Evaluation of dexmedetomine in anesthesia care for elderly patients with obstructive sleep apnea
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Abstract

It is estimated that by year 2030, there will be approximately 71.5 million elderly representing about 20% of the population. Compared with young patients, there is a 3-fold increase in risks associated with surgery, which constitutes a unique challenge to anesthesia care providers. In addition, comorbid diseases in the elderly patients add significantly more risks. Certain diseases make elderly patients particularly vulnerable to anesthesia, for example, the obstructive sleep apnea (OSA). However, there have not been sufficient studies to investigate the optimal anesthesia care to this special but common patient population. Commonly used anesthetics including propofol and opioids have significant cardiovascular and respiratory side effects, particularly in elderly patients. In recent years, dexmedetomidine has attracted a great attention to be able to optimize anesthesia care in specific patients. In this proposed study, we will investigate whether adding dexmedetomidine will provide a better and safer anesthesia care to elderly OSA patients. In addition, we will investigate whether dexmedetomidine will reduce the use of propofol and opioids in anesthesia care and the incidence of cardiovascular and respiratory side effects in this patient population. Proposed study will be the first to look into the clinical application of dexmedetomidine in elderly OSA patients. The results will help to guide safe anesthesia care to the elderly.
Chapter I: Introduction

The World Health Organization defines the ‘elderly’ as a person of 65 years or older. In the United States, the elderly population was 36.3 million in 2004, representing 12.4% of the U.S. population. By 2030, there will be approximately 71.5 million elderly, and representing about 20% of the population. Compared with young patients, there is a 3-fold increase in risks associated with surgery. However, in many situations, these elderly patients must undergo surgery to save their lives. This population presents itself as a unique challenge to health care providers, particularly anesthesia care providers (Morgan et al. 2006).

Besides inherent risks associated with anesthesia regardless the age of the patient, there are unique features in the elderly making them especially vulnerable to anesthesia. There are physiological changes associated with aging. Particularly, those changes in cardiovascular and respiratory systems of the elderly put these patients in particular risks under anesthesia. For example, decreased arterial elasticity and adrenergic activity will enhance the negative effect on cardiac output or conduction pathways in heart from both volatile and non-volatile anesthetics. Aging decreases pulmonary elasticity and increases chest wall rigidity. Along with decreased respiratory muscle weakness and blunted chemoreflex responses, the elderly patients are particularly vulnerable to drugs with respiratory depression capability, which is the character of nearly all anesthetics, including popular propofol and opioids. Furthermore, aging induces reduction in the reserve of both renal and hepatic function. Thus it is necessary to adjust the dose of anesthetics in the elderly, usually lowering the dose to reduce side effects. Unfortunately, side effects are inevitable when using proper anesthetics to achieve satisfactory anesthesia in the elderly patients.
In addition, comorbid diseases in the elderly patients level addition risks to them. Certain diseases make elderly patients particularly vulnerable to anesthesia. A good example is the obstructive sleep apnea (OSA). OSA is common in the elderly. Epidemiology studies put its occurrence at 11-66% of the population, depending on specific studies (Russel & Duntley, 2011). The characteristic symptom of the OSA patients is the frequent interruption of breathing activity during sleep. OSA is often associated with increased perioperative cardiovascular and respiratory complications, including hypertension, hypoxia, arrhythmias, myocardial infarction, pulmonary infection, etc. Thus for anesthesia care providers, this patient population deserves extra caution during perioperative care. Endeavors to finding a better and safer anesthetic to this specific patient population will have significant impact on future clinical practice. In this proposal, we will explore the potential benefits of a new anesthetic medicine dexmedetomidine in anesthesia care for this patient population.

Statement of the Problem

The purpose of this study is to evaluate the efficiency of dexmedetomidine in safe anesthesia care for elderly patients with OSA. Cardiovascular and respiratory functions in these patients are compromised even without other comorbid diseases. Commonly used anesthetics, including propofol and opioids, have negative effects on cardiovascular and respiratory functions and will cause increased anesthesia risks and perioperative complications in these patients. Dexmedetomidine, a new anesthesia drug with few and mild side effects, has been demonstrated to reduce the use of propofol and opioids during anesthesia in a limited number of studies, thus reducing associated risks. It is expected that the results from proposed study will help clinicians provide a safe and balanced anesthesia to the patients.

Significance of the Study
Currently, most commonly used recipes for balanced anesthesia include the use of propofol and opioids. Both have significant side effects, particularly the depression effect on cardiovascular and respiratory systems. For elderly patients suffering from OSA, respiratory depression effect is particularly harmful. Anesthesia care provider should be extremely careful when providing anesthesia care in this specific population. In recent years, clinicians have been looking for alternatives for safer anesthesia. Dexmedetomidine (Precedex®) is a central alpha2-adrenoreceptor agonist, has received interest during recent years. Dexmedetomidine leads to dose-dependent sedation, analgesia, and blunts the sympathetic reactions to surgical stress. It has found to have an opioid-sparing effect and reduce the dose of other intravenous anesthetics. Its side effects are mild, including hypotension and bradycardia. Noticeably, dexmedetomidine does not significantly depress respiratory drive. This character would be particularly valuable in OSA patients. OSA patients tend to have obstructed airways easily during anesthesia. Further reduction in respiratory drive would further exacerbate autonomic dysfunction associated with OSA. In recent years, multiple studies have demonstrated that dexmedetomidine is a safe and effective anesthetic. However, its application in elderly OSA patients has not been studied.

Recent census found that there are 40 million people in the United States are the elderly. It is projected that this number will reach more than 89 million by 2050. Based on epidemiology data regarding the occurrence of OSA in elderly patients (Russel & Duntley, 2011), a significant portion of this population will suffer from complications associated with OSA. Due to the aging, many of these patients will receive some type of surgery before they die. When surgery is inevitable, any incidence of perioperative complication will be a significant financial and psychological burden on patients and their families, and the society. Significant harm will be done to the general health of the patient. Any improvement in providing safer anesthesia will
benefit these patients. In recent studies, dexmedetomidine has approved itself to be a safe adjunct to anesthesia. This current proposal will for the first time provide systemic information about its application in a specific population. The results will be used to guide our future practice to provide safe anesthesia care to elderly patients. In addition, data will be used to further extend the use of dexmedetomidine in anesthesia care.

**Delimitations**

1. This study will be performed in 6 program-affiliated major hospitals in Fort Lauderdale area. We will only include people 65 years or older in our project, both male and female. To reduce confounding factors, we will only include those patients without known significant cardiovascular, respiratory, and neurological diseases except OSA. Thus, specific population for our project will be those who receive anesthesia for reasons other than cardiovascular, respiratory and neurological causes, including medical procedures.

2. Patients will be divided into two groups, those with or without OSA. In each group, patients will be randomly assigned to receive dexmedetomidine in addition to standard anesthesia plan including both propofol and opioids or standard anesthesia plan only. Based on previous studies with similar design, each hospital will recruit a total of 40 patients, eventually into 4 subgroups. Thus, in total there will be 240 patients for this project, with 60 in each subgroup. Based on the working load at each hospital, it is expected that this project can be finished within 3 years.

3. In each hospital, there will be a designated anesthesia staff to review the patient data and decide the eligibility of each patient. Then this designated staff will follow the random number to group each eligible patient. All anesthesia care providers in the project will receive training of standard anesthesia plan of this project.
4. All data will eventually be collected and sent to analysis team, where a statistician will analyze the data, and results will be reported to the principle investigator (PI). Subsequently, PI will further analyze and interpret the data, and prepare the results for publication.

5. Dexmedetomidine will be given as continuous intravenous infusion at a rate of 0.2 µg/kg/hr and start from the beginning of anesthesia induction and end at the completion of anesthesia.

6. Propofol will be given at an initial dose of 1.5 mg/kg as intravenous bolus. Total dose will be depending on anesthesia effect.

7. Fentanyl will be given as intravenous bolus at a dosing range of 0.5-2 µg/kg/hr to relieve pain and autonomic response induced by procedures including intubation.

8. Demographic data of patients will include age, gender, history of previous anesthesia, drinking, smoking, drug using, and race. Anesthesia data will include dose of propofol and fentanyl used in whole case, number of adverse events (hypotension, bradycardia, hypoxemia), emergence time.

Limitations

1. This is a multi-center study at local level. Thus the result can only be applied to the population in this specific reason and could risk over-interpretation if applying it to patients in other hospitals. Future study involve multiple hospitals across the country will help to solve this limitations. In current research design, it will be necessary to perform statistical analysis within the population from the same hospital in addition to that

2. The skills of the anesthesia care provider affect the use of anesthetics and occurrence of anesthesia accidents. The difference in skill level among different anesthesia care providers will have negative impact on the results of this study design. To address this problem, it is necessary
to emphasize the use of standard protocol and recruit sufficient number of patients at each clinical site.

3. This study will only test one single dose of dexmedetomidine, which is based on previous studies and may not represent the optimal dose. Future study will be needed covering the whole dosing range approved by the FDA.

Assumptions

1. The data collected in current study design, particularly blood pressure, heart rate, dose of each drug used, apnea incidence and emergence time, is sufficient to answer the question about whether dexmedetomidine can provide extra benefits to the patients.

2. It is assumed that clinical dexmedetomidine in our protocol has no long-term negative effects on the patients.

3. We assume that designated staff at each clinical site will be able to access all necessary documents and follow the protocol.

4. We assume that cardiovascular and respiratory systems are the major factors deciding the safety of a particular anesthetic. Based on that assumption, research design is not based on functional parameters of other systems, particularly renal and neurological systems, although standard ASA monitoring will be performed on each patient and data will be analyzed.

Hypotheses

It is hypothesized that dexmedetomidine will reduce the use of propofol and opioids in elderly patients, compared to those patients not receiving dexmedetomidine. It is further hypothesized that dexmedetomidine will not increase the incidence of apnea during anesthesia or further exacerbate cardiovascular incidents. It is hypothesized that in elderly patients with OSA, dexmedetomidine will be able to provide a safer anesthesia when added into standard anesthesia
Running Head: DEXMEDETOMIDINE AND ANESTHESIA CARE IN THE ELDERLY

plan. On the other hand, it is hypothesized that in elderly patients with OSA, standard anesthesia plan alone is associated with more frequent adverse respiratory and cardiovascular events.

**Definition of terms**

1. **Apnea** – Complete stop of breathing. In the diagnosis of OSA, apnea is defined as 10 seconds or more of total cessation of airflow despite continuous respiratory effort against a closed glottis.

2. **Apnea-hypopnea index (AHI)** – The sum of apneas and hypopneas during sleep divided by the sleep time in hours.

3. **Bradycardia** – In anesthesia care, bradycardia is a heart rate below 50 beats/minute.

4. **Dexmedetomidine** – Dexmedetomidine is a central alpha2-adrenoreceptor agonist. It has sedative, analgesic, and sympatholytic effects. Its action on sympathetic system contributes to its main side effects including mild hypotension and bradycardia.

5. **Hypopnea** – It is defined as a 50% decrease in airflow or a decrease sufficient to lead to 4% or greater decrease in arterial oxygen saturation.

6. **Hypotension** – In anesthesia care, hypotension is defined as the arterial blood pressure level drops at least 20% of baseline level.

7. **Hypoxemia** – In anesthesia care, hypoxemia is defined as oxygen saturation below 90% if measured with pulse oximeter or arterial blood gas shows arterial oxygen partial pressure below 80 mmHg.

8. **Obstructive sleep apnea (OSA)** – A disorder characterized by repetitive collapse and reopening of the upper airway during sleep. Clinical Guideline from the American Academy of Sleep Medicine defines OSA as patient with an AHI at least 5.
9. **Opioids** – This class of drug provides strong analgesic effects by binding to specific
receptors at various sites along the pain pathways in the central nervous system. Opioids depress
breathing activity. This is mediating by opioid receptor subtypes in brainstem respiratory center.

10. **Propofol** – The chemical name is 2,6-diisopropylphenol. Propofol induces general
anesthesia by facilitating the central inhibitory neurotransmission mediated by GABA. Propofol
is fast acting anesthetic with rapid recovery. Its main side effects include hypotension and apnea.
Chapter II: Literature Review

Introduction

Propofol is currently the most popular intravenous anesthetic agent in the United States. Propofol is fast acting, and can be cleared from the body very fast after the completion of infusion, making it ideal for total intravenous anesthesia (TIVA), managed anesthesia care (MAC), and sedation for medical procedures. However, propofol can cause significant hemodynamic disturbance including hypotension and respiratory depression. These side effects could be fatal, if the person administrating it is incapable or could not maintain sufficient level of vigilance, such as in the death of Michael Jackson in 2009. They also put certain patient population under particularly high risk, such as the elderly patients. The elderly patients usually have compromised organ functions and would easily be decompensated after dramatic change in physiological function, such as during anesthesia. Realizing the potential risk of propofol in anesthesia care, the American Society of Anesthesiologist (ASA) issued a statement emphasizing that for the safety of the patients, propofol should only be administrated by skilled anesthesia providers (American Society of Anesthesiologists, 2004). While anesthesia professionals are looking for approaches to improve the safety of propofol administration, there are also ongoing searches for safe alternatives. The purpose of this project is to evaluate the effectiveness of dexmedetomidine, an central-acting $\alpha_2$-adrenoreceptor agonist, in balanced anesthesia care for elderly patients with obstructive sleep apnea (OSA).

Previous Studies

The $\alpha_2$-adrenoreceptor agonists have been in clinical use for decades as anti-hypotensive medicine. These drugs lower arterial blood pressure by inhibiting sympathetic tone to peripheral blood vessels via central neural mechanisms. The $\alpha_2$-adrenoreceptor is a G protein-coupled receptor (GPCR) associated with the $G_i$ protein. Its inhibitory effect is mediated by inhibiting the
activity of adenylate cyclase. The activation of neuronal α₂-adrenoreceptor inhibits pre-synaptic neurotransmitter release and post-synaptic neuronal excitation (Morgan et al, 2006). With the popularity of β-blockers and angiotensin-converting enzyme inhibitors and their confirmed long-term benefits for hypertension patients, these drugs are not normally considered anymore. However, in recent years, clinical studies have found that some of the α₂-adrenoreceptor agonists have both sedation and analgesia effect with mild hemodynamic effect, suggesting potential anesthesia application. Currently dexmedetomidine is the only drug in this class approved for anesthetic use. Available data suggests that dexmedetomidine can be a valuable replacement of propofol in certain clinical settings.

Dexmedetomidine can produce sedation and analgesia. In addition, when used in combination, it potentiates opioid-induced analgesia, benzodiazepine-induced hypnosis, and has potent minimal alveolar concentration (MAC)-sparing effects when administrated with non-volatile anesthetic gases. Dexmedetomidine does not depress respiration. Most inhaled or intravenous anesthetics inhibit breathing activity, including respiratory responses to hypoxia or hypercapnia. This character of dexmedetomidine is particularly valuable for patients under intensive care, as these patients usually have impaired respiratory function, or the elderly patients commonly suffering from chronic cardiovascular and/or pulmonary diseases. Currently, dexmedetomidine is only approved to use as continuous intravenous sedation of initially intubated and mechanically ventilated patients in the intensive care unit. After a decade of clinical application in this setting, dexmedetomidine has proved itself to be a safe anesthetic agent with excellent track record in the adult, pediatric and geriatric populations (Carollo et al. 2008; Chrysostomou & Schmitt, 2008; Coursin et al. 2001). Dexmedetomidine provided
sufficient level of sedation and analgesia for those patients with mild and manageable side effects, including hypotension and occasionally bradycardia.

Clinical application has proved that dexmedetomidine can replace propofol as an anesthetic agent in certain clinical settings including the intensive care unit (Carollo et al. 2008; Chrysostomou & Schmitt, 2008; Coursin et al. 2001). One study compared the opioid requirement and time to extubation in patients undergoing coronary artery bypass graft surgery anesthetized with either dexmedetomidine or propofol. The results show there is no significant difference regarding those two parameters, supporting that dexmedetomidine is as safe and effective as propofol (Reichert et al. 2011). In a randomized, prospective clinical trial with patients for cardiac surgeries, dexmedetomidine is proved to be more effective than morphine, but with less side effects including delirium (Shehabi et al. 2009). Taken together, these studies confirmed the versatility and safety of dexmedetomidine in anesthesia application.

New trials have been focusing on drug combination and sedation for procedures. One study investigated the effectiveness of the combination of ketamine and dexmedetomidine in pediatric patients undergoing cardiac catheterization. The combination provided satisfactory and safe sedation for the patients. Few side effects were noticed, except for mild bradycardia. No incident of hypotension or respiratory depression was reported. The results strongly support the combination of ketamine and dexmedetomidine to be an effective and safe sedative medicine for cardiac catheterization in pediatric patients (Mester et al. 2008). A critical finding of this study is that the combination of ketamine and dexmedetomidine provides more balanced anesthesia with fewer side effects than single drug recipe. It has also been reported that intramuscular dexmedetomidine can provide great sedation in preparing pediatric patients for MRI and CT exams. Only mild hypotension was noticed in a small portion of patients and all only needed
observation without any incidents. This study supports the new indication for dexmedetomidine in preparing pediatric patients for imaging exams or other short-duration procedures (Mason et al. 2011). In conclusion, current clinical data support the notion to use dexmedetomidine as an important adjunct to general anesthesia and as a component of procedural sedation techniques.

Major side effects of dexmedetomidine are hypotension and bradycardia, reflecting its effect on central sympathetic system. But its cardiovascular effect is well tolerated in patients under anesthesia. Actually, because of these side effects are anti-sympathoexcitation, low-dose intravenous dexmedetomidine has been used in those clinical scenarios where sympathoexcitation needs to be blocked, such as in cardiac surgery (Kabukçu et al. 2011) or during endotracheal tube intubation (Menda et al. 2010).

Although minimal respiratory depression effect of dexmedetomidine has well been utilized in regular anesthesia care, there are very few studies to evaluate its effectiveness in patients with chronic pulmonary diseases. Chawla et al. (2010) evaluated the use of dexmedetomidine in anesthesia care for adult patients with (OSA). In this randomized prospective study regarding anesthesia care for airway reconstruction surgeries. The authors found that, compared to control group, dexmedetomidine group reached similar hemodynamic stability regarding the incidence of hypotension. Furthermore, dexmedetomidine significantly reduced the perioperative use of vasodilators nitroglycerin and hydralazine. In addition, dexmedetomidine group received more procedures than control group, although there was no difference in the usage of opioids, which was closely associated with the number of surgical procedures. This is the only study available to investigate the impact of dexmedetomidine on OSA patients. Even so, this study still did not differentiate the role of the age.
In recent years, there are significant progresses in understanding the anesthesia effect of dexmedetomidine. The $\alpha_2$-adrenoreceptor consists of three receptor subtypes, $\alpha_{2A}$-, $\alpha_{2B}$-, and $\alpha_{2C}$-adrenoreceptors. Studies have shown that the sedative effect is mediated by acting on $\alpha_2$-adrenoreceptors located in central sleep pathways. By measuring the expression of c-Fos protein, a neuronal marker of activation, scientists found that dexmedetomidine elicits a pattern of neuronal activation in the locus ceruleus, the tuberomammillary nucleus and the ventrolateral preoptic nucleus, all components of sleep-promoting pathways (Nelson, et al. 2003). In addition, this activation pattern was lost in $\alpha_2$-adrenoreceptor knock-out animals, so did the sedation effect, further confirming the role of $\alpha_2$-adrenoreceptors. The value of this study is that it not just identified the central acting sites of dexmedetomidine, but also revealed potential targets for new drug development.

The cellular/molecular mechanisms underlying the analgesia and sedation effects are much more complicated. Studies show that sedation and analgesia are both mediated by $\alpha_{2A}$-adrenoreceptor subtype in the central nervous system. But the analgesia effect can be independent of either $\alpha_{2A}$- or $\alpha_{2B}$-adrenoreceptor subtype (Stone et al. 2007). These pharmacological characteristics are of clinical relevance since in certain clinical settings only analgesia is needed while sedation is unwanted. Opioids are potent respiratory depressant while dexmedetomidine has minimal depressing effect. Thus dexmedetomidine may be of clinical value in pain management in patients with impaired pulmonary function. At the same time, these data also suggest that it is possible to develop highly selective $\alpha_2$-adrenoreceptor agonist to activate only certain receptor subtypes to avoid unwanted effect. Additional data indicates that the sedation effect of dexmedetomidine may be $\alpha_{2A}$-adrenoreceptor-independent and mediated by li-imidazoline receptor (Dahmani et al. 2008). Nevertheless, it is a long way to go before we
fully understand how α₂-adrenoreceptor agonists work as anesthetics. Until then, we may find more use for this class of drugs.

Currently, dexmedetomidine is the only approved α₂-adrenoreceptor agonist for continuous intravenous sedation in the intensive care setting for up to 24 hours. The benefits of its long-term use still wait to be evaluated thoroughly. In the near future, the focus is on expanding the application of dexmedetomidine in those short procedures (Lehtimäki et al. 2008; Nelson et al. 2003; Stone et al. 2007). Drug combination seems to be beneficial as it will further reduce already mild hemodynamic disturbance and the dosage of other anesthetic agents. Along with the progress in the investigation of the pharmacological mechanisms of α₂-adrenoreceptor agonists, it would be expected that there will soon be new drugs in this class (Stone et al. 2007).

Summary

There are large amount of data indicating that dexmedetomidine can be safely used in anesthesia care. In addition, data shows that dexmedetomidine can reduce the dose of propofol or opioids used in anesthesia care. However, it is also obvious that these studies largely ignored the elderly patients. These patients may benefit greatly from the use of dexmedetomidine due to its mild and manageable side effects. It is projected that in the United States, there will be approximately 71.5 million elderly by 2030, and representing about 20% of the population. OSA is common in the elderly (Russel & Duntley, 2011). Study specifically designed to develop safe anesthesia in this population is of clinical significance. Sadly, no study has been published on this subject. Only one related study was found. Chawla et al. (2010) evaluated the use of dexmedetomidine in anesthesia care for adult patients with (OSA). As discussed above, the results from this study clearly demonstrated that dexmedetomidine can be safely used in adult OSA patients and its application has significant clinical benefits. Thus, there is no doubt that we
should specifically study dexmedetomidine in the elderly OSA patients. The proposed project will serve this purpose. This is a whole new research field that has not received sufficient attention yet. The results from this project will have great clinical impact in guiding our clinical practice. Previous studies have provided sound foundation to support our hypothesis. However, none of them touched this specific population. It is anticipated that dexmedetomidine will be demonstrated to play a greater role in anesthesia care for the elderly patients.
Chapter III: Methodology

Introduction

American is steadily becoming a so-called ‘silver society’ with increasingly large portion of the elderly. This trend brings health care provider a challenge to provide better care to these patients, as most of these people suffering from one or more chronic diseases and the anesthesia risks in these patients are inherently high. On the other hand, it is estimated that by 2040, health care for the elderly will constitute about half of health care in financial cost in this country, which is also a great opportunity for health care industry. For better service to elderly patients, it is necessary to specifically study health care to this population.

Statistically, the elderly will have at least one surgery before the end of their lives. Thus, it is necessary to have sufficient clinical research in order to provide safe anesthesia care to the elderly patients. In this proposed study, we will focus on elderly OSA patients. This patient population is at particular risk to anesthesia due to the fact that all common anesthetics significant depress cardiovascular and respiratory function, which is particularly compromised in this patient group. We will test whether a new anesthetic drug dexmedetomidine will help to provide safer and better anesthesia care to elderly OSA patients.

Research Participants

The purpose of this study is to evaluate the efficiency of dexmedetomidine in safe anesthesia care for elderly patients with OSA. It will be performed in 6 NSU AA program-affiliated major hospitals in Fort Lauderdale area. We will only include people 65 years or older in our project, both male and female. We will only include those patients without known significant cardiovascular, respiratory, and neurological diseases except OSA. Thus the baseline condition of these patients will not have direct effect on cardiovascular and respiratory function.
As a result, specific population for our project will be those who receive anesthesia for reasons other than cardiovascular, respiratory and neurological causes, including both surgeries and medical procedures.

**Research Design**

This study has a case-control prospective experimental design. As defined by this design, each OSA patient will be matched by a non-OSA patient regardless of the type of or surgery. The patient will be randomly assigned to receive dexmedetomidine or not. This type of design is not as powerful as the randomized prospective design but is more cost- and time-efficient. For the target patient population in our study, this design will be able to provide valid results in a relatively short period of time with a less number of participants.

**Instruments**

No additional specific medical equipment will be required for this study. All cardiovascular and respiratory parameters during anesthesia will be collected from the anesthesia station as these data are stored electronically. Pre- and post-operative parameters will be collected from monitoring equipment and patient charts. All are standard practices in each participating hospital. At each participating hospital, assigned staff will be provided a laptop specifically for data collection. At the end of each month, all available data will be processed and logged in an Excel sheet and sent to Principle Investigator (PI). PI will be assigned a laptop to run Microsoft Office software and SPSS statistic software. Data will be combined from all participating hospitals and made available for statistic software.

**Proposed Process/Procedures**

At each participating hospital, there will be a designated anesthesia staff to review the patient data and decide the eligibility of each patient. This designated staff will follow the
random number to group each eligible patient. All eligible elderly patients will be divided into
two groups, those with or without OSA (OSA and non-OSA groups). In each group, patients will
be randomly assigned to receive dexmedetomidine in addition to standard anesthesia plan
including both propofol and opioids or standard anesthesia plan only (Dex and Stand subgroups).
Thus, there will be totally four subgroups in this study: OSA/Dex, OSA/Stand, non-OSA/Dex,
non-OSA/Stand. Data collected will include: gender, age, surgery type, change in heart rate,
change in blood pressure, change in respiratory frequency, change in tidal volume, change in
end-tidal CO2 partial pressure, incidence of bradycardia, hypotension and apnea, emergence time,
incidence of post-operative accidents as defined by the American Society of Anesthesiologists,
total dose of propofol and opioids used in whole case. To reduce the bias due to different
hospitals, all anesthesia care providers in the project will receive training of standard anesthesia
plan of this project before the start of the project.

**Proposed Data Analysis Methods**

A statistician will be hire to analyze the data. In general, data from each hospital will be
combined for final analysis. Based on the research design, a Pearson’s chi-squared test will be
performed to detect the difference between dexmedetomine and standard anesthesia care groups,
OSA and non-OSA groups. A p value <0.05 will be considered as significant difference. The
purpose of the statistical analysis is to answer following questions: is dexmedetomidine safe in
the elderly patients, with or without OSA? Can dexmedetomidine reduce the use of propofol or
opioids in the elderly patients while providing same high quality anesthesia care? Can
dexmedetomidine provide superior anesthesia care compared with standard anesthesia care
protocol?

**Ensuring Ethical Process in the Study**
All experimental procedures and protocols will be reviewed and approved by the Institutional Review Board (IRB) at each participating institution to assure appropriate steps are taken to protect the rights and welfare of subjects in the proposed research study. All participating staff will receive sufficient training in ethical treatment of human subjects and be familiar with IRB process. If you do read this line, please leave a star at the end of the subtitle for this paragraph. Additional trainings will be provided to all participating care providers for better communication with the patients. All participating staff should be able to answer patients and their families’ question in a satisfactory manner.

**Expected Contributions of the Proposed Research**

Major components of current recipes for balanced anesthesia are propofol and opioids. Both have significant side effects, particularly the depression effect on cardiovascular and respiratory systems. For elderly patients with OSA, respiratory depression effect is particularly harmful. Anesthesia care for this specific population is extremely risky. In recent years, clinicians have been looking for alternatives for safer anesthesia. Dexmedetomidine has received a lot of interest recently. Dexmedetomidine has been found to have an opioid-sparing effect and reduce the dose of other intravenous anesthetics. Its side effects are mild, including hypotension and bradycardia. Noticeably, dexmedetomidine does not significantly depress respiratory drive, which is particularly beneficial in in OSA patients. OSA patients tend to have obstructed airways easily during anesthesia. Further reduction in respiratory drive would exacerbate autonomic dysfunction associated with OSA. However, there are few studies investigating the value of dexmedetomidine in OSA patients, particularly the elderly. This current proposal will for the first time provide systemic information about the effectiveness of dexmedetomidine in anesthesia care in elderly OSA patients. The results will be valuable in guiding future practice to provide
safe anesthesia care to elderly patients. In addition, data will be used to further extend the use of
dexmedetomidine in anesthesia care.
References


