Adam C. Adler, MS, MD, FAAP, FASE
Assistant Professor of Pediatric Anesthesiology
Department of Anesthesiology, Perioperative and Pain Medicine
Baylor College of Medicine
Texas Children's Hospital
6621 Fannin, Suite (A3300)/(W17417)
Houston, TX 77030
Phone: (832) 824-5800
Email: axadler@texaschildrens.org

April 13, 2021

Protocol for NCT #NCT03285243
Title: Effect of Monochromatic Light on Incidence of Emergence Delirium in Children

Sincerely,

Adam C. Adler, MS, MD, FAAP, FASE
Department of Anesthesiology, Perioperative and Pain Medicine
Texas Children's Hospital

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: H-39878
Status: Admin Mods Required
Initial Submit Date: 8/15/2017

Section Aa: Title & PI

A1. Main Title

EFFECT OF MONOCHROMATIC LIGHT ON INCIDENCE OF EMERGENCE DELIRIUM IN CHILDREN; A SINGLE BLINDED RANDOMIZED CONTROLLED TRIAL

A2. Principal Investigator

Name:	ADAM ADLER	Phone:	832-824-5800
Id:	195273	Fax:	

Department: TCH ANESTHESIOLOGY
Center:

Email: axadler@texaschildrens.org
Mail Stn: BCM320

A3. Administrative Contact

Name: KIMBERLY DIANE MITCHELL
Id: 043942

Phone: 832-824-5800
Fax:
Email: katkins@bcm.tmc.edu
Mail Stn: BCM320

A3a. Financial Conflict of Interest

Does any member of study personnel (Investigator (including investigator's spouse and/or dependent children)) that are involved in the design, conduct, or reporting of the research have a Significant Financial Interest (SFI) that would reasonably appear to be affected by the research for which funding is sought and/or associated with an entity/business that would reasonably appear to be affected by the research?

No

Section Ab: General Information

A4. Co-Investigators

Name: DEAN ANDROPOULOS
Id: 041898
Department: TCH ANESTHESIOLOGY
Center:

Phone: 832-826-5822
Fax: 832-825-1903
Email: dra@bcm.tmc.edu
Mail Stn: BCM320

Name: CHARLES MINARD
Id: 174095
Department: OFFICE OF RESEARCH: BIOINFORMATICS RES CTR
Center:

Phone: 713-798-2353
Fax:
Email: minard@bcm.tmc.edu
Mail Stn: BCM451

Name: DEEPAK MEHTA
Id: 190754
Department: TCH BASED SURGICAL/HOSP/OTHER
Center:

Phone: 832-822-3267
Fax:
Email: dkmehta@bcm.tmc.edu
Mail Stn: NA102

Name: ARVIND CHANDRAKANTAN
Id: 195204
Department: TCH ANESTHESIOLOGY
Center:

Phone: 832-824-5800
Fax:
Email: chandrak@bcm.tmc.edu
Mail Stn: BCM320

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?

No

A9. ClinicalTrails.gov Registration

Does this protocol/trial require registration on ClinicalTrials.gov due to it: meeting the definition of an Applicable Clinical Trial, being required under the terms and conditions of an award, or being proposed to be published in ICMJE journals?

No, this clinical is not a clinical trial, or does not meet the definition of an Applicable Clinical Trial, or does not need to be registered under the terms and conditions of an award, or is not a clinical trial with results intended to be reported in an journal belonging to the ICMJE. Registration is not required.

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

Emergence delirium/emergence agitation (ED/EA) is a behavioral phenomenon of unclear etiology consisting of short lived behavioral changes that can be both traumatic to families and pose a safety risk to patients and staff. ED is characterized by a variety of presentations, including crying, excitation and agitation, that occur during the early stage of recovery from general anesthesia, generally in the first 30 minutes. Involuntary activity in the bed and even thrashing about during an episode of ED can lead to dislodgement of IV cannulas, surgical dressings and or surgically placed items such as drains and catheters. Emergence delirium occurs in children of all ages following an anesthetic with halogenated agents (e.g. sevoflurane/isoflurane) with or without having undergone a surgical procedure (e.g. MRI patients). Electroencephalograms (EEG) in patients experiencing emergence delirium show diffuse background slowing. Presently, the treatment for ED is to revert the patient back to a hypnotic state mainly with sedatives so that they may ¿reset¿ themselves postulating that by re-inducing a hypnotic state, the brain has time to resolve this issue. The hypothesis of this study is that during ED, there is failure of organized EEG activity, especially alpha wave activity and that by enhancing alpha activity, the incidence of ED may be reduced without the need for additional pharmaceuticals which may be costly, delay recovery and are not without adverse effects specifically cardiopulmonary depression.

Monochromatic light (ML) has been used in a variety of clinical and non-clinical applications to affect a variety of changes. Exposure to light of short wavelength within the visible spectrum (450-470nm) has been associated with effects on circadian rhythm, neuroendocrine and neurobehavioral changes and enhanced cognitive performance. Blue ML has been studied safely to enhance work-place alertness and productivity. Clinically, blue ML has been used safely for decades in the neonatal intensive care unit to treat jaundice.

Blue ML, has been known to suppress melatonin secretion and enhance alertness and workplace performance. The effect occurs within the retinal photoreceptive ganglion cells which mediate the observed responses. The effect is even present in visually blind persons lacking outer retinal function. Short exposure to bursts of blue

light has revealed enhanced neural activity on functional MRI. Use of blue ML has been shown to enhance EEG activity in the alpha range (awake range) compared with light of greater wavelengths. Using blue ML in the operating room may enhance alpha EEG activity, (a circadian marker for alertness) it may be possible to reduce the incidence of emergence delirium in the post-operative period and therefore the amount of (non-pain) sedative medication needed in recovery.

Section D: Purpose and Objectives

Emergence delirium is associated with a safety risk to patients and staff members in the fact that these children are uncontrollable and often thrashing which may result in self-inflicted injury (falls and collision with bedframe) or perturbation of intravenous or surgically placed devices. At present, the treatment involves re-sedating these patients (e.g. propofol or dexmedetomidine). These medications are certainly not without risk. If intravenous access has been lost, intra-nasal or intra-muscular administration of medications can be dangerous or impractical to administer at times of delirium.

The primary aim of this study is to ascertain if perioperative exposure to non-invasive monochromatic blue light can reduce the incidence of emergence delirium.

The secondary aim involves assessing the need for rescue interventions (e.g. hypnotic agents ¿ propofol or dexmedetomidine).

Section E: Protocol Risks/Subjects

E1. Risk Category

Category 1: Research not involving greater than minimum risk.

E2. Subjects

Gender:
Both

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

Ethnicity:

Primary Language:
Arabic, English, Spanish

Groups to be recruited will include:
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?

All patients will undergo standard anesthetics in accordance with local practice at Texas Children's Hospital. To avoid undue coercion, during the consent process, it will be stressed to parents that study participation is completely voluntary and will not alter the care provided. The family will be notified that they may opt out at any time and that standard of care will be provided throughout. Confidentiality will be maintained using study specific numbers and a random number generator to avoid collecting any identifying patient information.

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.

This is a double blinded randomized control trial. The placebo arm will serve as the control group. After enrollment and consent, each patient will be randomized to either placebo or intervention group. 110 sealed envelopes randomizing patients to the exposure group A (monochromatic light) or bulb B (placebo) white light bulb with blue outer coating.

Inclusion Criteria:

Healthy patients ages 2-6 years undergoing routine tonsillectomy and adenoidectomy requiring general anesthesia would be identified for inclusion

Exclusion Criteria:

Exclusion criteria would include: American Society of Anesthesiology classification other than 1,2; history of migraine headaches, ocular disorders, seizure history, psychiatric conditions, parental refusal, developmental delay and those patients on medication for attention deficit disorders or caffeine stimulants. Patients with contraindications to receiving inhalation agents, use of premedication with midazolam or dexmedetomidine would also be excluded.

F2. Procedure

Intra-operative Care (Standard Care) A standard and routine anesthetic will ensue for these patients in line with routine operative practices at Texas Children¿s Hospital, including an inhalational induction (mask) using sevoflurane 8%v/v with oxygen/nitrous oxide 3/7 L/min respectively, followed by intravenous cannula placement. Propofol will be administered if needed to facilitate oral endotracheal intubation at the discretion of the anesthesia attending. Dexamethasone (0.5mg/kg), ondansetron (0.1mg/kg) and morphine (0.1-0.2mg/kg) will be administered for anti-inflammatory, antiemetic and analgesic effects respectively. Intravenous fluid (lactated ringer solution) will be continuously infused with the appropriate volume to be determined by the anesthesia provider. Maintenance of anesthesia will be with sevoflurane with the concertation titrated to maintain an appropriate level of hypnosis as determined by the anesthesia provider. At the conclusion of the surgery, the patient will undergo routine deep extubation according to the routine practice of the anesthesia providers of record.

Postoperative evaluation for emergence delirium (Study Portion) On arrival to the PACU, the Drager

phototherapy lamp will be illuminated over the patients head and neck. Randomization will determine if the patient will be exposed to ML blue light or the placebo bulb (white bulb with blue over coating). The PACU staff and the anesthesiologist will be blinded to study arm. The placebo bulb will provide blue light of all wavelengths as to not compromise blinding. The light will remain active and over the patient until the patient has been in the post anesthesia recovery unit (PACU) for 30 minutes. Two PACU nurses blinded to the patient group will be asked to complete the PAED scoring scale for evaluation of emergence delirium. They will be asked to complete the scoring evaluation upon arrival to the PACU and at 10 minutes, 20 minutes and 30 minutes following arrival. Two nursing evaluations will be used to reduce inter-observer bias.

(Standard Care) A patient experiencing emergence delirium will receive standard pharmacologic treatment as determined by the anesthesiology provider irrespective of study participation. Blinding of the nurse and anesthesia team will help to ensure that the nursing staff will call the anesthesia providers with any and all usual questions and the anesthesia provider to react and treat potential ED as per usual practice without being biased by the study. The study will end at this point without the need for additional follow-up or patient contact related to the study.

Section G: Sample Size/Data Analysis

G1. Sample Size

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

Local: 110 Worldwide: 110

Please indicate why you chose the sample size proposed:

The PAED behavioral scale will be used to assess the incidence of emergence delirium. The PAED scale is a reliable tool to measure ED and involves five items: eye contact, purposeful actions, awareness of the surroundings, restlessness, and inconsolability. While other scales exist, the PAED scale is the standard for assessment of ED and is the only validated scale. A PAED score of >12 will be used to define ED.

A sample size of 110 subjects (55 per group) would be required to detect a significant difference between treatment arms with 80% power if the proportion of patients with PAED>12 is 0.25 in the controls (Proportion1) and 0.05 in the active treatment arm (Proportion2) assuming alpha=0.05. For the primary outcome, the proportion of patients with PAED >12, the Fisher¿s exact test will be used to compare proportions.

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?

A sample size of 110 subjects (55 per group) would be required to detect a significant difference between treatment arms with 80% power if the proportion of patients with PAED>12 is 0.25 in the controls (Proportion1) and 0.05 in the active treatment arm (Proportion2) assuming alpha=0.05. For the primary outcome, the proportion of patients with PAED >12, the Fisher¿s exact test will be used to compare proportions.

Section H: Potential Risks/Discomforts

H1. 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 study procedure poses no additional risk to patients. The major risk is loss of confidentiality. Use of monochromatic light has been safely tested in numerous human studies and used routinely in the NICU without identified patient risk using the same Drager machines at TCH. The moment the patient is awake and making purposeful eye contact with the PACU RN, the lights will be terminated. The risk of phototherapy is well known

from nearly 40 years of clinical use in neonates. The risk of phototherapy is predominantly in neonates, especially preterm infants with jaundice, all requiring prolonged and continuous exposure to high intensity light for many days. This study will not include any neonates (with immature retina) or long term exposure of >30 min. The study will be terminated the moment the patient is awake and making purposeful eye contact with the PACU RN to avoid unnecessary discomfort.

H2. Data and safety monitoring plan

Do the study activities impart greater than minimal risk to subjects?

No

H3. Coordination of information among sites for multi-site research

Is the BCM Principal Investigator acting as the SPONSOR-INVESTIGATOR for this multi-site research?

No or Not Applicable

Is BCM the COORDINATING CENTER for this multi-site research?

No or Not Applicable

Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.

The study may potenitally reduced the incidence of emergence delirium and the use of pharmacologic agents required by the study patient group.

Describe potential benefit(s) to society of the planned work.

The study benefits include improved understanding of emergence delirium and potential for both reduction in the incidence of emergence delirium and the use of pharmacologic agents.

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.

The risk to the patient is minimal as this is a widely accepted therapy and adjunct both medically and commercially. The benefit would be a potential to reduced the exposure to medications that may result in cardiopulmonary depression.

Section J: Consent Procedures

J1. Waiver of Consent

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

No

J1a. Waiver of requirement for written documentation of Consent

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

No

J2. Consent Procedures

Who will recruit subjects for this study?

PI
PI's staff
Third Party: research associates from the Dept of Anesthesiolog

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.

All patients undergoing Adenotonsillectomy meeting inclusion criteria will be identified. Personnel other than the anesthesia and nursing providers will obtain consent from the parents/legal guardian on the day of surgery. Consent forms will be signed on the day of surgery by the parent/legal guardian. The consenting party will be informed that the study will not change care of the patient or influence the anesthetic care. They will be informed that there is no obligation to participate and that failure to participate will not result in any change in care provided to their child. They will be informed that consent may be withdrawn at any time.

Participants speaking Spanish or arabic as their primary language will be approached (as these are the most common, non-english languages encountered at TCH) using hospital approved interpreters and the IRB approved translated consent forms.

Procedure- After consent, participants will be randomly assigned to a group, One group will be exposed to special blue light and one group to a white light blue that has been colored blue. Your child will undergo routine anesthesia as described by and according to their anesthesia provider. After the surgery, your child will be taken into the recovery room to wake up. Depending on their randomly selected group, they will be exposed to one of the two blue lights as described above for the first thirty minutes in the recovery area or until your child wakes up, whichever is first. Nursing staff will evaluate your child as usual and will call the anesthesia provider if there are any signs of emergence delirium. The experimental portion of this is specifically the blue light which is not a form of therapy for emergence delirium. Should your child experience emergence delirium, their anesthesiology provider will be notified and they will determine what standard therapy will be used. Standard therapies include administration of dexmedetomidine, propofol or opioids. The experimental blue light will be terminated at this time.

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?

Yes

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

No

Specific information concerning alcohol abuse:

No

Specific information concerning drug abuse:

No

Specific information concerning sickle cell anemia:

No

Specific information concerning HIV:

No

Specific information concerning psychiatry notes:

No

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

Yes

Full Social Security #:

No

Partial Social Security # (Last four digits):

No

Billing or financial records:

No

Photographs, videotapes, and/or audiotapes of you:

No

Identifiable biospecimens

NA

Other:

No

At what institution will the physical research data be kept?

All physical data will be kept in secured cabinets, locked and in areas with badge access in the offices of the Dept of Anesthesiology, preoperative and pain medicine at Texas Children's Hospital.

How will such physical research data be secured?

All physical data will be kept in secured cabinets, locked and in areas with badge access in the offices of the Dept of Anesthesiology, preoperative and pain medicine at Texas Children's Hospital.

At what institution will the electronic research data be kept?

All data will be stored at TCH on TCH encrypted servers

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

Yes

Such electronic research data will be secured via Other:

No

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

No

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

Transmission of data will be only via secured encrypted email on BCM or TCH servers.

Will you obtain a Certificate of Confidentiality for this study?

No

Please further discuss any potential confidentiality issues related to this study.

N/A

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.

Not applicable

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:

Not applicable

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 research study involve the use of ANY device?

Yes

Device 1: Drager phototherapy 4000

Section Q: Consent Form(s)

Participation in Post op delirium by blue light therapy

Section R: Advertisements

None