Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) for the Prevention of Emergence Agitation and Delirium After Adenotonsillectomy in Children: A Randomized, Double-Blind, Interventional Study

Informed Consent Form · Participant Information Sheet

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Dear Parents/Guardians,

We invite your child to participate in a research study titled "Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) for the Prevention of Emergence Agitation and Delirium After Adenotonsillectomy in Children: A Randomized, Double-Blind, Interventional Study."

This study aims to explore whether taVNS can help prevent or alleviate postoperative agitation and emergence delirium (ED) in children after adenotonsillectomy.

This consent form provides you with essential information to help you decide whether to allow your child to take part in this clinical study. Participation in this research is entirely voluntary, and your decision will not affect your child's routine medical care or treatment in this hospital.

If you agree to participate, our research team will make every effort to ensure your child's safety and protect his or her rights throughout the study.

Please read this document carefully. If you have any questions, do not hesitate to contact the responsible investigators.

Study Introduction

1. Background and Study Objectives

1.1 Study Background and Significance

Postoperative agitation and emergence delirium (ED) refer to a series of negative behavioral symptoms that occur during the early recovery period from general anesthesia in children, such as crying, struggling, and disorientation. The incidence ranges from 25% to 80%.

The occurrence of ED not only delays recovery, increases postoperative complications and medical costs, but also reduces parental satisfaction with anesthesia — making it a pressing issue in pediatric anesthesia management.

At present, the exact etiology of ED remains unclear, though it is closely related to exposure to general anesthetics. Multiple studies have shown that inhalational agents such as isoflurane, halothane, sevoflurane, and desflurane are associated with the development of ED, with sevoflurane being particularly significant in increasing the risk of pediatric anesthesia emergence delirium (PAED).In addition to anesthetic drugs, the type of surgery also plays an important role in the

incidence of ED. Studies indicate that ED occurs less frequently after thyroidectomy or circumcision but more commonly following ophthalmologic or otorhinolaryngologic (ENT) surgeries.Furthermore, preoperative anxiety and postoperative pain are also strongly associated with ED. The higher the preoperative anxiety level, the greater the risk of ED. According to the modified Yale Preoperative Anxiety Scale (mYPAS), every 10-point increase in the score corresponds to approximately a 10% increase in ED risk. Postoperative pain is likewise recognized as an important triggering factor for ED. Therefore, reducing children's preoperative anxiety and appropriately managing postoperative pain may help lower the incidence of ED following sevoflurane anesthesia.

To prevent or treat ED, a variety of pharmacological and non-pharmacological interventions have been attempted; however, their overall efficacy remains uncertain.Drugs such as fentanyl, propofol, and dexmedetomidine can mitigate symptoms but may cause respiratory depression or prolong recovery due to their sedative effects. Midazolam has been reported to effectively reduce the incidence of ED in children. Compared with intranasal or oral administration, intravenous (IV) administration is the most commonly used route for preventing emergence delirium. A single dose of 0.5 mL/kg IV midazolam administered at the start or end of surgery has been shown to reduce the incidence of ED. However, due to its relatively long half-life (0.79–2.83 hours) and the activity of its metabolite 1-hydroxymidazolam, midazolam may delay postoperative recovery.

In terms of non-pharmacological interventions, behavioral strategies such as playing handheld video games or watching videos have been shown to alleviate preoperative anxiety. However, these methods are not applicable to anesthetized or unconscious children. Although parental presence during induction can help reduce anxiety to some extent, this approach is often difficult to implement due to operating room constraints and may interfere with surgical procedures.

In recent years, with deeper understanding of autonomic nervous system (ANS) function, it has been found that vagal nerve activity plays a crucial role in maintaining physiological stability, reducing postoperative complications, and promoting recovery. Enhancing vagal tone has been shown to reduce postoperative pain scores, alleviate depression and anxiety, and improve sleep quality. These effects are primarily attributed to cholinergic anti-inflammatory, anxiolytic, antidepressant, and analgesic mechanisms.However, systemic inflammation, regional anesthesia, and general anesthesia may impair autonomic regulation during the perioperative period, leading to decreased vagal tone and enhanced sympathetic activity.Transcutaneous auricular vagus nerve stimulation (taVNS), a safe and non-invasive neuromodulatory technique, uses an external device attached to the auricular concha to stimulate the auricular branch of the vagus nerve. This stimulation activates vagal pathways, exerting cholinergic anti-inflammatory and analgesic effects, and mitigates the body's stress response.Therefore, taVNS holds great promise as a novel strategy

for improving perioperative outcomes.

Based on this background, we plan to conduct a randomized, double-blind, controlled trial to systematically evaluate the efficacy of taVNS in preventing postoperative ED in children undergoing adenotonsillectomy. This study may provide a safe, non-invasive strategy for managing pediatric postoperative ED and offer new theoretical and clinical evidence supporting the role of autonomic neuromodulation in perioperative care.

1.2 Study Objective

To investigate the effects of taVNS intervention on postoperative emergence delirium (ED) in children undergoing adenotonsillectomy.

2. Who Should Not Participate in the Study

Children will be excluded from participation if they meet any of the following criteria:

1) ASA classification 3–4, or presence of hepatic or renal dysfunction, cardiovascular disease, or endocrine disorders.
2) Presence of neuromuscular diseases or dermatitis of the left auricle.
3) Recent respiratory tract infection, developmental delay, or autism spectrum disorder.
4) Children currently receiving specialized care or living in social welfare institutions, or any other factors that may interfere with participation.
5) Children currently participating in other clinical trials.

3. What Participation Involves

This study is a randomized, double-blind, interventional trial, and we aim to enroll 120 participants. If you agree to allow your child to participate, you will be asked to sign this informed consent form.

Next, your child will be assessed for inclusion and exclusion criteria. If your child meets all inclusion criteria and none of the exclusion criteria, he or she will be enrolled in the study. Each child will then have a 50% chance of being assigned to the intervention group (active stimulation) or the control group (sham stimulation). Group assignment will be determined by computer-generated randomization, and neither you nor your child's doctor will have the ability to influence this process.

This is a blinded study, meaning that both the assessing physician and you will not know your child's group assignment until the study is completed, unless there is an emergency that requires unblinding. If you do not wish to participate in this intervention, you may decline or withdraw at any time and discuss alternative treatment options with your doctor.

Intervention Procedures

Active Stimulation Group:

Children assigned to the active stimulation group will receive electrical stimulation of the left auricular concha with the following parameters:

Frequency: 25 Hz

Pulse width: 300 μs

Stimulation pattern: 30 seconds on / 30 seconds off

Duration: consecutive 3 days

The first stimulation begins after your child arrives in the preoperative preparation area, assisted by you to wear the device.

Stimulation continues postoperatively in the PACU until your child leaves the PACU, at which point the device will be removed.

Intensity: starting at level 1, increased stepwise by 1 level (approximately 0.4 V per step) until your child reports a mild tingling sensation, then adjusted to the highest tolerable intensity without pain.

On postoperative days 1 and 2, stimulation will be applied for 0.5 hours in the morning and 0.5 hours in the afternoon.

A trained operator will be present throughout the stimulation sessions.

Sham Stimulation Group:

Children assigned to the sham stimulation group will undergo the same procedure and duration, but the device will be turned off after intensity adjustment.

Note: Children in either group may or may not feel any sensation from the stimulation.

Clinical Data Collection

The following clinical data, collected through routine assessments, will be recorded:

A. Primary Outcome

Incidence of ED

1) ED is diagnosed when PAED ≥ 10 and FLACC < 4.
2) If PAED ≥ 10 and FLACC ≥ 4, the child will first receive analgesic treatment: Fentanyl 0.5 μg/kg IV if FLACC ≥ 4.After 5 minutes, PAED will be reassessed. If PAED ≥ 10 persists, ED is confirmed regardless of FLACC score.

B. Secondary Outcomes

1)Postoperative Pain Incidence

Defined as FLACC ≥ 4. FLACC will be assessed at 0, 5, 10, 20, and 30

minutes after emergence from anesthesia.

2)Pediatric Quality of Recovery (PedSQoR)

1) Evaluated on postoperative days 1 and 2.
2) PedSQoR consists of 20 items, reflecting physical, emotional, and psychological recovery.
3) Proxy Report: for children 2–7 years, completed by parents/guardians.
4) Self-Report: for children 8–17 years, completed by the child.
5) Total score ranges from 20 to 100, with higher scores indicating better recovery quality.

3）Recovery Time

Time from cessation of sevoflurane until your child is awake and able to respond to verbal name calling, including delays due to ED.

4）Postoperative Analgesic Consumption and Pain Scores

Record the number of oral ibuprofen doses and total dose at 4, 6, 12, 24, and 48 hours postoperatively, along with VAS pain scores (both at rest and during deep breathing).

5）Adverse Events

Record all other adverse events during hospitalization, including nausea, vomiting, pneumonia, and taVNS-related complications.

4. Potential Benefits of Participation

If the results of this study show that taVNS has a beneficial effect on postoperative emergence delirium (ED) in children undergoing adenotonsillectomy, and your child happens to be assigned to the intervention group, your child may benefit from this treatment. However, your child may not receive any direct benefit from participation.

Regardless of direct benefit, the data provided by your child will contribute valuable information to research on this condition, helping researchers better understand its pathophysiology and explore potential treatment strategies. Ultimately, this could benefit your child's future care and other children with the same condition.

5. Potential Risks, Discomforts, and Inconveniences

When your child undergoes taVNS, the research team will strictly follow operating procedures. Since this is a non-invasive procedure with low stimulation intensity, the main adverse events may include mild pain, flu-like symptoms, and local skin discomfort. These effects are temporary and resolve once the taVNS treatment is stopped. To date, there have been no reports of serious adverse events in the literature.

If stress or anxiety occurs during the procedure, the operation will be paused or continued based

on the child's willingness.

In the event of any injury or adverse reaction, the research team will provide prompt medical care.

6. Costs

Participation in this study will include 3 days of free taVNS treatment (including sham stimulation) and postoperative ED assessments at no cost. All other clinical assessments are part of routine care, and any associated costs will be the responsibility of the participant's family.

Participation in this study will not increase your child's routine medical costs, and no additional compensation will be provided. If any injury occurs that is deemed related to the study, the study team will provide necessary medical treatment at no cost to you.

7. Confidentiality

If you decide to participate, all information and data collected during the study will be kept strictly confidential. Your child's study data will be identified by a research code number, not by name. Any information that could identify your child will not be shared with anyone outside the research team without your permission.

All research personnel are required to maintain confidentiality regarding your child's identity and data. Your child's records will be stored in locked cabinets and accessed only by authorized researchers. To ensure compliance with regulations, government agencies or ethics committees may review your child's records at the research site as required.

Any publications resulting from this study will not disclose your child's personal information.

8. How to Obtain More Information

You may ask questions about this study at any time. Your child's doctor will provide contact information to address your questions.

If you have complaints about participation in the study, please contact the Hospital Ethics Committee Office.

If important new information arises during the study that may affect your child's participation, your doctor will inform you promptly.

9. Voluntary Participation and Withdrawal

Participation in this study is entirely voluntary. Your child may refuse to participate or withdraw at any time without affecting your relationship with your doctor, your child's medical care, or any other rights or benefits.

For your child's safety and best interest, the doctor or research team may discontinue participation at any time.

If your child withdraws from the study for any reason, you may be asked to provide information on the use of study procedures. If deemed necessary, your child may also undergo laboratory tests or physical examinations, which can help protect your child's health.

10. What Should You Do Now?

Whether to participate is your decision. You may discuss the study with your family or friends before making a decision.

Before deciding, please ask your doctor any questions necessary until you fully understand the study.

Thank you for reading this information.

If you decide to participate, please inform your doctor or research assistant, who will arrange all study-related procedures for your child.

Please keep this document for your records.