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Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: H-45486
Status: Closed
Initial Submit Date: 4/2/2019

Section Aa: Title & PI

A1. Main Title

EFFECT OF OPIOIDS ON VENTILATION IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA

A2. Principal Investigator

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Section Ab: General Information

A4. Co-Investigators

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A5. Funding Source:

Baylor College of Medicine (Internal Funding Only)

A6a. Institution(s) where work will be performed:

TCH: Texas Children's Hospital

A6b. Research conducted outside of the United States:

Country:
Facility/Institution:
Contact/Investigator:
Phone Number:

If documentation of assurances has not been sent to the Office of Research, please explain:

A7. Research Category:

A8. Therapeutic Intent

Does this trial have therapeutic intent?
Not set yet

A9. ClinicalTrials.gov Registration

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

Ventilatory suppression in children following opioid administration is of obvious concern, especially following routine surgical procedures (i.e. adenotonsillectomy). It is thought that patients with obstructive sleep apnea (OSA) have increased sensitivity to opioids, and especially in opioid naïve patients. Recent evidence in adults suggests that patients with moderate to severe OSA may not predispose patients to increased opioid sensitivity in the form of respiratory depression when compared with patients that do not have OSA. It is well known that OSA in children is significantly different from OSA in adults (e.g. gender predilection, central vs. peripheral causation). The manifestation and etiologies are very different in pediatric OSA making it a vastly different disease process. The aim of this study is to identify if children with known OSA experience opioid induced respiratory depression with greater incidence then in children without OSA.

Section D: Purpose and Objectives

The sole objective in this study is to evaluate if routine amounts of opioids given for tonsillectomy in children have greater amounts of respiratory depression in children with documented obstructive sleep apnea when compared with patients that do not have obstructive sleep apnea

Section E: Protocol Risks/Subjects

E1. Risk Category

Category 3: Research involving greater than minimal risk and no prospect of direct benefit to the individual subject, but likely to yield generalizable knowledge about the subject's disorder or condition.

E2. Subjects

Gender:
Both

Age:
Child (3-12 yrs), Infant/Toddler (0-36 mos)

Ethnicity:
All Ethnicities

Primary Language:
English, Spanish

Groups to be recruited will include:
Asymptomatic patients with chronic conditions, healthy; Patients

Which if any of the following vulnerable populations will be recruited as subjects?
Children

Vulnerable populations require special protections. How will you obtain informed consent, protect subject confidentiality, and prevent undue coercion?
Parents will be approached as ask to participate in the study. They will be informed that this is completely voluntary and that they can choose to avoid participation and or revoke their participation at any point. Their participation or lack there of will not change or alter the care their child will receive. The risks include loss to confidentiality and we will reduce this risk by only having the PI and co-investigators collect data which will be stored only on the BCM firewall. Additionally, there is a risk of apnea with all opioids however this risk is routinely managed by pediatric anesthesiologists and encountered in nearly all anesthetics.

E3. Pregnant woman/fetus

Will pregnant women and/or fetuses (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E4. Neonates

Will neonates of uncertain viability or nonviable neonates (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E5. Children

Will children be enrolled in the research?
Yes

Section F: Design/Procedure

F1. Design

Select one category that most adequately describes your research:
c) Pilot

Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.
The Principal and/or co-investigators will identify children meeting enrollment criteria from the daily operative list at Texas Children's Hospital main campus. Those meeting enrollment criteria will be approached by the PI and or co-investigators.

The study is a prospective randomized trial to identify the effect of opioids on children with obstructive sleep apnea

Inclusion Criteria:
-Patients undergoing tonsillectomy or adenotonsillectomy at Texas Childrens Hospital main campus. -Ages 2 to 8 years - Polysomnography with AHI >6 (study group) -Polysomnography with AHI =0 or negative OSA 15 questionnaire (control group)

Exclusion Criteria:
Ages >8 years Patients requiring pre-medication Parental refusal Opioid allergy/intolerance Patients requiring propofol for intubation Patients with known or suspected difficult airway Obesity ¿ body mass index exceeding 30- (control group only) Known cardiovascular disorders Known pulmonary disorders aside from asthma Patients with chronic oxygen requirement History of Prematurity <35 weeks of gestation Personal of family history of malignant hyperthermia Recent Illness

F2. Procedure

Patient Identification The Principal and/or co-investigators will identify children meeting enrollment criteria from the daily operative list at Texas Childrens Hospital main campus. Those meeting enrollment criteria will be approached by the PI and or co-investigators.

Control Group: -Patients requiring tonsillectomy/adenotonsillectomy without suspected OSA Children presenting for tonsillectomy/adenotonsillectomy for recurrent infection. Children with negative sleep studies will be included. Those without formal sleep studies will be screened using the OSA 18 questionnaire, a validated clinical assessment score for pediatric sleep-disordered breathing. Those with negative questionnaire scores will be included.

Study Group: -Patients with Moderate to Severe OSA as documented by formal polysomnography For the study group, patients will be included if they have undergone formal sleep study evaluations. Stratification will be based on the polysomnography testing using the apnea hypopnea index (AHI) and or the number desaturation events according to the McGill Scoring system for pediatric OSA. Patients with AHI greater than 6 will be considered to have moderate to severe OSA and thus eligible for inclusion

All patients will undergo general anesthesia per the usual practice at Texas Childrens Hospital according to the preferences of the anesthesiology attending physician. Induction will be with sevoflurane+/-nitrous oxide followed by intravenous access securement. Endotracheal intubation using a RAE endotracheal tube will be performed with the size selected using the formula: Predicted Size Cuffed Tube = (Age / 4) + 3. Following endotracheal intubation, spontaneous ventilation will be maintained without the use of continuous positive pressure. Sevoflurane will be reduced to maintain between 0.5-0.7 MAC according to the Drager Apollo anesthesia machine. The patient will be allowed to establish their respiratory equilibrium for 3 minutes following intubation on 0.21% oxygen. Baseline tidal volume (TV), respiratory rate (RR) and end-tidal carbon dioxide (ETCO2) will be recorded. fentanyl 1mcg/kg will be administrated as a bolus (usual clinical practice). The TV, RR, ETCO2 will be recorded, at 5 and 10 minutes following opioid administration. Apnea or desaturation <92%) will be treated by assisting ventilation as required (standard practice). After 10 minutes,(to study a repeated dose effect) a second dose of 1/mcg/kg will be administered with the same TV, RR, ETCO2 recorded for 5 minutes.

Surgery will commence as usual with additional medication to be administered at the discretion of the anesthesiology providers. No change to standard practice will occur the research portion will be prospectively recording the TV, RR, ETCO2 following opioid administration to calculate change from baseline (pre-opioid). routine fentanyl administration for these procedures is 2 mcg/kg

Section G: Sample Size/Data Analysis

G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?
Local: 50 Worldwide: 50

Please indicate why you chose the sample size proposed:
Our sample size is based on a recent 2019 landmark paper investigating a similar question in adults with obstructive sleep apnea we propose to enroll 20 control patients and 30 patients with documented obstructive sleep apnea

G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?
The primary outcome will be measurement of continuous variables of tidal volume, respiratory rate and end tidal CO2. these will be reported as means with SD. regression analysis will be performed for patients falling into the moderate and severe categories of obstructive sleep apnea by sleep study.

Section H: Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:
The risks include loss to confidentiality and we will reduce this risk by only having the PI and co-investigators collect data which will be stored only on the BCM firewall. Additionally, there is a risk of apnea with all opioids however this risk is routinely managed by pediatric anesthesiologists and encountered in nearly all anesthetics.

There is no long term follow up or patient related efforts required to participate.

Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.
There is no planned benefit for the patient enrolled

Describe potential benefit(s) to society of the planned work.
the societal benefit is understanding the impact of opioids based on obstructive sleep apnea. The risk of opioid induced respiratory depression can be significant and even lethal as it has been demonstrated repeatedly over recent years

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.
This study is a risk category 3, moderate risk which in this case is apnea. The risks to the patient is apnea which occurs in nearly all anesthetics and routinely managed by pediatric anesthesiologists. There is also the risk of loss of confidentiality which will be minimized by limiting data access to those on the protocol only

Section J: Consent Procedures

J1. Waiver of Consent

Will any portion of this research require a waiver of consent and authorization?
NA

J1a. Waiver of requirement for written documentation of Consent

Will this research require a waiver of the requirement for written documentation of informed consent?
NA

J2. Consent Procedures

Who will recruit subjects for this study?
PI
PI's staff

Describe how research population will be identified, recruitment procedures, any waiting period between informing the prospective participant and obtaining consent, steps taken to minimize the possibility of coercion or undue influence and consent procedures in detail.
The PI and Co-investigator will identify patients prior to the day of surgery that meet inclusion/exclusion criteria. Participants/parents will be approached in the preoperative area for potential enrollment. The study will be explained to the participants parent/guardian and we will explain that all care will be standard regardless of their participation. They will be informed that their participation is optional, and can be revoked at any time without penalty. They will also be informed that no cost is associated with participation.

Are foreign language consent forms required for this protocol?
Yes

Which of the following ways will you document informed consent in languages other than English?
Short-Form consent documents

J3. Privacy and Intrusiveness

Will the research involve observation or intrusion in situations where the subjects would normally have an expectation of privacy?
No

J4. Children

Will children be enrolled in the research?
Yes

J5. Neonates

Will non-viable neonates or neonates of uncertain viability be involved in research?
No

J6. Consent Capacity - Adults who lack capacity

Will Adult subjects who lack the capacity to give informed consent be enrolled in the research?
No

J7. Prisoners

Will Prisoners be enrolled in the research?
No

Section K: Research Related Health Information and Confidentiality

Will research data include identifiable subject information?
NA

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
NA

Specific information concerning alcohol abuse:
NA

Specific information concerning drug abuse:
NA

Specific information concerning sickle cell anemia:
NA

Specific information concerning HIV:
NA

Specific information concerning psychiatry notes:
NA

Demographic information (name, D.O.B., age, gender, race, etc.):
NA

Full Social Security #:
NA

Partial Social Security # (Last four digits):
NA

Billing or financial records:
NA

Photographs, videotapes, and/or audiotapes of you:
NA

Identifiable biospecimens
NA

Other:
NA

At what institution will the physical research data be kept?
NA

How will such physical research data be secured?
NA

At what institution will the electronic research data be kept?
NA

Such electronic research data will be secured via BCM IT Services- provided secured network storage of electronic research data (Non-Portable devices only):
NA

Such electronic research data will be secured via Other:
NA

Will there be anyone besides the PI, the study staff, the IRB and the sponsor, who will have access to identifiable research data?
NA

Please describe the methods of transmission of any research data (including PHI, sensitive, and non-sensitive data) to sponsors and/or collaborators.
NA

Will you obtain a Certificate of Confidentiality for this study?
No

Please further discuss any potential confidentiality issues related to this study.
the only risk to this study is potential loss of confidentiality which will be minimized by only using BCM/TCH behind the BCM firewall using BCM Box and keeping all information with the PI and Con-investigator

Section L: Cost/Payment

Delineate clinical procedures from research procedures. Will subject's insurance (or subject) be responsible for research related costs? If so state for which items subject's insurance (or subject) will be responsible (surgery, device, drugs, etc). If appropriate, discuss the availability of financial counseling.
none

If subjects will be paid (money, gift certificates, coupons, etc.) to participate in this research project, please note the total dollar amount (or dollar value amount) and distribution plan (one payment, pro-rated payment, paid upon completion, etc) of the payment.

Dollar Amount:
0

Distribution Plan:

Section M: Genetics

How would you classify your genetic study?

Discuss the potential for psychological, social, and/or physical harm subsequent to participation in this research. Please discuss, considering the following areas: risks to privacy, confidentiality, insurability, employability, immigration status, paternity status, educational opportunities, or social stigma.

Will subjects be offered any type of genetic education or counseling, and if so, who will provide the education or counseling and under what conditions will it be provided? If there is the possibility that a family's pedigree will be presented or published, please describe how you will protect family member's confidentiality?

Section N: Sample Collection

None

Section O: Drug Studies

Does the research involve the use of ANY drug* or biologic? (*A drug is defined as any substance that is used to elicit a pharmacologic or physiologic response whether it is for treatment or diagnostic purposes)
No

Does the research involve the use of ANY gene transfer agent for human gene transfer research?
No

O1. Current Drugs

Is this study placebo-controlled?
No

Will the research involve a radioactive drug?
No

Section P: Device Studies

Does this study need an IDE?
No

Regarding your device study, could potential harm to subjects be life-threatening?
No

Regarding your device study, could potential harm to subjects result in permanent impairment of a body function?
No

Regarding your device study, could potential harm to subjects result in permanent damage to a body structure?
No

Section Q. Consent Form(s)

Research Study on Narcotics and sleep apnea

Section R: Advertisements

None