Comparative Study of Superficial Cervical Plexus Block and Nerve of Arnold Block with Intravenous antiemetic drugs Dexamethasone and Ondansetron and Incidence of Post-operative Nausea Vomiting for Inner Ear Surgery

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1.0 Background

Patients that undergo inner ear surgery often complain of postoperative nausea and vomiting (PONV) despite prophylactic antiemetic regiments with 5HT3 antagonists, steroids and vigorous hydration. Patients still experience this unpleasant feeling that may prolong hospital stay and can lead to nutritional issues such as dehydration and huge patient and family dissatisfaction. We would like to explore the use of regional anesthesia and potential antiemetic proprieties and compare it's efficacy to the existing therapy.

PONV is an unpleasant complication following anesthesia, it is well known that patients undergoing certain surgical procedures such as those involving the inner ear, the tympanomastoid cells, and the cochlear organ may be more prone to PONV. This complication can be anticipated in those instances and prophylactically treated with antiemetics, Vigorous hydration and cautious selection of anesthetic technique and avoidance of drugs known to promote nausea[1, 2, 3]. Despite all the measures described above, vomiting still occurs often, leaving patients and their families wondering if more can be done[4, 5].

Regional anesthesia has a therapeutic and preventive role in the incidence of PONV by reducing post-operative pain and opioids consumption.

2.0 Rationale and Specific Aim

We would like to compare the therapeutic and cost effectiveness of established therapies for postoperative nausea and vomiting to regional nerve blocks of the head and neck area an intervention known for analgesia but for which the antiemetic effects hasn't been entirely explored.

Our rational is based on the knowledge of the anatomical innervation of the inner ear and the role of the parasympathetic nervous system in the emetic act[1]. A lot of focus has been given on its counterpart the sympathetic nervous system and its role in painful conditions. We believe that the nerve blockade of the parasympathetic innervation can have some beneficial effect in the post-surgical patient.

The role of the vagal nerve response in the act of vomiting has been extensively studied. Observation that the Vagus nerves are predominantly sensory nerves has been shown through direct electrophysiological recordings of this afferent traffic from the vagal distribution in the GI tract to the brain stem. Vagal afferent terminals stained with horseradish peroxidase (HRP) appear to project to the dorsal motor vagal nucleus (DMVN) and to the area postrema. This latter projection may provide a visceral input for vomiting[1, 2, 3]. In fact electrical stimulation of vagal afferent fibers readily evokes vomiting in experimental animals. Furthermore, stimulation of the concha of the ear which is innervated by the (sensory) auricular branch of the Vagus nerve produced activation of the solitary nucleus and its following projections: parabrachial nucleus, thalamus, amygdala, paracentral lobule, and insula shown during fMRI[1, 2, 3]

This latter distribution is of interest to our study since it involves the area of surgery where the auricular branch of the vagus nerve should easily accessible for anesthetic blockade.

There shouldn't be a surprise that most of the anti-emetics in use today have a mechanism of action that involves the modulation of the vagal effect during the emetic act[1, 2, 3].

We hypothesize another potential antiemetic mechanism by the blockade of the auricular branch of the Vagus nerve at the ear canal (commonly described as nerve of Arnold) in conjunction with a block of the greater auricular nerve and lesser occipital nerve at the superficial cervical plexus level[8, 9, 10]. The block would cover both the sensory innervation and of the ear canal and the inner ear. A regional anesthetic block prior to the surgical intervention on the inner ear at the superficial cervical plexus block is performed. This latter is a branch of the vagus nerve at the superficial cervical plexus (erb's point). The block would inhibit the vagal afferent to area postrema through inhibition of afferent vagal input to the medullary center.

The emetic act (vomiting) is a highly integrated physiologic reflex involving both the somatic and autonomic nervous system. We do not know how much of a relation there is between the vagal nerve branches involvement and incidence of nausea and vomiting effects are from the inner ear injury and or the inflammatory response type of response triggering the area postrema. The usual prophylactic treatment of PONV has been limited to anti-emetics such 5-HT3 and dexamethasone[6, 7], along with aggressive fluid therapy and adequate analgesia.

We are proposing to conduct a comparative study of the therapeutic and cost effectiveness of regional anesthesia and antiemetic therapy in the prevention and treatment of PONV in children undergoing inner ear surgical procedures.

3.0 Inclusion/Exclusion

Inclusion Criteria
Patient Age 1-18 yo
Scheduled to have cochlear implantation, tympanomastoidectomy, inner ear surgery
Past history of PONV susceptibility

Exclusion Criteria
Patient/ Parents refusal
Infection at the site of local anesthetic injection
Known coagulopathy
Existing VP shunt
Severe mental disability
Any known allergic to dexamethasone (Decadron) and/or ondansetron (Zofran)

4.0 Enrollment/Randomization

Subject will be approached by Dr. Yates, the surgeon at his office the day of the preoperative office visit appointment or by any member of the study team the day of the surgery in the preoperative area.

After appropriate assent and consent is obtained subject will be given an identifier and will undergo randomization using a computer program.

Subject will be assigned to either one of the three groups.

Study will involve pediatric patients Age 1-18 years old who are scheduled to undergo inner ear surgery. Subjects will be randomization into three different groups. Each group will consist of 20 patients; we intend to enroll 60 participants total.

Group A Nerve of Arnold block with superficial cervical plexus block (SCPB)
Group B IV dexamethasone (Decadron) + ondansetron (Zofran)
Group C Block + IV dexamethasone (Decadron + ondansetron (Zofran)

5.0 Study Procedures

After proper informed consent and/or assent have been obtained, all patients will receive a general anesthesia using standard of care. For all patients randomized to receive regional nerve block (Group A & C) a time out before regional anesthesia will be performed stating patient identification and proposed surgical procedure with location of the block to be performed and the medications to be injected.

Patients randomized to receive regional anesthesia will be prepared following standard universal precautions with application of sterile cleaning solution of chlorhexidine (Chloraprep) or alcohol prior to injections.

The site of local anesthetic injection will be identified according to the landmarks defined by their respective anatomical descriptions. The nerve of Arnold block is located at junction of the ear tragus and external 1/3 of ear canal which will be injected using a 30 G needle with 0.5 ml of Bupivacaine 0.25%. na

The Superficial Cervical Plexus located at Erb's Point, posterior border of the sternocleidomastoid muscle and a bisecting horizontal line drawn from the cricoid cartilage at the level of the sixth vertebrae, which is slightly posterior to the external jugular vein, this site will be injected with 3-5ml of bupivacaine 0.25% with 1:200000 of epinephrine. Surgical procedures lasting longer than 4hrs will require a repeat injection with 2.5-3 ml of bupivacaine 0.25% with1:200000 epinephrine at this latter location after completion of the surgical procedure prior emergence from anesthesia.

Group A: to receive a homolateral (same side) to surgical site or bilateral if surgery involves both ears regional block at the Erb's point and Nerve of Arnold.

The block will be performed prior to surgical incision and may be repeated at Erb's point only with half the initial volume of local anesthetic (1.5 ml -2.5ml) at completion of surgery prior emergence from anesthesia, if the procedure lasted more than 4 hours after the initial block.

Group B: will receive an anti-emetic drug regiment comprising of dexamethasone 150mcg/kg IV (max dose of 10 mg) and ondansetron 150mc/kg IV (max single dose of 4 mg) at any time after induction of anesthesia and as soon as an intravenous line is available. If, at the anesthesiologist's discretion, ondansetron is re-dose at the end of procedure, a max total dose of 8 mg may be given.

Group C: Will receive both a homolateral or bilateral if surgery involves both ears, a regional block at Erb's point (superficial cervical plexus block) and will receive an anti-emetic drug regiment comprising of dexamethasone 150mcg/kg IV (max dose of 10 mg) and ondansetron 150mc/kg IV (max single dose of 4 mg) at any time after induction of anesthesia and as soon as an intravenous line is available. If, at the anesthesiologist's discretion, ondansetron is re-dose at the end of procedure, a max total dose of 8 mg may be given.

All three groups will receive a standardized general anesthetic regiment, prior to induction the patient *might* require an oral dose of versed 0.5mg/kg as premedication for separation anxiety. Patients will also receive induction of anesthesia either inhalational oxygen in sevoflurane or intravenous induction if subject patient has an IV access, muscle relaxants will be avoided to preserve facial nerve monitoring as required by the surgical approach. Anesthesia will be maintained with oxygen in sevoflurane or desflurane. Prior to emergence of anesthesia and at any point during the procedure, patients may receive IV analgesics (acetaminophen, morphine, fentanyl, ketamine) for postoperative analgesia according to the standard recommended pediatric dosing regiments commonly used at Riley Hospital.

All three groups will receive the standard PACU protocol for pain management and anti-nausea and vomiting intervention. Following patient's recovery starting upon emergence (t_0), all symptoms indicating nausea and/or vomiting and pain will be recorded and every 15min (t_{15}) thereafter in PACU than every 4-6 hrs. while on the inpatient unit for 24 hrs and will be treated as deemed necessary. For pain assessment a FLACC scale and Visual Analogue Scale (VAS) will be used. Complaints of, or signs or symptoms of, nausea, retching and/or vomiting will be documented in the PACU or floor for 24 hours post-operatively. For patients discharged to home prior to the 24 hours, follow up will be done by phone call using the Rhodes INRV to report post-operative nausea and vomiting.
We will also review patients chart for requests or demands for any pain medications and anti-emetics, documentation of their usage as well as times of discharge from the recovery room to the floor and their discharge from the hospital. For cost comparison and analysis we will look at itemized billing for medical services related to anesthesia, pharmacy use and IV fluid use, antiemetic interventions, medication for pain throughout hospital stay from recovery room to time of discharge from the hospital. For patients that are discharged the same day of their surgery they will be given The Rhodes INRV survey to fill out at home and will be called by phone the following day to collect that information.

A cost analysis between the three study groups taking into account all the items above will be done to compare overall cost of care between the three study groups.

6.0 Reporting of Adverse Events or Unanticipated Problems Involving Risk to Participants or Others

Risk related to the Blocks
Bleeding
Infection at the site
Intravascular local anesthetic injection
Anaphylactic/allergic reaction
Rare spread of local to deeper structures, inadvertent Phrenic nerve blockade (the injection are superficial, subcutaneous with specific landmarks)
Failure of the block to produce pain relief or to prevent nausea and vomiting
Complications related to the surgical procedure including but not limited to:
Facial nerve blockade

Risk of General Anesthesia

All precautions will be taken care of to avoid the above complications by adhering to standard of practice with strict adherence to standard ASA monitoring will be used at all time, observance of the time out procedure and surgical site marking, using universal precautions for sterility and observance of safe injection technique for the regional blocks with intermittent aspiration and injection to avoid intravascular injection and use of live imaging with ultrasound guidance if necessary.

7.0 Study Withdrawal/Discontinuation

Subject patient can withdraw from study at their own will and they can do so by letting know the principal investigator or members of the study team. Failure to comply with study protocol may result in withdrawal of patient subject from the study. Should any unanticipated adverse events known to have a direct relation to the procedure occur, the study will be discontinued and IRB will be notified.

8.0 Statistical Considerations

A sample size of 20 subjects per group was selected to provide 80% power for finding a difference between all three groups with nausea/vomiting of 90% vs. 50%, assuming two-sided chi-square tests conducted at a 5% significance level. At completion of study we will submit our data to statistical analysis.

9.0 Privacy/Confidentiality Issues

Adequate provisions to protect the privacy interests of research subjects and the confidentiality of research data will be taken in accordance of IUSM research policy. All patient information

will be kept confidential and all data will be carefully processed and stored in accord with federal and institutional regulatory policies. Paper collected study information will be stored in the locked anesthesia offices. Data may also be entered and stored into a secure electronic database (example REDCap).

The principal investigators and all research study team members are properly trained and will ensure these provisions exist and are followed.

Pediatric patients will be approached in the presence of their parents for enrollment either in the privacy of ENT office or their private cubicle in the day surgery area at Riley Hospital. A proper consent and assent for children of age 7 or older will be obtained by members of the research team this will be done by either principal investigators Dr. Nouri and Dr. Yates or anesthesia nurse research coordinator.

10.0 Follow-up and Record Retention

Records will be retained for 7 years after the study is completed in order to properly analyze the results. All paperwork, data collection sheets will be physically shredded after being scanned and stored electronically in a password protected database for an indefinite duration.

11.0 Analysis of Results

At completion of study we will submit our data for expert statistical analysis.

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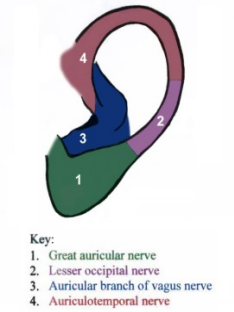
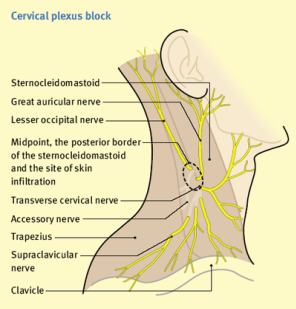
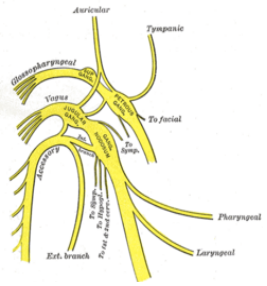
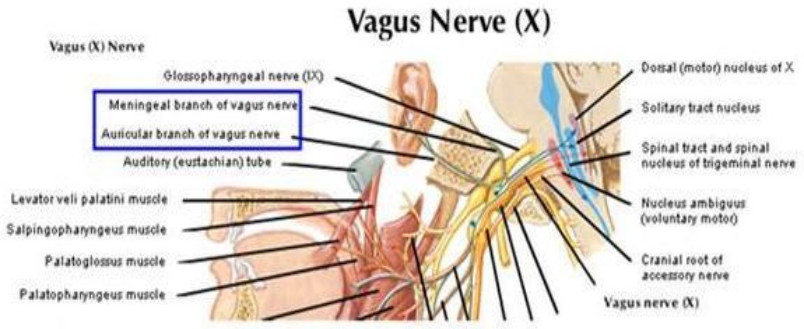


Ear Innervation



Superficial Cervical Plexus Anatomical Relations and Injection Site





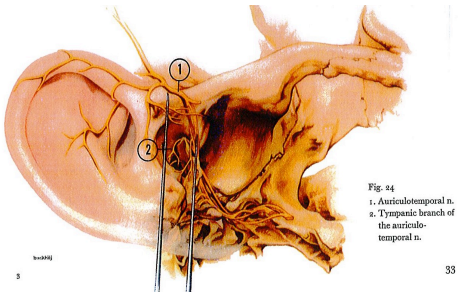
RHODES INDEX OF NAUSEA, VOMITING AND RETCHING

Patient initials _____
Date _____
Day of week _____
Time of day _____

Directions: Please mark the box in each row that most clearly corresponds to your experience. Please make **one** mark on **each line**.

1. In the last 12 hours, I threw up ____ times.	7 or more	5-6	3-4	1-2	I did not throw up
2. In the last 12 hours, from retching and dry heaves, I have felt ____ distress.	no	mild	moderate	great	severe
3. In the last 12 hours, from vomiting or throwing up, I have felt ____ distress.	severe	great	moderate	mild	no
4. In the last 12 hours, I have felt nauseated or sick to my stomach.	not at all	1 hour or less	2-3 hours	4-6 hours	more than 6 hours
5. In the last 12 hours, from nausea/sickness to my stomach, I have felt ____ distress.	no	mild	moderate	great	severe
6. In the last 12 hours, each time I threw up, I produced a ____ amount.	very large (3 cups or more)	large (2-3 cups)	moderate (1/2-2 cups)	small (up to 1/2 cup)	I did not throw up
7. In the last 12 hours, I have felt nauseated or sick to my stomach ____ times.	7 or more	5-6	3-4	1-2	no
8. In the last 12 hours, I have had periods of retching or dry heaves without bringing anything up ____ times.	no	1-2	3-4	5-6	7 or more

Superficial cervical Plexus infiltration



Nerve of Arnold Injection