

Summer Student Research Program
Project Description

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PROJECT TITLE (200 Characters max):

Comparison of Dexmedetomidine vs. Propofol in Vitreoretinal Surgery Under Sub-Tenons' Block

HYPOTHESIS:

Dexmedetomidine alone, and in a reduced dose during sedation, can prevent or decrease the incidence of adverse effect such as hypertension, hypotension, bradycardia, hemodynamic instability and provide adequate sedation for patient and surgeon satisfaction during vitreoretinal surgery, under Sub-tenons' block. This will be compared to propofol sedation.

PROJECT DESCRIPTION (Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)

This is a double blind randomized study for both the patient and the operating surgeon. A total of 200 patients will be enrolled.

Study Population: All patients undergoing elective vitreoretinal surgery under sub-Tenon block, male and female 18 to 65 yrs old, ASA 1-3 with good liver and renal function. Excluded in the study will be those patients with:

- renal and hepatic insufficiency (any patient history of renal and /or liver problems will be eliminated from the study),
- uncontrolled diabetes (any patient on hypoglycemic agents with a fasting blood sugar greater than 150)
- uncontrolled hypertension, (any patient on anti-hypertensive drugs with a systolic blood pressure greater than 160 or diastolic 100)
- severe cardiac disease Class III or Class IV (as defined by the New York Heart Association [NYHA]) –Class III- patients with marked limitation of activity who are comfortable only at rest or mild exertion, Class IV patients confined to bed or chair, any physical activity brings on symptoms or discomfort
- heart blocks (not Paced) ,
- chronic use of sedatives, narcotics alcohol or illicit drugs,
- allergy to any of the study drugs,
- pregnancy and inability to tolerate the sedative technique of the study drugs.

Method: This is a double-masked, prospective, randomized study for both patient and operating surgeon. A total of 200 patients will be enrolled after an approval from Institutional Review Board and informed consent has been obtained from the patient. Subjects will be randomized into two study groups of 100 in each group. Group D (Dexmedetomidine) will received a bolus of 0.5 ug/kg intravenously of dexmedetomidine administered over a period of 10-15 minutes . This will be followed by an infusion of 0.2 – 0.7 ug/kg/min of drug. Group P (Propofol) a bolus dose of 1 mg/kg

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of propofol will be administered intravenously and then followed by infusion of 25-100 ug/kg/min. The criteria for infusion dose will be as follows: the anesthesia investigators will start with the lowest dose in the dose range mentioned and titrate to effect. The effect will be a Bispectral Index Scale (BIS) range of 70-80 and a University of Michigan Sedation Score (UMSS) of 2. There will be no other supplemental sedative drugs administered to both study groups. Baseline blood pressure, heart rate, EKG, respiration, pulse oximetry, level of consciousness will be recorded prior to the administration of the bolus loading doses of the study drugs. During the administration of the bolus loading dose, the subject will be observed for changes in blood pressure, heart rate, cardiac rhythm, pulse oximetry and respiration. Occurrence of hypotension (blood pressure 20% below the baseline) and bradycardia (heart rate below 50) will be managed with phenylephrine 100 ug or ephedrine 5 mg and atropine 0.4 mg in incremental doses until baseline value has been achieved. The subject will receive 3 liters of oxygen via nasal cannula during the course of the procedure. Topical tetracaine 0.5% ophthalmic solution and 2% lidocaine gel will be placed in the operative eye by the surgeon and the site will be prepped and draped in the usual sterile fashion. The surgeon will perform a sub-Tenon block with a mixture of equal volume of 3-6ml 0.50% marcaine and 2% lidocaine local anesthetics on the operative eye. Level of sedation will be measured by BIS monitor and University of Michigan Sedation Scale (UMSS) intraoperatively. BIS value will be assessed and recorded every 5 minutes. UMSS score will be assessed every 15 minutes by the surgeon. Any patient in the study groups who does not tolerate sedation technique of the study drug, USMM score of 0 or a BIS value greater than 85 will receive 1-2mg of midazolam and/or 50-100 ug fentanyl as a rescue drug and this patient will be excluded from the study. Should the BIS value be less than 80 and/or UMSS value exceed 3, the infusion will be decreased to titrate to a level of moderate sedation. Chin lift and/or insertion of a oral airway will be used to support the airway until moderate sedation is achieved. A BIS value of less than 60 will be considered over-sedation and appropriate actions will be taken to reduce drug dosage and maintain airway patency. Intraoperative hemodynamic stability will be defined as blood pressure between within $\pm 20\%$ of the baseline and a heart rate no lower than 50. Infusions of the study drug will be discontinued within 5 minutes before the end of the surgical procedure. In the PACU, both study groups will be observed for two hours and the following will be assessed: blood pressure, heart rate, O₂ saturation, pain score, post-op pain medication requirement and nausea/vomiting. Postoperative pain of 4 or 5 on VAS Pain scale will be treated with Tylenol 650mg orally. If the subject is not relieved in 30 minutes he/she will be provided Percocet 325mg. If the subject's pain score is 6 or greater than Percocet 325mg will be administered initially. If the subject is experiencing nausea or vomiting and is unable to take oral medication for the pain, he/she will be administered Morphine 2mg intravenously. Should the subject be experiencing nausea or vomiting they will be administered Zofran 4mg IV and if not relieved Compazine 5-10 mg IV will be administered. During recovery period, the patient (when fully recovered), and the surgeon will be asked as to the degree of their satisfaction with the used study drug.

Statistical Analysis:

Data analysis will be performed using the anonymous information compiled by the study team and transferred into a confidential study database.

A Sample size of 200 patients was calculated based on 20% difference on the incident rate of hemodynamic unstable events between groups, with a two sided α of 0.05 and a power of 80%. The primary outcomes, such as hemodynamic and BIS reading, will be analyzed using repeated measures analysis of variance (ANOVA). Satisfaction scores, Pain score, UMSS will be compared using Mann-Whitney tests. Categorical data will be analyzed using Chi-Square test for larger contingency tables and Fisher exact test for 2x2 contingency tables with

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unpaired data. Data will be expressed as means \pm SD, number (%), or median (minimum-maximum). All statistical analysis will be performed using SPSS software (version 16.0, SPSS Inc., Chicago, IL) A p-value < 0.05 will be considered statistically significant.

IS THIS PROJECT SUPPORTED BY EXTRAMURAL FUNDS?

Yes or No

(IF YES, PLEASE SUPPLY THE GRANTING AGENCY'S NAME)

Hospira, Inc is providing the drug dexmedetomidine as well as a small amount of funding.

THIS PROJECT IS: Clinical Laboratory Behavioral Other

THIS PROJECT IS CANCER-RELATED N/A

Please explain Cancer relevance

THIS PROJECT IS HEART, LUNG & BLOOD- RELATED N/A

Please explain Heart, Lung, Blood relevance

THIS PROJECT EMPLOYS RADIOISOTOPES N/A

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS

PENDING

APPROVED

IRB PROTOCOL # M0120090202

THIS PROJECT IS SUITABLE FOR:

UNDERGRADUATE STUDENTS ENTERING FRESHMAN
SOPHOMORES ALL STUDENTS

THIS PROJECT IS WORK-STUDY: Yes or No

THIS PROJECT WILL BE POSTED DURING ACADEMIC YEAR

FOR INTERESTED VOLUNTEERS?: Yes or No

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?

The student will benefit from their participation in a structured research study. They will be exposed to Good Clinical Practice (GCP) which ensures the rights and safety of clinical trial subjects and the integrity of clinical data obtained during the conduct of a

clinical trial. The student will have the opportunity to have a comprehensive review of the protocol, participate in subject-investigator interactions, ongoing and risk appropriate safety monitoring throughout the conduct of the study and assist in data collection, analysis and reporting. They will be exposed to regulatory study documents and if the situation arises assist in the maintenance of same.

Additionally student will benefit from the experience of interviewing the subject's and reviewing the medical history to assess the individual eligibility for inclusion into the study. They will benefit from the experience of spending time in the Operating Room.