Effect of preoperative intervention with folic acid and vitamin B12 on postoperative neurobehavioral changes in children

Informed consent

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Introduction

We sincerely invite your child to participate in this research called "Effects of preoperative folic acid and vitamin B12 intervention on postoperative neurobehavioral changes in children" This research aims to investigate the effects of therapeutic folic acid upon postoperative delirium neurobehavior in children. It is our responsibility to let you understand the purpose and content of the research before your agreement. Please read the consents one item by another intensively and let us know anything unclear.

What is the purpose of the research?

Awake stage delirium (ED) and long-term cognitive dysfunction are two common complications for children, who undergo surgery under general anesthesia. Folic acid, as a one-carbon unit transferase coenzyme, is an important factor acting on the nervous system. Vitamin B12 participates in methyl conversion and folate metabolism, and promotes the conversion of 5-methyltetrahydrofolate to tetrahydrofolate. General anesthesia is a common anesthesia method for children surgery. Our previous studies have shown that preoperative folic acid supplementation can reduce myelin sheath damage and cognitive impairment caused by general anesthesia. Therefore, the purpose of this research was to investigate the effects of folic acid and vitamin B12 interventions preoperatively, which might cause the delirium and long-term cognitive dysfunction after pediatric surgeries.

How is the research conducted?

This research is a randomized, double-blind, placebo-controlled, prospective research. The participants would take a certain amount of folic acid and VitB12 or pure brown sugar water without folic acid and Vitb12 on the third day before surgery. Observation and evaluation would be performed on the operation day. All the data would be recorded.

Before the operation, inform the patients and their families that they would randomly

receive folic acid, VitB12 orplacebo therapy. Due to the pale yellow color after folic acid dissolution, it is planned to dissolve folic acid tablets and VitB12 in 20ml of brown sugar water to ensure the consistency of the drug properties in the intervention group and placebo group, and to avoid the risks of blindness. All participants will be randomly divided into intervention group and placebo group.

Intervention group: patients took folic acid and VitB12 tablets for 3 days before surgery (2 years old children 0.4mg / d + VitB12 1.2μg / d, dissolved in 20ml brown sugar water once a day.). Placebo group: Patients took the same dose of brown sugar water for 3 consecutive days before surgery.

The dosages of folic acid and VitB12 wouldn't be above children's tolerable upper intake levels (UL), The maximum daily intake dosage has been extensively verified by toxicology experiments and has no significant side effects and dangers for almost all individuals. Adopting this dose can avoid the adverse reactions caused by folic acid intervention to the greatest extent. Folic acid, VitB12 and placebo are all in light-shielding bottles, and the researchers assign the medicine to the children every day. Patients and their families, anesthesiologists, surgeons, research recorders, and evaluators are unaware of the grouping and the composition of the drugs issued.

What are the possible circumstances of the suspension of the test?

In the course of the trial, any person who is allergic to the drug or serious adverse events and complications will undergo emergency blinding and first aid treatments. Any emergency blinding cases, or cases in which participants and guardians request to withdraw from the research halfway, are considered to be aborted.

How many people participated in this research?

This research is expected to recruit 360 children hospitalized for surgery, who are randomly divided into two groups of 180 patients per group.

Main observation indicators of the research:

PAED scores were performed at the time of awakening, extubation, and every 10min after extubation for 30 min in total (total score 0 ~ 20, score ≥10 is defined as delirium in the awakening period). Long-term neurobehavioral changes are assessed using Gesell scale.

Research secondary observation indicators:

(1) Changes in the induction period of anesthesia, intubation, and the operation center rate (HR) and mean blood pressure (MBP);

(2) Changes in HR and MBP after entering the resuscitation room (T1), 5 minutes before extubation (T2), during extubation (T3), and 2 minutes after extubation (T4);

(3) Extubation time and Wake-up time

(4) Ramsay sedation score after recovery, extubation and every 10min within 30min after extubation

(5) The postoperative pain CHEOPs scores were taken at the time of extubation and every 10 minutes within 30 minutes after extubation (the total score was less than 6 points, there was no pain, and ≥10 points for corresponding analgesia treatment);

(6) The use of narcotic drugs (e.g. : Pentazocine , Propofol)

(7) Changes in serum IL-6, TNF-α, folic acid and vitamin B12 concentrations before and after surgery. Preoperative and postoperative blood sequencing detection metabolomics.

(8) Other adverse events during the recovery period (e.g.: nausea and vomiting, bronchospasm, respiratory depression, etc.)

(9) Gesell scale score changes every six months before the age of three

(10) Postoperative child score (PHBQ)

(11) PAED scale score

Is research dangerous?

Folic acid and vitamin B12 are water-soluble B vitamins, which are mainly absorbed in the duodenum and proximal jejunum .Human body stores folic acid for 5-20mg. Folic acid is mainly excreted through urine and feces, with a daily excretion of 2 to 5ug. Folic acid has few adverse reactions, and in patients with normal renal function, toxic reactions rarely occur. Occasionally, allergic reactions can be seen. Some symptoms of folic acid allergic reactions include skin rash, itching, swelling, dizziness, and difficulty breathing. Vitamin B12 adverse reactions are rarer. Currently, there is still no clear evidence that Vitamin B12 may cause damage to the human body. If this trial caused any severe complications, the hospital would make compensation according to the degree of damage and in accordance with relevant national laws and regulations.

Expected duration of participation in the trial:

The follow-up is expected to continue until the child is 3 years old

If you do not participate in this research, are there any alternatives?

If you decide not to participate in this research, the other alternative is to receive general anesthesia for routine clinical procedures.

Inclusion criteria:

(1) ASA grade is Ⅰ ～ Ⅱ;

(2) Children aged 6 months to 2 years old;

(3) It is planned to undergo head, neck and maxillofacial surgery under general anesthesia, and the anesthesia time is less than 6 hours;

Exclusion criteria:

(1) Children with a history of respiratory tract infection within 1 week;

(2) Children with congenital malformations such as congenital heart disease;

(3) Children with central nervous system diseases or mental disorders or mental disorders;

(4) Children with long-term use of sedative or analgesic drugs;

(5) Children with severe liver and kidney dysfunction;

(6) Received folic acid and VitB12 supplement treatment or taken related derivatives;

(7) Have taken drugs that affect absorption within the past month, such as sulfonamides, aspirin, etc. . . .

(8) Those who have participated in other relevant clinical research in the past 3 months;

(9) Children with stunting

Benefit

It may improve the agitation and delirium of the child's postoperative recovery to a certain extent, reduce the risk of long-term neurobehavioral changes, promote patient recovery, and reduce the incidence of adverse events.

Do I need additional medical expenses?

There are no additional medical expenses in this clinical trial.

Reparation

In the event of damage related to this research, the hospital will compensate in accordance with the degree of damage and in accordance with relevant national laws and regulations.

There are no additional compensations for this research.

Is my information confidential?

During the research, all your information are strictly confidential. Only relevant personnel can view your medical records, so that they can check the accuracy of the collected information and ensure that the research is carried out normally. Any electronically transmitted information will be renamed to ensure the confidentiality of the information. All information in the computer will be protected by using a password. The results of this research may be reported at medical conferences and published in scientific journals. However, any personal information that is identifiable to you will not be used.

Participant rights

In this research, it is possible for your child to belong to any group. You have the right to decide whether your child will participate in the research. Participation in this research is completely voluntary. If you cannot decide immediately, you have enough time to discuss with relatives and friends before making a decision. If you decide not to take part in this research, it will not affect your normal treatment with medical staff. If you decide to participate in this research, we hope that your child can complete the test. Of course, you have the right to withdraw at any time without any reason.

During the test, you can always know the information related to this test. If you receive information that may affect the participant continued participation in the trial, you will be notified in a timely manner.

Participant Responsibilities

As a participant, you have the following responsibilities: to provide relevant medical history and current physical conditions; to inform the research doctor of any discomfort in this research; not to take other related drugs or food; to tell the researcher whether he has recently participated in other studies or is currently taking Participate in other research.

Who will do this test?

This research was implemented by the Department of Anesthesiology, Shanghai Ninth People's Hospital and completed in cooperation.

Who should I contact for more information?

After reading the introduction and discussing with your doctor, if you have other questions or

concerns, please contact the following persons:

Researcher: Lei Zhang

Phone number: 0086-18717822662

Address: Department of Anesthesiology, the Ninth People's Hospital, Shanghai Jiao tong University School of Medicine

Who approved the research?

This research has been approved by the Medical Ethics Committee of the Ninth People's Hospital Affiliated to Shanghai Jiao tong University School of Medicine. Anyone who has questions or complaints about this research can directly contact the Medical Ethics Committee: 0086-021-63057795.

Signature page of the participant's informed consent

The researcher has explained the purpose, process, and possible risks and benefits of taking the test drug to me. I have carefully read the instructions for the participants and have sufficient time to ask questions. At present, I have no doubts. My participation in this trial is voluntary, and I can withdraw from the trial at any time for any reason without suffering any loss. I will follow the guidance of the research doctor during the trial. If there are any adverse events during the trial, I will immediately notify the clinical trial physician and other researchers. If this test causes any obvious damage to my health (the content mentioned in the test plan and instructions), I will receive active treatment and compensation from the organizer.

I know that if I have used other medicines myself without discussing with the researchers in advance, or failing to notify my research doctor in time when there is a problem with my health, it will affect the protection I receive in the trial. I agree that the data obtained from this experiment can be used for recording, storage and processing. In addition, I agree that the organizer representative, the ethics committee, and the representative of the government could check my case records following the principle of confidentiality. I confirm the information collected in this research is true, accurate and reliable.

In conclusion, I agree to join in this clinical research. I have obtained a copy of this signed informed consent form.

Participant's name: Guardian's name (regular script):

Guardian's signature:

Participant signature: Relationship with participant:

Participant telephone number: Guardian telephone number:

Date of signature: _____ Month _____ Day _____ Year （Participant）

Date of signature: _____ Month _____ Day _____ Year （Guardian）

(Note: If the participant is incapacitated, the guardian will sign for it)

Researcher's name: Researcher's telephone number:

Researcher's signature: Date of signature: _____ Month _____Day _____Year