access. Internal jugular central venous catheters had tubing that was threaded through the neck collar without substantial air leak. Finally, out of bed activity was possible when the arm straps secured the helmet's position.

Despite these impressive results, many questions remain as these results are intended to be hypothesis...
generating. Multicenter trials are needed to demonstrate external validity of these findings. A major tenant of the management of ARDS is limiting tidal volume to 6cc/kg of ideal body weight such that deep sedation and paralysis are recommended in severe cases to ensure controlled mechanical ventilation. The tidal volumes with the helmet are unknowable but clearly vary with spontaneous breathing and are not necessarily limited to less than 6cc/kg for each breath. Yet despite this variability in tidal volume depth, patients had improved outcomes. These controversial findings question the primacy of controlled invasive mechanical ventilation in ARDS. Furthermore, high flow nasal cannula (HFNC) is emerging as an alternative interface in hypoxemic respiratory failure. While the high fresh gas flow’s effects on dead space can improve the work of breathing, the PEEP effects are negligible. Therefore HFNC’s efficacy in comparison to helmet NIV in severe hypoxic respiratory failure that may require enhanced PEEP titration remains unknown. Finally, further investigation is needed to understand which patients may benefit from enhanced PEEP titration with helmet NIV without the risk of delaying inevitable intubation. These preliminary findings have the potential to change the landscape for NIV in ARDS and warrant further investigation.

References


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Epidemiology

In recent years, studies of obstructive sleep apnea (OSA) in the Asian population have revealed important differences when compared to the Western population.1,2,3,4 These differences include the prevalence, symptoms and contributory causes of OSA. Consequently, data from Western studies on OSA, may not be extrapolated wholesale to an Asian population.

Singapore is a multiracial, developed country within Southeast Asia, with a population of 5.6 million, comprising 75% Chinese, 15% Malays and 10% Indians.5 Our country has a multi-payer public healthcare financing framework, whereby mandatory public health insurance universally covers for inpatient hospitalisations and catastrophic illnesses, while the majority of the outpatient expenses are borne by patients.

A 2016 study showed that one in three Singaporeans in the general population are estimated to have moderate to severe OSA.6 This alarming prevalence surpasses that of the Western population, where 9% and 24% of middle aged females and males are reported to have OSA, despite our lower obesity rates.7,8 It was further estimated that up to 90% of the Singaporean subjects are undiagnosed. The study also revealed the importance of ethnicity, as the Chinese and Malays were found to have higher predisposition to OSA compared to their Indian counterparts. Although Chinese and Malay share similar prevalence for OSA, the former has a significantly lower obesity rate (14% vs 34.9%).6 This can partially be explained by the Chinese’ restrictive craniofacial anatomy, some of which include a smaller, receding mandible and smaller posterior airway space.9,10

OSA Screening

These findings have significant implications on our perioperative OSA screening process: anaesthesiologists in perioperative clinics may not only need to use the appropriate population-adjusted obesity cut-off to calculate their STOP-Bang scores, they must also have a higher index of suspicion for OSA, based on patients’ ethnicity and craniofacial features.

There have been studies looking at the validity of the STOP-Bang questionnaire in the Asian population.11,12,13 A Singapore study measuring STOP-Bang performance demonstrated moderate sensitivity and specificity (66.2% and 74.7%), with negative predictive value of ≥85%.12 Interestingly, the study found that using a lower obesity cut-off did not improve the questionnaire’s performance. In contrast, another study from neighbouring Thailand found that the sensitivity and specificity of STOP-Bang was improved by using lower BMI and neck circumference cutoffs.13

Differences in Awareness and Attitudes of OSA

Public awareness of OSA and its health consequences are poor amongst our local population. In a 2012 cross-sectional study, 256 Singaporeans were asked to complete STOP-Bang questionnaire and a home-based sleep study, continued on next page
followed by a survey assessing their knowledge in sleep apnea.14 Only slightly over a third could correctly define OSA. Lower education levels, Malay and Indian ethnicity, and patients with moderate to severe OSA were identified as predictors for lower levels of OSA awareness.

In our experience, one of our major challenges stem from poor patient acceptance towards treatment modalities, such as continuous positive airway pressure (CPAP) or dental devices. Part of the reason for this might be due to large out-of-pocket payments as health insurance generally does not provide coverage for OSA treatments.

**OSA Management in the perioperative setting**

The use of perioperative CPAP in OSA patients already on CPAP therapy reduces incidence of reintubations, ICU admissions and adverse cardiovascular events.15,16

Most hospitals in Singapore would advise diagnosed patients on CPAP therapy to bring their home CPAP machines to hospitals and continue its use perioperatively.

However, for the larger proportion of undiagnosed, or diagnosed but non-adherent patients, there is a clinical dilemma on whether perioperative CPAP should be initiated. Currently, evidence in this area is mixed.17,18,19 While the trend may be towards initiating CPAP in undiagnosed OSA patients, high healthcare costs and limited resources serve as major barriers to its widespread implementation. At present, the perioperative practice for this subgroup remains varied in Singapore. In one large tertiary centre, patients are routinely screened for OSA in the preoperative anaesthetic clinic. If the patient scores ≥ 5 on STOP-Bang, they are referred to the sleep physicians for a formal polysomnography in the post-operative period. In another smaller public tertiary hospital, OSA screening is done by the surgeons, who typically see the patients earlier than anaesthesiologists do. Patients with a high STOP-Bang score are referred to a sleep physician, who will then expedite the polysomnography and initiation of CPAP prior to surgery. This hospital has also enhanced their non-invasive ventilation capabilities in designated surgical wards to manage OSA patients on CPAP. This obviates the need to admit these patients to a high-dependency unit, particularly if they have no other medical or surgical indications warranting the admission.

**Where to from here?**

With a 90% undiagnosed OSA rate, it is inarguable that more needs to be done for screening and detection in Singapore. Population screening for OSA should be extended to the primary care level, so that a greater proportion of patients presenting at the perioperative clinic for surgery would already be formally diagnosed, if not also started on therapy. Although STOP-Bang has been shown to be a robust and well performing screening tool in the Asian population, future studies could look into the incremental value of adding ethnicity and anthropometric measurements amongst the variables. More studies should also be done to investigate the role of perioperative CPAP in previously undiagnosed patients. Lastly, while most Singapore tertiary public hospitals have a sleep unit comprising of a sleep physician and otolaryngologist, it is worthwhile considering the inclusion of a perioperative physician, dental surgeon and respiratory therapist to add value to, and make the care a more holistic one.

**References**


Sleep Apnea continued from previous page

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