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Message from the President

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In this last message as the SASM President, I would like to express my deepest gratitude to the SASM Board, Committee Chairs, and Committee members as well as the Past Presidents for their help, support and encouragement throughout the past year. It is due to their dedication and hard work that SASM remains a preeminent society. I would also like to thank our Executive Director, Marie Odden and her staff who have worked tirelessly on behalf of SASM.

I have enjoyed my term as SASM President and it was an experience that I shall always treasure. SASM is a wonderful and vibrant organization, and I am confident that it will continue to further enhance membership benefits including foster education, scientific progress, and research in the field of anesthesia and sleep medicine.

During my term, the organizational structure was updated to reflect the growth of our society. This has required changes in the bylaws, which I hope will be approved by the general body during our annual meeting in Boston. I would like to thank Dr. David Hillman, Chair of the Bylaws Committee, for guiding us through this process. Other projects that are being pursued are the development of clinical practice guidelines, advisories, and statements that address clinical dilemmas we face in day-to-day practice when managing patients with sleep-disordered breathing. The guidelines on preoperative screening and assessment of adult patients with obstructive sleep apnea, which was led by Dr. Frances Chung, has been already been published. Another project of the Pediatric Subcommittee, led by Dr. Kimmo Murto, attempts to identify the controversial issues related to the care of children at risk for obstructive sleep apnea. This is a part of a bigger project of developing guidance for appropriate selection of children undergoing airway surgery on an outpatient basis. This project is being conducted in collaboration with the Guidelines Committee of the Society For Ambulatory Anesthesia (SAMBA). The Narcolepsy Task Force, under the leadership of Drs. Dennis Auckley and Rahul Kakkar has developed guidelines for perioperative care of patients with narcolepsy. Also, the Intraoperative Care Task Force, under the leadership of Drs. Crispiana Cozowicz and Stavros Memtsoudis, is currently working very hard to develop guidelines for intraoperative management of patients with obstructive sleep apnea. As you can imagine this is a significant undertaking that requires considerable commitment. I am positive that these guidelines will be of great value to our members and improve patient safety.

I am pleased to report that SASM is in good financial health. However, we need to obtain more corporate support that would allow us to pursue various projects that expand membership benefits. In addition, we need to increase our membership. The Membership Committee, under the leadership of Drs. Meltem Yilmaz and Ellen Soffin, has developed creative approaches towards increasing our membership. In fact, I am proud that these ideas are being adopted by other societies. Another approach to increasing our membership is through the international outreach program, an endeavor that would

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Editor's File

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As the summer ends, the upcoming SASM meeting in Boston is fast approaching. This year's program promises to be varied and thought-provoking. This issue of the newsletter features updates on some of the recent literature that is increasing our knowledge regarding the mechanisms for OSA and other sleep breathing disorders, which may potentially improve our ability to manage OSA during the perioperative period. This issue also features the latest evidence on management of various sleep breathing disorders in adults, children, during pregnancy, and in Australia.

In this issue, Yamini Subramani, MD reviews the emerging evidence supporting OSA as a heterogeneous disorder with varying endotypes and phenotypes. She discusses some of the potential implications for providing targeted perioperative management and treatment of OSA depending on the underlying endotype and phenotype of OSA.

The perioperative considerations for management of patients with Obesity Hypoventilation Syndrome are reviewed by Vina Meliana, MBBS, FANZCA. With the increase in obesity globally, perioperative clinicians are more likely to encounter patients with this condition undergoing surgical procedures. Dr. Meliana discusses the challenges of perioperative management of these high risk patients.

Peter Gay, MD reviews recent evidence for the use of high-flow nasal oxygen therapy vs. conventional therapy on clinical outcomes. He discusses some of the limitations of previous studies on this mode of therapy that has recently been receiving increased interest.

Management of children undergoing drug-induced sleep endoscopy (DISE) poses unique challenges. In this issue, Suryakumar Narayanasamy, MD, Mohamed Mahmoud, MD, and Rajeev Subramanyam, MD describe the use of different anesthetic regimens for DISE in children.

Jennifer E. Dominguez, MD, MHS reviews the first results from the large prospective Nulliparous Pregnancy Outcomes Sleep Disordered Breathing (nuMom2b-SDB) substudy. The findings of this study will be of interest to all clinicians managing pregnant patients with sleep breathing disorders.

Finally, Alister Ooi, FANZCA, MBBS describes the perioperative management of OSA in Australia.

I look forward to seeing you at the SASM Annual Meeting in Boston, Massachusetts from October 19-20, 2017.

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provide education and professional guidance to our international colleagues. SASM has expanded to Asia - under the leadership of Dr. Frances Chung, and to Europe - under the leadership of Dr. Stavros Memtsoudis.

The Newsletter Subcommittee, under the leadership of Dr. Jean Wong, has worked hard to provide us with excellent newsletters that continue to update us on the activities of SASM and provide us with articles on current trends and controversies surrounding perioperative care of patients with sleep-disordered breathing. One of the highlights of SASM activities is its annual meeting. I would like to encourage all of our members to make plans to attend the upcoming 7th Annual Meeting planned by Drs. Babak Mokhlesi and Stavros Memtsoudis. Please note that I have mentioned only a few of the many activities that are being performed by several other committees (e.g., Obstetric Subcommittee, Clinical Committee, and Scientific Updates Subcommittee). In fact, each and every committee has been very active and making efforts to grow our society through increasing membership benefits as well as improving patient care and safety.

As the practice of sleep medicine grows, so will SASM. SASM has many young and enthusiastic members looking forward to assume leadership responsibilities required to maintain and grow SASM as a premier international society. However, along with the potential for growth, there will be new challenges. The future accomplishments of SASM will only be possible with the hard work and dedication of the SASM members who serve on various committees. I would like to emphasize that the time commitments are very satisfying, and will allow you to gain valuable experience as well as develop lifelong friendships.

Finally, I thank you for giving me the honor of being your President. I will always value the friendships I have developed over the years of my involvement with SASM. I look forward to see you in Boston.

Best wishes!

Understanding Phenotypes of Obstructive Sleep Apnea

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Obstructive Sleep Apnea (OSA) is increasingly being recognized as a heterogeneous disorder with both anatomical (upper airway) and non-anatomical traits, defining various endotypes and phenotypes.[1] Due to this heterogeneity, the response to continuous positive airway pressure (CPAP) therapy is variable. It may be useful to understand the clinically important endotypes and phenotypes of OSA as there is a scope for alternate treatment targeting the underlying mechanism of OSA, apart from empirical CPAP therapy.

A 'phenotype' is defined as an observable expression of an individual's characteristics, whereas an 'endotype' is defined by a unique or distinctive functional or pathophysiological mechanism. Pathogenic mechanisms of OSA based on craniofacial morphology, obesity, arousal functions, upper airway muscle activity, ventilatory control stability and nocturnal rostral fluid shift constitute potential endotypes of OSA.

Anatomy:

Obesity and craniofacial abnormalities are the two anatomical endotypes of OSA, accounting for two-thirds of the variation in OSA severity measured by apnea hypopnea index (AHI).[2] Obesity, being a modifiable risk factor, is amenable to treatment with weight loss measures through diet and bariatric surgery, associated with an improvement in the severity of OSA.[3] Likewise, craniofacial characteristics are also relevant to target OSA treatment by altering upper airway bony and soft tissue anatomy. Oral appliances and surgical procedures like maxillary-mandibular advancement and uvulopalatopharyngoplasty[4] can alter craniofacial morphology and can serve as alternatives to CPAP for some patients.

Genioglossal hyporesponsiveness:

Hyporesponsive genioglossus is a physiological endotype of OSA which is amenable to treatment with electrical stimulation of the hypoglossal nerve or the genioglossus muscle directly. [5–7] Serotonergic drugs like paroxetine and mirtazapine can also help in dilating upper airway muscles, but they do not have consistent effects on AHI.[8,9]

Arousal threshold:

OSA patients may have a variable threshold to arouse in response to respiratory disturbance, giving rise to possible endotypes of high and low arousal threshold. The notable differences between the two categories are described in Table 2.

Low arousal threshold contributes to OSA, in approximately one third of patients, by disrupting continuity of sleep and limiting the sufficient accumulation of respiratory stimuli to restore upper airway patency and airflow during sleep.[10] Although not validated, Edwards et al described criteria to identify low arousal threshold from the standard clinically available variables such as AHI, nadir SpO2 and frequency of hypopneas. The criterion for each variable was AHI < 30 events/hour, nadir SpO2 > 82.5%, frequency of hypopneas > 58%.[11] **Patients with low respiratory arousal threshold may benefit pharmacologically from certain sedatives** like eszopiclone[12] and trazodone[13] which improve sleep quality and reduce OSA severity.

Patients with a preexisting high arousal threshold may be at increased risk of adverse respiratory events when sedatives and opioids are used in the perioperative period.[14] The sedative drugs can precipitate a respiratory arrest leading to sudden unexpected death in these patients as they are in a state of "arousal dependent survival".

Table 1. OSA endotypes of low and high arousal threshold:

Low arousal threshold	High arousal threshold
Wakes up with minimal respiratory stimulus	Does not wake up until there is significant hypoxia/hypercarbia
Obstructive symptoms may be amenable to treatment with sedatives	Sedatives can precipitate a respiratory arrest
OSA likely to be mild to moderate	OSA is predominantly severe

OSA – Obstructive sleep apnea

At present, there is no conventional way to identify the patients with low or high arousal threshold preoperatively. Hence continuous postoperative monitoring is recommended with high resolution pulse oximetry to detect early desaturation and initiate treatment.[15] Monitoring end-tidal carbon dioxide using capnography can detect hypoventilation earlier in these patients.[16]

Loop gain:

Certain OSA patients have a propensity to develop a cyclical breathing pattern whereby the patient oscillates between obstructive breathing events (sleep) and arousal (wakefulness). An increase in ventilatory drive activates the upper airway muscles and promotes patency, whereas a decrease in ventilatory drive relaxes the upper airway muscles and fascilitates closure. This ventilatory instability is described as a high loop gain, which is another OSA en-

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dotype. OSA patients with high loop gain have an oversensitive ventilatory control system to hypoxia and hypercapnia. It is difficult to measure loop gain in clinical practice[17] as the methods are experimental and are not currently routinely measured in sleep laboratories.[18] Oxygen and acetazolamide are effective in reducing loop gain and may possibly benefit OSA.[19,20]

Rostral fluid shift:

The prevalence of sleep apnea is much higher in patients with fluid-retaining states such as congestive heart failure and end-stage renal disease than in the general population.[21,22] Fluid accumulates in the intravascular and interstitial spaces of the legs due to gravity during the day, and upon lying down at night redistributes rostrally, due to gravity. This hypothesis is called "rostral fluid shift".[23] Potential interventions of benefit include diuretics, sodium restriction, compression stockings, elevating the head of the bed, exercise interventions and ultrafiltration.

Clinical phenotypes of OSA:

Clinical phenotypes of OSA may be described in terms of demographics, ethnicity, sleep stages and position. A specific phenotype may encompass several endotypes.[24]

.OSA in elderly males:

Males are two to three times more likely to have OSA than females[25] with longer periods of apnea and more significant oxygen desaturations, despite a lower BMI.[26,27] The male predisposition to OSA appears to be anatomically based with increased fat deposition around the pharyngeal airway,[28] increased length of the vulnerable pharyngeal airway and the android pattern of fat deposition around the abdomen.[29]

Likewise, elderly patients with OSA are a unique group with a distinct phenotype.[30] Reduced airway caliber due to preferential deposition of fat around the pharynx, decreased genioglossal function[31] and higher surface tension of the upper airway[32] predispose the elderly population to OSA. Hence airway anatomy/collapsibility plays a greater role in older adults whereas a sensitive ventilatory control system is a prominent trait in younger adults with OSA.[30] Table 2 illustrates the differences in manifestations of OSA between the young and elderly patients.

OSA in various ethnic populations:

The relative importance of the anatomical determinants of OSA varies between ethnicities. The Asian OSA populations are found to primarily display features of craniofacial skeletal restriction, African Americans display more obesity and enlarged upper airway soft tissues, whereas Caucasians show evidence of both bony and soft tissue abnormalities4 (Table 4). Surgical treatment to alter the craniofacial anatomy carries a higher success rate in treating OSA in certain patients who refuse CPAP.[33]

OSA in REM sleep:

Hypopneas and apneas are known to be longer in duration and cause an increase in the severity of hypoxemia during REM compared with non-REM sleep in patients with OSA.[34]

REM sleep is known to be associated with reduced responsiveness of the genioglossus muscle to negative intrapharyngeal pressure.[35,36]

Treatment measures targeted to improve the genioglossus muscle tone may reduce obstructive events occurring in REM sleep. Transnasal insufflation could also help REM-related OSA as it possibly stabilizes the hypotonic upper airway musculature by increasing the end-expiratory intrapharyngeal pressure.[37]

Supine position related OSA:

Supine position related OSA is a dominant phenotype of OSA with a prevalence of 20% to 60% in the general population.[38] It may be attributable to unfavorable upper airway anatomy, reduced lung volume and inability of airway dilator muscles to compensate for the airway collapse in the supine position.

Table 2. OSA phenotype in young vs. elderly:

OSA in young	OSA in elderly
High loop gain	Loop gain is normal, stabilized breathing
Arousal threshold is normal/high	Predominantly low arousal threshold
Decreased airway surface tension	Increased airway surface tension
OSA pathogenesis is predominantly physiology driven	Predominantly anatomy-driven pathogenesis of OSA

OSA – Obstructive sleep apnea

Recognition of supine position related OSA may be therapeutically useful as these patients respond to oral appliances and positional devices avoiding supine sleep, better than other types of non-postural OSA.[39]

Role of endotypes and phenotypes in the perioperative management of OSA:

It may be useful for the perioperative team to have knowledge of the various endotypes and phenotypes of OSA to provide optimal perioperative management. Obesity and abnormal craniofacial morphology can be associated with poor glottic visualization and unexpected difficult intubation in OSA patients. The sniffing and ramped up positions can facilitate intubation. Recently, a closed malpractice claims of 12 surgical patients with OSA who were found 'dead-in-bed' was reported.[40] Certain surgical patients with OSA have a high arousal threshold and may be more sensitive to opioids and sedatives with a higher risk of respiratory arrest.[14] Regional anesthesia, by an opioid sparing effect, decreases airway collapsibility and respiratory depression and is beneficial in these patients.[41] It is useful to have patients with supine-related OSA in lateral or semi-upright positions throughout the perioperative period.

In conclusion, OSA has recently been recognized as a complex multifactorial disease with distinct endotypes and phenotypes. Hence, understanding the pathophysiological mechanisms of OSA is critical to the success of individualized therapeutic approaches.

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Perioperative Management of Obstructive Sleep Apnoea in Australia

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Introduction

Obstructive sleep apnoea (OSA) is a clinical syndrome involving recurrent periods of partial or complete upper airway obstruction during sleep, potentially resulting in respiratory complications and cardiovascular dysfunction. The cornerstone of management of OSA is Continuous Positive Airway Pressure (CPAP), with the aim of reducing the airway obstruction during sleep.

The respiratory effects of OSA can be magnified by the effects of anaesthesia and surgery, with significant implications for patient management during the perioperative period. Multiple studies have demonstrated a higher incidence of post-operative desaturation, respiratory failure and adverse cardiac events in patients with OSA.[1-3] Facilitating best perioperative outcomes for this at-risk cohort requires preoperative identification of patients with OSA in high risk populations, followed by risk stratification of those with the disease to allow appropriate planning of perioperative management and post-operative monitoring to minimise morbidity and mortality related to OSA.

Perioperative management of OSA in Australia seems largely consistent with international guidelines regarding these principles.[4,5]

Identification of previously undiagnosed OSA in high risk populations

A proportion of patients presenting for surgery will have undiagnosed OSA. Certain populations, such as the morbidly obese (and hence the bariatric surgical population), are at higher risk of having undiagnosed moderate to severe OSA, particularly given the reciprocal relation between the two conditions.[6]

In Australia, the well-validated STOP-BANG questionnaire[7] is commonly used as a preliminary screening tool for those thought to be at risk of OSA. Patients who score equal to or greater than 4 on the questionnaire are thought to warrant further investigation for the presence of moderate to severe OSA, with a score of less than 2 considered to almost exclude the presence of severe OSA.

At our metropolitan tertiary health centre, all patients with known or suspected OSA are recommended to be seen in Pre-Admission Clinic by an anaesthetist prior to surgery. The STOP-BANG questionnaire is applied to all patients who are thought to be at risk of OSA who have not previously undergone polysomnography. This includes morbidly obese patients (BMI >40), patients for bariatric surgical procedures, patients with significant cardiovascular or respiratory disease and known previous difficult intubation.

In elective cases, patients with a score of greater than or equal to 4 are referred to the Respiratory/Sleep team for a sleep study prior to booking a date for the procedure, to allow stabilisation on CPAP pre-operatively if required.

An especially high risk subset of OSA patients are those thought to suffer from Obesity Hypoventilation Syndrome (OHV). This conveys a significant increase in perioperative cardiopulmonary complications even above those with OSA, with a 10-fold risk of post-operative respiratory failure and 5-fold risk of post-operative cardiac failure8. At our centre, it is suggested that any patients noted to have a BMI>45, elevated bicarbonate levels and signs suggestive of pulmonary hypertension and right heart failure be considered for arterial blood gas sampling in addition to referral to Sleep Clinic.

Access to Sleep Medicine physicians and expected waiting time to be seen in clinic varies between different health services and regions, with access not surprisingly more difficult in centres without a dedicated Sleep unit and more remote regions. Even in large metropolitan centres, the waiting time for a Sleep Clinic appointment and formal polysomnography can be several weeks.

Risk stratification in patients with known OSA

Risk stratification of patients with known or suspected OSA in Australia requires consideration of both patient and surgical risk factors pertinent to the condition. This allows an appropriate location to be selected for planned procedure and planning of appropriate perioperative management.

Patient factors largely pertain to the severity of OSA (including the presence of OHV) and the patient's usage and compliance with CPAP therapy. Surgical factors relate to the nature of the surgery and the expected analgesic requirements post procedure. Surgical procedures considered high risk include airway surgery and any major procedures expected to have high post-operative analgesic needs with the potential for significant opioid use.

Patients noncompliant with previously established CPAP therapy are strongly encouraged to use their CPAP during the perioperative period to lower their associated risk level. They may also be referred to Sleep Clinic pre-operatively where possible to attempt to address any specific issues interfering with compliance to CPAP therapy.

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High risk patients having major elective procedures are booked at health centres with appropriate levels of post-operative medical and nursing support available, including an Intensive Care Unit if non-invasive (or even invasive) ventilation becomes necessary.

OSA patients need to be carefully considered regarding their suitability for Day Care Surgery, particularly in the absence of CPAP therapy. The Australian and New Zealand College of Anaesthetists (ANZCA) has published several Professional Documents guiding perioperative care. OSA is specifically mentioned in the guidelines regarding Day Care Procedures,[9] with the suggestion that patients with confirmed or suspected OSA should have 'minimal postoperative opioid requirement' and that 'ideally discharge analgesia should not include opioids'.

Intraoperative management

Intraoperative management of patients with OSA in Australia is at the discretion of the treating anaesthetist but largely complies with local and international practice guidelines. Some common principles include minimisation of the use of opioids and other longer acting sedative agents (e.g. benzodiazepines) which may increase the degree of postoperative sedation. To this end, multimodal analgesia and regional anaesthetic techniques may be useful, especially if able to contribute to persistent post-operative analgesia. Extubation is widely recognised to be a particularly high risk period for patients with OSA and is suggested to be performed awake and with full reversal of any residual neuromuscular blockade.

Other potential considerations include the use of invasive arterial blood pressure monitoring, particularly in patients thought at risk of OHV and can prove useful postoperatively if sequential blood gas analysis is required.

Postoperative monitoring

One of the primary concerns guiding the monitoring of patients with OSA during the postoperative period is the possibility of unrecognised respiratory depression and persistent airway obstruction in the unmonitored patient, in the worst cases leading to anoxic brain injury and death. Continuous oximetry monitoring potentially allows earlier detection of respiratory compromise and is one of the main methods for monitoring of patients thought to be at high risk. Appropriate nurse to patient ratios in the chosen area of postoperative care are another important consideration, particularly if assistance is likely to be required regarding the use of CPAP therapy.

The setting in which continuous monitoring is available varies widely between institutions. In many smaller hospitals, continuous monitoring may not be available at all, deeming them unsuitable for the perioperative management of very high risk OSA patients. Some larger hospitals with a High Dependency Unit or Intensive Care Unit may only be able to provide continuous monitoring in these high acuity environments, resulting in surgical patients thought to be at high risk from OSA competing for a scarce resource with unwell patients from the Emergency Department and from the wards. This can lead to a difficult decision on whether to proceed with an elective procedure on the day of surgery if no HDU/ICU beds are available. In emergency surgical situations where the case cannot be deferred, the Post Anaesthesia Care Unit (PACU) may be used as a temporary alternative until a monitored ward bed becomes available, but this has implications for theatre capacity and throughput particularly during after-hours periods with lower numbers of staff.

Large tertiary health care centres may be able to provide continuous oximetry monitoring in a non-HDU/ICU environment, most commonly on Respiratory wards but also in some hospitals as a remote monitoring device on a standard ward reporting back to a central continuously staffed station. This may be appropriate in the absence of other comorbidities or surgical requirements for a higher acuity environment.

Despite this, most patients with OSA of more moderate severity are considered low enough risk to be cared for post-operatively in an unmonitored environment. However, these patients are still recognised as more complex and more stringent criteria may need to be met in PACU prior to discharge to the ward. This may include a more prolonged PACU stay, a return to pre-operative oxygen saturation values with or without oxygen supplementation and an absence of hypopnoea or apnoea for a defined period of time. Oxygen supplementation, if used, should be targeted to a level thought to minimise the risk of potential loss of hypoxic drive with resulting further hypoventilation.

Postoperative management of CPAP therapy

All OSA patients on pre-existing CPAP treatment in the community are expected to bring their CPAP equipment to the hospital for use during their admission. These machines are checked by a member of the respiratory team prior to use on the wards. In the absence of any surgical contraindications, CPAP may be commenced as soon as is practical post-operatively, including in PACU if necessary. It is worth noting in the bariatric surgical population that concerns about CPAP causing gastric distention and increasing the risk of anastomotic leaks following upper GI surgery appear to be unfounded.[10] If CPAP or other forms of non-invasive ventilation are thought to be required in a CPAP naïve patient it is likely a strong indication for management in an HDU/ICU environment.

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Obesity Hypoventilation Syndrome in the Perioperative Period

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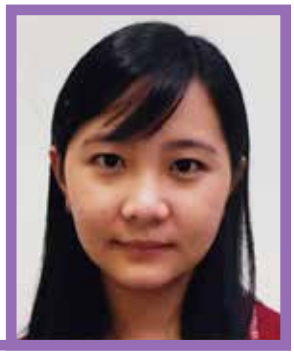

Obesity hypoventilation syndrome (OHS), also known as Pickwickian syndrome, has recently gained the much-needed attention it deserves. OHS is associated with significant health burden and resource utilisation.[1] Patients with untreated OHS have multiple cardio-respiratory and metabolic comorbidities, predisposing them to poor quality of life, frequent hospitalisations and premature death.[2,3] Unfortunately, patients are often not diagnosed until they present to hospital with type 2 respiratory failure, typically in their fifth and sixth decades of life,[2] or they are often misdiagnosed as having chronic obstructive lung disease/ asthma.[4] In the perioperative setting, evidence for postoperative outcomes are scarce.[5] However, it is not surprising that the limited data available exposed high risk of adverse events.[3,5] In a recent study, patients with unrecognised OHS undergoing non-cardiac surgery were found to have significantly higher risk of respiratory failure, heart failure, intensive care unit (ICU) admission, prolonged intubation and hospital stay when compared to patients with obstructive sleep apnea without hypoventilation.[6] In addition, mortality data in patients with OHS undergoing bariatric surgery is high at 2-8%.[7]

The diagnosis of OHS traditionally requires a combination of awake hypoventilation ($PaCO_2$ > 45mmHg) in an obese individual with a body mass index (BMI) >30 kg/m2. Essential to the diagnosis is the exclusion of other causes of chronic alveolar hypoventilation.[8] A consensus regarding the addition of serum bicarbonate to the diagnostic criteria have yet to be established.[4] OHS is estimated to affect 0.15 – 0.6% of the general population.[5] The likelihood of OHS, however, rises dramatically as BMI increases, with up to 50% of super obese patients (BMI ≥ 50kg/m2) estimated to have the condition.[5] Despite the significant morbidity associated with OHS, anesthesiologists often have limited awareness about this complex disorder.

A recent review article summarises the issues relevant to the anesthesiologists looking after patients with OHS in the perioperative setting.[5] Preoperative screening is a vital first step to identify obese patients with the condition. The clinical predictors of OHS include – serum bicarbonate, apnea hypopnea index (AHI) and oxygen nadir during sleep.[9] A two-step screening process utilising serum bicarbonate level, a marker for metabolic compensation of chronic respiratory acidosis, and AHI was proposed.[3] Serum bicarbonate level >27mEq/l has 92% sensitivity in predicting hypercapnia on arterial blood gas.[9] The addition of an AHI threshold of 100 to serum bicarbonate improves test specificity.[3] In the absence of a sleep study result, the STOP-Bang questionnaire can be used as a screening tool. A STOP-Bang score > 3, high serum bicarbonate and awake hypoxia with SpO_2 <90% may identify the majority of patients with OHS.3 Other independent predictors for daytime hypercapnia in patient with OSA include higher BMI and restrictive chest wall mechanics.[10] The presence of hypercapnia should be confirmed using an arterial blood gas and trigger further evaluation to exclude severe obstructive or interstitial pulmonary disease, neuromuscular conditions and chest wall deformities.[8] In addition, an echocardiogram should be considered to confirm or exclude the presence of pulmonary hypertension/cor-pulmonale.[3,5] Polysomnography are used to confirm OHS diagnosis, provide additional information regarding the type and severity of sleep disordered breathing (SDB) and evaluate treatment effectiveness. Therapies for OHS should be multimodal, aimed at weight reduction, controlling SDB and improving respiratory drive (Table 1).[4] The use of positive airway pressure with CPAP or bi-level positive airway pressure (BPAP) provides the most immediate benefit in gas exchange and severity of SDB.[3,4] The decision whether to delay elective surgery should be individualised, based on risk benefit ratio and should take into consideration the invasiveness of the surgery, type of anaesthesia, analgesia requirement and severity of comorbid conditions.[5]

Intraoperative management of patients with OHS are often challenging because of the associated obesity, severe OSA and other co-morbid conditions.[3,5] The Society for Obesity and Bariatric Anaesthesia has recently published guidelines on the perioperative management of this patient population.[11] The use of regional anaesthesia is advocated whenever possible and the use of ultrasound imaging may improve block success rate. Some of the concerns highlighted with general anaesthesia include difficult intubation and bag-mask ventilation, opioid sensitivity, cardiorespiratory events and thrombosis risk.[11] Meticulous planning with adequate equipment, back up plans and skilled personnel is essential. Optimal intubating positioning using ramping pillow to achieve the head elevated laryngoscopy position (HELP) and the use of videolarnyngoscope often facilitate successful intubation.[11] Techniques such as preoxygenation with positive end-expiratory pressure (PEEP) of 10cmH2O and apneic oxygenation using transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) prolong safe oxygenation time during intubation attempts.[12] The use of protective ventilation strategies with intermittent lung recruitment maneuvers and PEEP is recommended to avoid volutrauma and improve intraoperative oxygenation. Awake extubation done

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in the upright sitting position after ensuring adequate reversal of neuromuscular blockade minimises risk of atelectasis and hypoxia.[11]

High level of vigilance and close monitoring is also required in the postoperative period. The risk of respiratory failure and decompensation is high, due to multiple factors such as sedation, residual respiratory depressant effect from anaesthetic agents, opioid induced ventilation impairment and deconditioning.[3,5] Continuing PAP therapy is vital in minimising this risk. In the intensive care unit setting, it has been shown to reduce failed extubation in the morbidly obese patients.[13] Supplemental oxygen should be cautiously titrated to avoid acute hyperoxia-induced hypercapnia and worsening acidemia.[14] The use of multimodal analgesia or regional technique should be employed to minimise opioid requirements. Monitoring for sedation level and recurrent respiratory events, such as apnea >10s, bradypnea <8 breaths/min, desaturation <90% and pain sedation mismatch should also be a routine practice in the postanesthesia care unit to detect high risk patients.[3,5]

With the predicted worsening global obesity epidemic, anesthesiologists and the perioperative physicians will no doubt encounter more patients with OHS in their clinical practice. Routine screening of high risk patients pre-operatively is key to recognising the condition, implementing appropriate treatment and measures to optimise associated comorbidities. The development of multidisciplinary care pathways as well as further research in the area of perioperative identification of high risk patients and strategies to improve postoperative outcome are needed.

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Nasal High Flow Oxygen Therapy

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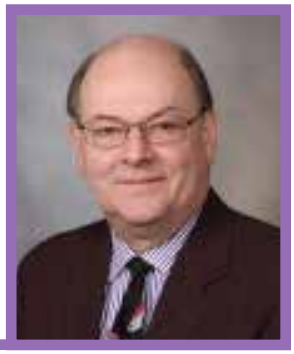

Nasal High Flow (NHF) oxygen therapy is a technique devised to deliver high flow oxygen in a maximally humidified, comfortable, and easily administered fashion. Conventional bubble humidifiers are most commonly used for humidifying medical gas delivered to spontaneously breathing patients, but the absolute humidity of the emergent gas remains low. Any time compressed gas is released the expansion results in significantly cooling and drying of the gas and when delivered directly especially in higher flows causes discomfort and increased airway resistance. NHF is administered via an air/oxygen blender that is more aggressively heated and humidified being delivered by a single limb heated circuit capable of up to 60 LPM and an FiO2 of 100%.

When originally designed, the focus was to enhance mucociliary clearance and found efficacy in bronchiectasis. While applying this therapy, it was noted that along with the marked improvement in oxygenation and ventilation, there was high patient tolerance and it was easily transitioned to the hospitalized patient when introduced to the market in 2006. Aside from the increased comfort and dyspnea relief as well as secretion clearance benefit, other mechanisms contributing to therapeutic efficacy are believed to be related to high gas flow and FiO2. This leads to less air entrainment, low level PAP, reduced dead space, and perhaps stretch receptor and other central and reflex neurally-mediated alterations in breathing pattern.

Several recent RCT studies lend further support and credence to aggressive clinical use in the hospital. An Italian study entitled **"Nasal High-Flow versus Venturi Mask Oxygen Therapy after Extubation- Effects on Oxygenation, Comfort, and Clinical Outcome" by Maggiore et al was published in AJRCCM 2014. Vol. 190(3): 282-88.** They compared the effects of the Venturi mask O2 and nasal high-flow (NHF) therapy on PaO2/FIO2 SET ratio after extubation over 48 hours with secondary endpoints of effects on patient discomfort, adverse events, and clinical outcomes. They used an RCT open-label trial on 105 pts with a PaO2/FIO2 ratio < 300 immediately before extubation. They showed from the 24th hour on, PaO2/FIO2SET was higher with the NHF (287 vs. 247 at 24 h; P = 0.03) and there were fewer pts that had interface displacements (32% vs. 56%; P = 0.01), oxygen desaturations (40% vs. 75%; P , 0.001), required reintubation (4% vs. 21%; P = 0.01), or any form of ventilator support (7% vs. 35%; P , 0.001) in the NHF group. They concluded that compared with the Venturi mask, NHF results in better oxygenation for the same set FIO2 after extubation was associated with better comfort, fewer desaturations and interface displacements, and a lower re-intubation rate. The study can be criticized because it was unblended, did not measure the true FIO2 delivered to patients, the comfort assessment purely subjective, and the ABG was done only at the end of treatment period.

A large Spanish trial lends further support and credence to aggressive clinical use in the hospital and examined this issue and was published as the **"Effect of Post-extubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Re-intubation in Low-Risk Patients- A Randomized Clinical Trial" by Hernandez et al. JAMA. 2016; 315(13): 1354-1361.** These investigators primary outcome was assessment of re-intubation within 72 hours in 527 adult critical patients at low risk for re-intubation and were randomized to undergo either high-flow (HFT) or conventional oxygen therapy (COT) for 24 hours after extubation. They found that the re-intubation rate within 72 hours was less in HFT group (13 pts [4.9%] vs 32 [12.2%] using COT (P = .004). the post-extubation respiratory failure rate was also less com-

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mon with HFT (22/264 patients [8.3%] vs 38/263 [14.4%] with COT (P = .03) but there was no differences in ICU LOS or mortality. There was concern about this study because there was an unusually higher risk of re-intubation in control groups which may be due to more medical than surgical patients in this group. This was also a heterogeneous patient population that was unblinded, and many re-intubated for secretion issues which had no a priori identified criteria. Lastly the number needed to treat for benefit is very high and therefore costly.

This same group of researchers followed with the **"Effect of Post-extubation High-Flow Nasal Cannula vs Non-invasive Ventilation on Re-intubation and Post-extubation Respiratory Failure in High-Risk Patients- A Randomized Clinical Trial" in JAMA. 2016; 316(15):1565-1574.** There were 604 patients randomized to either nasal high-flow O2 or NIV for 24 hours after extubation with the primary outcome being proof of non-inferiority of HFT vs NIV for re-intubation and post-extubation respiratory failure within 72 hours. There was no significant difference for the 66 pts (22.8%) in the HFT group vs 60 (19.1%) in the NIV group who were re-intubated and the 78 pts (26.9%) in HFT group vs 125 (39.8%) in the NIV group who experienced post-extubation respiratory failure. Median time to re-intubation and other secondary outcomes were similar in the 2 groups. However, the median post-randomization ICU LOS was lower in the high-flow group, 3 days vs 4 days (P=.048). Adverse effects requiring withdrawal of the therapy were observed in none of patients in the HFT group vs 42.9%patients in the NIV group (P < .001). Aside from the similar unblinded heterogeneous population concerns above, there is the obvious point that most of the patients were hypoxic and did not fall into categories typically defined for NIV intervention.

For those with further interest, a nice summation of recent findings can be obtained in **"Can high-flow nasal cannula reduce the rate of endotracheal intubation in adult patients with acute respiratory failure compared with conventional oxygen therapy and noninvasive positive pressure ventilation? A systematic review and meta-analysis. Yue-Nan Ni et al. In Press, available online- 10.1016/j.chest.2017.01.004.**

Women with OSA in Pregnancy May Be At Risk of Adverse Outcomes

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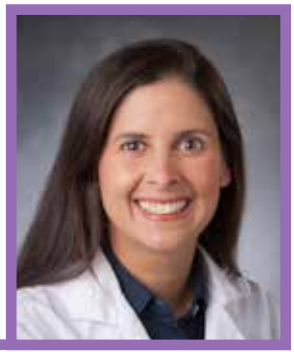

Those of us with an interest in sleep-disordered breathing during pregnancy have been anticipating the first published results of the large, prospective Nulliparous Pregnancy Outcomes Sleep Disordered Breathing (nuMom2b-SDB) substudy.1 A number of studies have shown that SDB is more common among women with other co-morbidities in pregnancy: chronic hypertension; pregnancy-induced hypertension (PIH); gestational diabetes; and cardiomyopathy.[1-7] However, not all studies have found a relationship between SDB and these co-morbidities,[8,9] and larger, prospective studies are needed to help clarify these associations.

The nuMom2b-SDB was a substudy of the larger, prospective cohort nuMom2b study conducted across 8 clinical sites in the United States between 2011-2013.[10] In January 2017, Facco et al. published the first results of their primary objective, whether SDB during pregnancy is a risk factor for adverse pregnancy outcomes. They reported an independent association between obstructive sleep apnea (OSA) in pregnancy and the risk of developing preeclampsia and gestational diabetes after controlling for several covariates.1

The substudy enrolled 3702 nulliparous women to complete extensive sleep questionnaires and undergo objective home sleep testing early in pregnancy (6 – 15 weeks gestation), and again mid-pregnancy (22 – 31 weeks gestation). Subjects with OSA on CPAP, severe asthma or on home oxygen were excluded. OSA was assessed with an unattended, Level 3 home sleep device, and defined as apnea-hypopnea index (AHI) greater than or equal to 5 events/hour. While the duration of sleep is not recorded by level 3 devices, sleep studies were interpreted by certified polysomnologists and sleep duration was estimated using several data points, as well as sleep diaries supplied by the subjects. This is a limitation of the study, as these devices have been shown to underestimate AHI by overestimating sleep time.[11] The study was powered with the assumption that 5% of subjects would have AHI > 5 in early pregnancy (180 women), and by mid-pregnancy 10% of subjects would have AHI > 5 (360 women). However, they found fewer women than expected with AHI > 5 (3.6% in early pregnancy and 8.3% in mid-pregnancy). The vast majority of these subjects had mild-moderate OSA (AHI 5-14.9/hour). This reflects one of the challenges of conducting research in this area, and may also reflect one of the limitations of the level 3 home sleep test. As shown by other studies as well, women with OSA were older, had higher body mass index, larger neck circumference, and were more likely to have chronic hypertension.

In mid-pregnancy, women with mild-moderate OSA (AHI 5-14.9/h) had an adjusted odds ratio (aOR) = 1.98 (95% CI, 1.12-3.48) for developing preeclampsia after adjusting for age, body mass index, pregnancy weight gain and chronic hypertension. Women with severe OSA (AHI > 15/h) had an even greater risk of preeclampsia with aOR = 4.27 (95% CI, 1.74 – 10.45). Preeclampsia was defined as all cases of mild, severe, superimposed, and eclampsia, regardless of the timing. While the number of women who developed preeclampsia in this cohort was consistent with population studies of the incidence of preeclampsia (approximately 3-6%), only 16 of the 114 OSA-positive women developed preeclampsia.[12]

The sub-study also demonstrated a significantly increased risk of gestational diabetes for women with OSA in both early and mid-pregnancy. In early pregnancy, women with mild-moderate OSA (AHI 5-14.9/h) had an aOR = 3.5 (95% CI, 1.64-7.44) of developing gestational diabetes later in pregnancy. This risk increased for women with severe OSA (AHI > 15/h) [aOR = 8.44 (95% CI, 1.90 – 37.60)]. The risk of developing gestational diabetes was even greater for women with OSA in mid-pregnancy. Again, the numbers of women with the co-morbidity of interest were small. In early pregnancy, 21/110 women with OSA developed gestational diabetes. In mid-pregnancy, 27/201 women with OSA went on to develop gestational diabetes. Only 5 of these subjects had AHI > 15.

The nuMom2b-SDB substudy will certainly yield other findings that will inform this area of clinical and research interest. While the findings reported to date regarding preeclampsia and gestational diabetes risk with OSA in pregnancy are interesting and consistent with other studies and meta-analyses, they should be interpreted cautiously given the small numbers of women with OSA in the cohort. Larger studies of women at higher risk of OSA may provide additional insight into their risk of developing these and other adverse pregnancy outcomes. The impact of treatment of OSA in pregnancy on adverse outcomes is still unknown, and warrants future studies.

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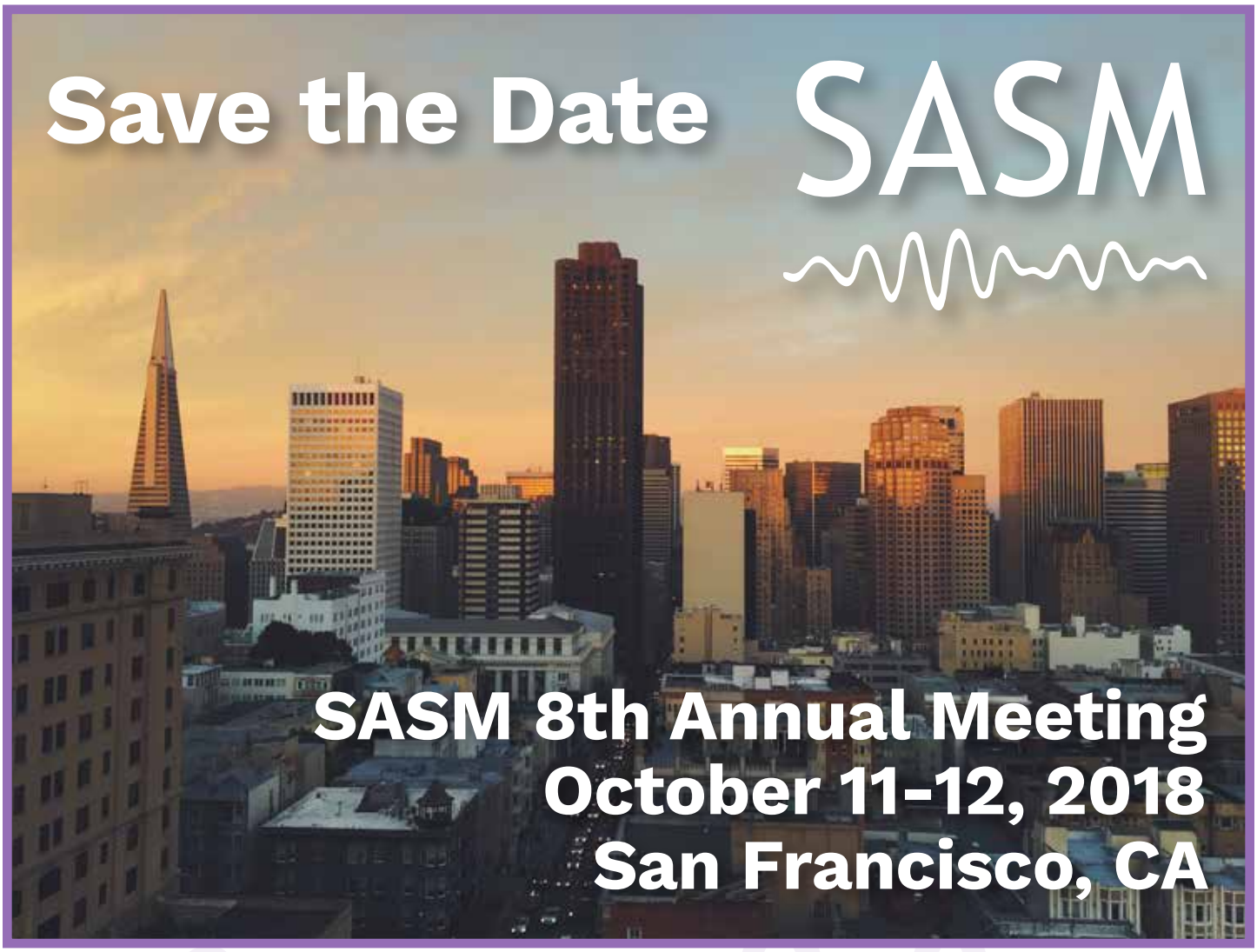

Drug-Induced Sleep Endoscopy (DISE) in Children

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Drug-induced sleep endoscopy (DISE) in children is a method to evaluate the airway in patients with refractory OSA. This involves an endoscopic evaluation of the upper airway under anesthesia. Additionally, in children with tracheal anomalies, the subglottis and tracheal airway can also be evaluated. DISE has been validated showing good inter-rater and test–retest reliability in adults and children.[1-2]

Children with OSA are sensitive to respiratory depressant effects of anesthetic agents and sedatives. The development of upper airway obstruction during anesthesia/sedation may confound the sleep endoscopy results. Hence, an ideal anesthetic regimen should mimic physiologic sleep as close as possible, allowing the patient to breath spontaneously with the natural airway. Choosing the appropriate drug and dose of the anesthetic or sedative agents required for adequate depth of anesthesia is also a major dilemma during DISE in children. Multiple anesthetic agents and sedatives including barbiturates, propofol, ketamine, benzodiazepines, opioids, dexmedetomidine have been used alone or in combination for dynamic airway evaluation.[3-7] Overdosing these agents can lead to oxygen desaturation and aborted procedures while under-dosing may result in frequent movement and prolong the duration of the procedure. There is no consensus on the ideal anesthetic agent for pediatric DISE.

We performed this study and compared three different options of anesthesia for patients presenting for DISE (Table 1). The goal was to identify the most effective drug regime among the three: dexmedetomidine plus ketamine (Group DK) vs. propofol (Group P) vs. sevoflurane plus propofol (Group SP) at Cincinnati Children's Hospital Medical Center.[8] Children in Group DK had significantly fewer desaturations to <85% when compared to Group P (P = 0.004) (Table 2). Overall, DISE was successfully completed in 93% (55/59) of cases; 100% (32/32) of children in Group DK, 92% in group P (12/13), and 78% in group SP (11/14). In Group P, the patient who failed completion of DISE could not maintain oxygen saturation above 85% despite continuous jaw thrust and ultimately required oral airway placement and cessation of the procedure before completion. Of the patients who were unsuccessful in Group SP, two patients had laryngospasm, and the third had extensive airway collapsibility that prevented full visualization and prohibited complete evaluation of the upper airway. Airway intervention was required in 3% of children in Group DK, 15% in Group P, and 21% in Group SP (P = 0.05).

We reviewed the preoperative overnight PSG reports, noting the severity of oxygen desaturations during natural sleep and used it as a guide to acceptable minimal arterial oxygen saturations for an individual patient. Oxygen saturation below 80% on preoperative PSG is identified as the single most important risk factor for perioperative respiratory complications in children after adenotonsillectomy.[9]

Dexmedetomidine is well described and successful for sedation for noninvasive procedures.[10] However, dexmedetomidine has been unsuccessful in providing adequate depth of anesthesia when used as a sole agent for invasive procedures.[11] High-doses of dexmedetomidine may lead to significant hemodynamic instability, specifically bradycardia and hypotension.[12-13] A combination of ketamine and dexmedetomidine bolus followed by a dexmedetomidine infusion has been shown to provide sedation without exacerbating respiratory problems in children with Down's syndrome and OSA.[14] This combination can provide fast onset amnesia, sedation, analgesia, and hemodynamic stability while maintaining spontaneous ventilation.[15-16]

Propofol acts through the inhibitory neurotransmitter GABA and has also been shown to induce a state of diminished responsiveness behaviorally similar to nonrapid eye movement (NREM) sleep.[17] It may compromise the airway by two mechanisms: (i) muscle relaxation and (ii) respiratory drive suppression. Ketamine has neither of these effects, most likely due to ketamine's mechanism of action on the blockade of N-methyl-D-aspartate (NMDA) receptors. A recent study examining the genioglossus electromyogram activity showed that ketamine was accompanied by lower levels of upper airway dilator muscle dysfunction compared to the equi-anesthetic concentration of propofol, with preservation of ventilation with a wide dose-range of ketamine.[18] The sedative effect of dexmedetomidine is mediated via stimulation of alpha-2 adrenoceptors in the locus coeruleus. Dexmedetomidine produces a state closely resembling physiological sleep,[19-20] which gives further support to earlier experimental evidence for activation of normal NREM sleep-promoting pathways.

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Table 1: Demographic and sleep characteristic Data						
	All Subjects (n=59)			Patients with PSG (n=49)		
	Group DK (n=32)	Group P (n=13)	Group SP (n=14)	Group DK (n=26)	Group P (n=10)	Group SP (n=13)
Age (months)	83.0 ± 80.8	105.7 ± 99.7	72.8 ± 56.6	89.7 ± 86.3	108.2 ± 106.1	72.0 ± 58.9
Weight (kg)	34.9 ± 38.5	39.4 ± 36.3	30.0 ± 27.6	38.9 ± 41.5	40.9 ± 41.1	29.8 ± 28.7
BMI (kg/m^2)	26.6 ± 21.3	27.4 ± 18.7	24.2 ± 16.5	28.8 ± 22.9	28.1 ± 21.1	24.0 ± 17.2
ASA						
II	5 (55.6)	1 (11.1)	3 (33.3)	4 (57.1)	0 (0.0)	3 (42.9)
III	26 (53.1)	12 (24.5)	11 (22.5)	21 (51.2)	10 (24.4)	10 (24.4)
IV	1 (100.0)	0	0	1 (100.0)	0	0
DS	9 (42.9)	8 (38.1)	4 (19.1)	9 (45.0)	7 (35.0)	4 (20.0)
OSA						
Mild				1 (25.0)	2 (50.0)	1 (25.0)
Moderate				10 (58.8)	2 (11.8)	5 (29.4)
Severe				15 (53.6)	6 (21.4)	7 (25.0)
RDI				15.2 ± 8.2	24.1 ± 28.2	11.6 ± 6.6
AHI				15.6 ± 10.5	30.2 ± 29.2	15.7 ± 11.9

AHI = Apnea/Hypopnea Index; ASA = American Society of Anesthesiologists scoring system; BMI = Body Mass Index; DS = Down Syndrome; DK = Dexmedetomidine+Ketamine; OSA = Obstructive Sleep Apnea; P = Propofol; RDI = Respiratory Disturbance Index; SP = Sevoflurane+Propofol

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Table 2: Comparison of outcomes between the groups												
	All Subjects (n=59			p-values			Patients with PSG (n=49)			p-values		
	Group DK (n=32)	Group P (n=13)	Group SP (n=14)	DK vs. P	DK vs. SP	P vs. SP	Group DK (n=26)	Group P (n=10)	Group SP (n=13)	DK vs. P	DK vs. SP	P vs. SP
Desaturation to < 85% during DISE n (%)	1 (3.1)	5 (38.5)	2 (14.3)	0.004 (-0.6, -0.1)	0.85 (-0.4, 0.1)	0.17 (-0.1, 0.5)	1 (3.9)	5 (50)	2 (15.4)	0.002 (-0.8, -0.2)	0.95 (-0.4,0.2)	0.05 (0.0, 0.7)
Desaturation to ≥ 85% - ≤90 during DISE n (%)	6 (18.8)	1 (7.7)	4 (28.6)	1.0 (-0.2, 0.4)	1.0 (-0.4, 0.2)	0.52 (-0.6, 0.2)	5 (19.2)	0 (0.0)	4 (30.8)	0.56 (-0.2, 0.5)	1.0 (-0.4, 0.2)	0.19 (-0.7, 0.1)
Successful completion n (%)	32 (100)	12 (92.3)	11 (78.6)	1.0 (-0.1, 0.3)	0.02 (0.0, 0.4)	0.44 (-0.1, 0.4)	26 (100)	9 (90)	10 (76.9)	0.94 (-0.1, 0.3)	0.04 (0.0, 0.5)	0.74 (-0.1, 0.4)

95% CI, 95% confidence interval; DISE, drug-induced sleep endoscopy; DK, dexmedetomidine + ketamine; P, propofol; PSG, polysomnography; SP, sevoflurane + propofol

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In our study, despite the complexity of the patients, the dexmedetomidine and ketamine (Group DK) combination was associated with fewer oxygen desaturations, a higher rate of successful completion, and better maintenance of blood pressure when compared to the described dose regimen of propofol, or sevoflurane plus propofol during DISE. At the dose used, propofol dosing appears to be associated with more morbidity.

In conclusion, we found that the described dose regimen of propofol used alone or in combination with sevoflurane appears to provide less favorable conditions for completion of DISE with more oxygen desaturations than a combination of dexmedetomidine and ketamine in children with OSA.

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