Informed Consent

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Title： Effects of Preconditioning by Nasal Splint and Mouth-breathing on Emergence Delirium after Functional Endoscopic Sinus Surgery in Chinese Adults

Institution： Shanghai General Hospital

Co-operative institution： None

We invite you to participate in a study on *Effects of Preconditioning by Nasal Splint and Mouth-breathing on Emergence Delirium after Functional Endoscopic Sinus Surgery in Chinese Adults.* It's a randomized controlled trial. Please read this informed consent carefully before you decide to participate in this study. If you have any questions that you do not understand, you may ask the investigator in charge of the study or members of the study working group to explain any terms or data that you do not understand.

INTRODUCTION

Emergence delirium (ED, or emergence agitation) is a well-known adverse phenomenon in the waking period of general anaesthesia (GA). It is described as a short-term state of confusion that occurs immediately after GA and lasts for 15 to 30 minutes. The sudden occurrence of ED may result in serious outcomes such as; increased pain, bleeding, removal of endotracheal tube, urinarycatheter, drainage tube, etc., sometimes even requiring additional medication and/or binding support. These may in turn increase the post-anaesthesia care unit (PACU) time, and the medical and nursing costs.

Otorhinolaryngology surgery or surgeries involving the ear, nose, and throat (ENT) are considered to be an independent risk factor for postoperative agitation. In 2006, Lepouse et al. showed a 12% incidence of ED after ENT surgery in adults,

while the overall ED incidence was 4.7%. In his study of 2000 cases in 2010, Yu et al. reported an ED incidence of 55.4% after ENT surgery, and a total ED incidence of 21.3% irrespective of the surgery type.

Functional Endoscopic Sinus Surgery (FESS) is one of the most commonly performed nasal surgeries. ED after FESS is not unfamiliar for each clinical anesthesiologist, but how to reduce ED occurrence effectively still remains a challenge.

AIMS

In this study, we adopt to find a non-invasive, non-pharmacological approach to prevent ED FESS in adults.

METHODS AND ANALYSIS

Who can take part in the trial?

1) patients undergoing FESS surgery in Shanghai General Hospital

2) age over 18 years

3) American Society of Anesthesiologists (ASA) Classification[1] class I-II, no serious cardiovascular disease

4) preoperative liver and kidney function within the normal range

5) those who, through publicity and mobilisation, know about the trial and voluntarily participate by signing the informed consent.

Who can't take part in the experiment?

1) ASA grade III-V, severe cardiovascular disease or poor blood pressure control

2) history of mental illness

3) history of sedative or anti-psychoticdrug use (neuroinhibitors, anxiolytics, antidepressants, benzodiazepines) for any reason

[1] **Definition ASA Classification:**
ASA-I: Healthy person.
ASA-II: Mild systemic disease UNDER CONTROL.
ASA-III: Severe systemic disease UNCONTROLLED.
ASA-IV: Severe systemic disease that is a CONSTANT THREAT to life.
ASA-V: A moribund person who is NOT expected to survive without the operation.

4) history of neurological diseases (cerebral infarction, transient ischaemic attack, Parkinson's disease, mental retardation, craniocerebral injury)

5) nasal malformation, history of nasal trauma, implantation of nasal prosthesis

6) surgical complications (socket perforation, massive bleeding requiring blood transfusion or reoperation, cerebrospinal fluid leakage, eyelid emphysema, intraorbital bleeding, meningitis, partial loss of vision, double vision, blindness, death)

Trial design

This study intends to adopt the method of prospective RCT. You will be randomly grouped (see below) in to the control group (C-group) or the pre-treatment group (P-group). The P-group will receive an intervention (see below) before FESS while C-group not. All the participants will experience the same anaesthesia scheme (see below) and the same postoperative pain control scheme (see below). We will observe and evaluate the occurrence of ED (see below) in both groups.

Grouping

The participants will be divided into C-group and P-group in a total ratio of 1:1 by means of simple randomisation. You won't know your grouping information until the morning of surgery day.

Intervention (pretreatment)

The intervention of this study is a kind of breathing method training, which is a non-invasive and non-drug method. However, we are very sorry that the detail of the preconditioning scheme of this study will be kept secret from you for the time being. You can get the information after the study from our researchers.

All participants will be admitted to the pre-anesthesia room 1 hour in advance. Patients in P-group will be received a breathing method training while patients in C-group not. Patients in P-group should not be included in C-group for any reason if he/she refuses the intervention. If you have any concerns, you can propose at any time and decide to withdraw from the study at any point, which will not have any impact on the subsequent operation and anesthesia.

Anaesthesia scheme

The subjects will not receive any preoperative medication. Once the patient

enters the operating room, routine vital signs such as electrocardiogram (ECG), noninvasive blood pressure (NBP), oxygen saturation (SpO_2) and end-tidal carbon dioxide ($EtCO_2$) will be monitored.GA will be induced in all patients with midazolam 0.05mg/kg, propofol 2mg/kg, sufentanil 0.25μg/kg. After the loss of consciousness, the nasal splint will be removed in the P-group, and rocuronium 0.6mg/kg given to both groups.

Endotracheal tube insertion will follow muscle relaxation. Using 60% oxygen (O_2) support, the $EtCO_2$ will be maintained between 35-45 mmHg. Desflurane at 0.8 and 1.0 minimum alveolar concentration (MAC) will be used for maintenance anaesthesia. Sufentanil 5-10 μg will be given before the nasal endoscopic procedures according to the patients' body weight and circulatory state. Due to the short operation time of FESS, no additional intraoperative sufentanil administration is required. When the surgery duration exceeds 1 hour, or in the event of increasing heart rate and blood pressure rise due to light anaesthesia, an additional dose of 5-10 μg sufentanil will be given depending on the body weight and vital signs of the patient. Also, if the surgical wound is larger than normal, an additional 5 μg sufentanil will be given before placing the nasal package. Neostigmine antagonist will be dosed based on the patients' muscle relaxation.

The extubation indicators will be tidal volume (VT) up to 5ml/kg and respiratory rate up to 12/min, with obvious swallowing reflex, and SpO_2 maintained at 95% or above after breathing air for 5 minutes. Due to possible intraoperative procedures such as sympathetic stimulation caused by adrenalin infiltration in the nasal cavity; nimodipine and esmolol will be used to control NBP and heart rate within the normal range.

Pain assessment and control

Postoperative PACU monitoring will include ECG, NBP, $SpO_2$and $EtCO_2$. Pain assessment will be carried out by a trained anaesthesia nurse blinded to grouping information. The numerical rating scale (NRS) will be used for pain assessment every 5 minutes immediately after extubation. The pain scale ranges from 0 to 10 with 0 representing no pain (painless) and 10 representing the most pain. Pain control will be

performed by the anesthesiologist in PACU. For scores of 4 or above, sufentanil 3-5 μg will be administered by intravenous injection and the NRS reassessed 5 minutes later to keep the pain below 4.

Observe and evaluate the occurrence of ED

Observation of ED assessment

Following postoperative extubation to any time within 30 minutes after FESS, the Riker sedation-agitation scale will be used.

Hierarchical evaluation of ED

If the above behaviour occurs in response to powerful stimulation such as suctioning phlegm, but stops with stimulus removal, the assessment is mild. If ED is observed without stimulation and lasts for at least 5 minutes, and does not require medical intervention, it is rated as moderate. It is rated as severe if lasts for at least 5 minutes and must be controlled with medication and/or physical restraint.

We also need your authorization and provide the following information:

The preoperative information collected will include age, gender, ASA classification, disease severity (computed tomography of the paranasal sinuses and nasal endoscopy), nasal congestion history, and smoking. In the pre-anaesthesia room, heart rate, SpO_2, and NBP before and after intervention, and the intervention effect will be recorded. The information collected during the surgery will include: operation time, anaesthesia time, intraoperative medication, changes in vital signs, absorbable foam filling site, presence or absence of indwelling catheter or drainage, etc. Postoperative information collected will include: ED assessment, hierarchical evaluation of ED, postoperative pain assessment, retention of tracheal intubation, PACU duration, and PACU medication, and any other relevant information.

Statistical analysis

IBM SPSS Statistics 20 statistical software will be used for statistical analyses. A Chi-square test will be used to compare the two groups, and t-tests will determine the statistical significance of continuous variables. All significance tests will be two-sided, and a two-tailed P-value of 0.05 or less will indicate statistical significance.

RESEARCH RISKS AND BENEFITS

Risks

The intervention in this study is a non-invasive and non-drug way, which does not increase the cost of medical treatment and nursing. No blood or tissue samples will be obtained. So there will be no side effects or sequelae.

Beneifits

You may not benefit directly from this study, but your participation will provide research evidence for the search for prevention methods for ED of FESS patients, which will be beneficial to the perioperative treatment and recovery of FESS patients in the future.

YOUR RIGHTS

You have the right to decide whether to participate in the test or not. If you cannot make a decision immediately, you have enough time to consider it. If necessary, you may consult with relatives, friends and other people you trust before making a decision.

If you decide not to participate in this study, it will not affect your relationship with the researcher, you will not face discrimination or retaliation, and your treatment and rights will not be affected. If you decide to participate in the study, we hope you can complete the study without special reasons, but you have the right to withdraw at any time during the study. If you decide to quit, please inform the researcher in time.

Before signing the informed consent, you may ask any questions about the technical terms, research methods and other relevant concerns in this informed consent form that you do not understand or have doubts about. The researchers will patiently answer any questions.

After the end of the study, you can keep track of the information related to you in the study.

PRIVACY PROTECTION

The personal information (such as name, gender, contact information, questionnaire, etc.) you provide to the researcher may be obtained by the following persons or units in addition to the normal research needs:

- Staff (inspectors, inspectors, etc.) of the research executing institution related to the test;
- State and local food and drug administration and other administrative agencies.

However, no one is allowed to disclose your personal information to others or other institutions without your permission, and no one or institution other than researchers and administrative institutions has the right to contact you about this study or directly provide you with information about this study.

The results of this study may be published as academic papers, but your personal information will not appear in any publicly published documents.

OTHERS

For the sake of your health, the researcher may withdraw you from this study without your consent if:

- If you continue to participate in this study, the risks may outweigh the benefits;
- You did not participate in the study according to the study protocol as instructed by the researcher;
- The test was terminated prematurely.

This informed consent is in duplicate, with one copy kept by the researcher and you.

COMPENSATION FOR DAMAGE CAUSED BY THE TEST

If your injury is caused directly by your participation in this study, you will not have to pay any medical expenses for treatment, which will be borne by the researcher.

CONTACTS

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Informed Consent

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Consent statement:

1. I have carefully read the instructions to the subjects and understood the relevant background of this study. The researcher has explained the characteristics and possible adverse reactions of the study to me in detail, and answered my questions.

2. I know that my treatment and rights will not be affected if I refuse to participate in this study. I will voluntarily participate in this study after knowing all the information of subjects and taking full consideration.

3. I am willing to follow the instructions of the researcher and participate in the experiment according to the research protocol. I have the right to quit at any time during the trial, but I need to inform the researcher before I quit.

4. During the trial, I will inform the researcher if any discomfort occurs.

Participant signature: **Date:**

/ /

Researcher signature: **Date:**

/ /

Signature of subject's agent (if any): **Date:**

Reason for can't sign by him/herself: / /

Relationship between participan and agent