



Preventive Effect of Transcutaneous Acupoint Electrical Stimulation in Treating Postoperative Nausea and Vomiting in Patients Craniotomy

Guobing Yin, Xiang Huang, Fang Kang, Mingyu Zhai and Juan Li*

Department of Anesthesiology, Anhui Provincial Hospital, China

Summary

To determine the anti-PONV effect of Transcutaneous Acupoint Electrical Stimulation (TAES) at Neiguan (PC6) and Zhigou (SJ6). All patients intravenous azasetron hydrochloride 10mg before the end of operation. Group TAES received transcutaneous acupoint electrical stimulation at bilateral Neiguan (PC6) and Zhigou (SJ6) lasted for 30min after patient was awake. The occurrence of PONV were recorded postoperatively (0-2 h, 2-6 h, 6-24 h and 24 h post-surgery). Blood samples were taken before operation (T1), at the end of the operation (T2), at 12 h (T3) and 24 h post-surgery (T4). A total 100 patients consented for the study, 92 patients [control group (N=47) and TAES (N=45)] were included into final data analysis. There were no significant differences in the baseline characteristics demographic information, surgical approach, and duration of surgery between the two groups ($P > 0.05$). The overall incidence between the control group and TAES group were 59.6% and 31.1%, respectively ($P < 0.05$). The incidence of PONV at 0-2 h ($P > 0.05$) between the two groups. However, the incidence of PONV within 2-6 h, 6-24 h and 24 h post-surgery were significantly less in TAES group than control group ($P < 0.05$). Compared with the control group, the severity of PONV were significantly less in TAES group ($P < 0.05$). A total of 14 patients in control group and 5 patients in TAES group required rescue anti-emetic therapy; the difference between the two groups was

statistically significant ($P < 0.05$). The serum concentration of plasma motilin was significantly decreased at T3 in TAES group ($P < 0.05$). The integration of TAES at PC6 and SJ6 can decrease the occurrence of PONV in patients of craniotomy, and its potential mechanism may be through the regulation of plasma motilin concentration.

Introduction

Postoperative Nausea and Vomiting (PONV) occurs in up to 30% of unselected surgical patients and is the most frequent side effect after anaesthesia [1-3]. PONV not only reduced patient satisfaction but also was rated worse than postoperative pain in some of the patients [4,5]. The 5-hydroxytryptamine type 3 receptor antagonists and dexamethasone are two antiemetic drugs with similar efficacy in patients with one or two risks for PONV after single-dose administration [6,7]. However, these drugs are only partly effective for patients at high risk for PONV and may produce undesirable adverse effects. So it is very important to find a noninvasive method for preventing the PONV. Early in 2006, the American Society of PeriAnesthesia Nurses (ASPAN) recommended pericardium 6 (P6; also known as Neiguan) acupoint stimulation (Class IIb, Level A) as a complementary intervention for PONV prophylaxis [8]. Although there is a great amount of research concerning P6 acupoint stimulation for preventing PONV few research focus on Zhigou (SJ6) acupoint stimulation for preventing PONV [9-12]. According to the theory of Traditional Chinese Medicine (TCM), performing surgery breaks the balanced state of the human body and disturbs the movement of both qi and blood. When this happens, stomach qi will reverse its direction and go upward, causing nausea and vomiting. When this happens, stomach qi will reverse its direction and go upward, causing nausea and vomiting. The main principle of treatment in this case is to regulate the function of the stomach to avoid the adverse flow of qi. P6 is an acupuncture point in the meridian named Jueyin Pericardium Meridian of Hand. One of P6's main functions is to regulate the function of the stomach to avoid the adverse flow of qi, thus it is an effective Acupoint for preventing nausea and vomiting [13]. He showed it is useful to stimulate SJ6 acupoint for preventing nausea and vomiting. While it has not been reported to combine the P6 and SJ6 to prevent PONV [12]. There is no research and the laboratory data concerning how P6 acupoint stimulation prevents PONV. We, therefore, performed an observer-blind, randomized and controlled study to evaluate the effects of the P6 combined J6 acupuncture point on the incidence of PONV after craniotomy and recorded the serum concentration of plasma motilin to observe the mechanism. Elevated intracranial pressure can also directly stimulate the hypothalamus, brain stem, cerebellum, pituitary pheochromocytoma, make it secrete abnormal, leading to a large number of MTL secretion, and the center through the integration of signals, further promote the secretion of MTL in the peripheral gastrointestinal tract. Excessive MTL acts on receptors in the central and gastrointestinal tract, resulting in gastrointestinal spasm and increased stress.

*Corresponding author: Juan Li, Department of Anesthesiology, Anhui Provincial Hospital, Hefei, Anhui, China 230036, China, Tel: +86 13956005465; E-mail: huamuzi1999@126.com

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Methods

Study design

This study was a single-center, prospective, randomized, double-blind, placebo-controlled trial and was reviewed and approved by the institutional ethics Committee of Anhu Povice Hospital (Number: 2015-36) and was registered at Chinese Clinical Trial Registry (October 30, 2015, Registration number: ChiCTR-IPR-15007303), and informed consent was obtained from all patients participating in the study. A total of 100 patients of American Society of Anesthesiologists physical status II-III, scheduled for craniotomy, were eligible for this trial between October 2015 and December 2016. Exclusion criteria were as follows: women in pregnancy or lactation patients with the complication of severe digestive, respiratory and circulatory system diseases; Patient characteristic and demographic data and influence factors that may influence PONV (e.g., PONV history and smoking history); emergency patients. Patients with operation time >8 h and operative blood loss >2500 mL were withdrawn from the study. The patients were randomly allocated into the following two groups: control group and TEAS group.

Randomization was conducted on the day of surgery as the patient arrived at the operating room. Both Acupoint stimulation and placebo treatment were performed by the same investigator, who was not involved in managing anesthesia care and surgery. Transcutaneous Electrical Acupoint Stimulation (TEAS) was achieved by an electrical neuromuscular stimulation device (SDZ-II Electronic acupuncture therapy apparatus, SuZhou Medical supplies company). Patients group TAES, positive electrode was pasted in the bilateral PC6 and SJ6 points while negative electrodes was placed 3 cm distal from the selected acupoint. Using 2/100 dilatational wave, the intensity was adjusted to patient's ability to tolerate stimulate 30 min after patient extubated and regain conscious. Patients in the control group, the placement of electrodes was the same as those of group TAES except no current applied.

Anesthesia Procedures

When patient is brought to operating room lying on the OR table we applied monitors first then a standardized anaesthetic protocol was followed. All patients were fasted for at least 8 h before anaesthesia. General anaesthesia was induced with midazolam 0.05 mg kg⁻¹ i.v., propofol 2-3 mg kg⁻¹ i.v., fentanyl 2-3 µg kg⁻¹ i.v., rocuronium bromide 0.8 mg kg⁻¹ i.v., and lidocaine 1 mg kg⁻¹ i.v. Anaesthesia was maintained with sevoflurane (1.0-1.5 minimal alveolar concentration expired) and oxygen (fractional inspired O₂=1.0). Additional doses of fentanyl and rocuronium were titrated to maintain an adequate level of anaesthesia (when bispectral index is 40-60) and muscle relaxation. Standard monitoring procedures were followed, including ECG, invasive blood pressure, pulse oximetry, capnography and inspiratory and expiratory sevoflurane concentrations. The patients, the anaesthetists, and the nursing staff were unaware of the group assignments. Nothing-by-mouth fasting was continued after surgery for 6 h after surgery. All patients stayed in the hospital for at least 24 h.

Data Collection

Blood samples were taken before induction (T1), at closure of skin (T2), and 12 h and 24 h after operation (T3, T4). After centrifugation, we took the plasma and stored in a refrigerator at -80°C, determination of plasma motilin concentration. The occurrence of

PONV was recorded at 0-2 h, 2-6 h and 6-24 h, and 24 h. PONV classification (0, I, II, III, IV), for more than grade II or wanted to be treated patients will be given 10 mg metoclopramide. PONV classification was showed as follows, Grade 0: non nauseating and vomiting; Grade I: with nauseating but without vomiting; Grade II: the time of the vomiting is 1-2; Grade III: the time of vomiting is 3-5; Grade IV the time of vomiting >=6. The needs for rescue antiemetic were recorded. Finally, each group was expressed by mean and standard deviation. Chi-square test was used to compare the difference between two categorical variables (such as gender and hearing recovery). Student's t test was used to compare the differences between two continuous variables. Wilcoxon rank sum test was used to compare the differences between the grade variables. SPSS statistics 17.0 was used for the statistical analysis. Since a global level of significance was not controlled, p-values smaller than 5% are termed noticeable instead of significant.

Results

Among the initial 100 patients, 92 completed the study and were included the final analysis, including 47 cases in the control group, 45 cases of TAES group. In the control group, 2 patients were transferred to the Intensive Care Unit (ICU) because of postoperative observation, and 1 patient were reported 48 hours after the operation, so the study was excluded. In group TAES, 3 patients had postoperative disturbance of consciousness and could not communicate smoothly. 2 cases reported 48 hours after operation were excluded. Finally, there were 47 cases in the control group and 45 cases in the TAES group. A total of 92 patients completed the study. The patient characteristic and demographic data were presented in table 1 and there were no significant differences between two groups (P > 0.05).

Variable	Control group (n=47)	TEAS group (n=45)	t/χ ² value	P value	
Male/Female (n)	25/22	23/22	0.40	0.84	
Age (year, ±s)	42.2±10.3	43.5±10.1	0.61	0.54	
BMI (kg/m ² \bar{x} ±s)	22.2±1.6	21.8±1.8	1.13	0.26	
Smoke history (n)	19	17	0.07	0.80	
Surgical cite	Supratentorial (n)	38	35	0.13	0.72
	Subtentorial (n)	9	10		
operation time (min, \bar{x} ±s)	264±38	271±42	0.84	0.40	

Table 1: Comparison of two group in ratio of gender, age, BMI, smokers and surgical cite and operation time.

The total PONV incidence in the control group and the TAES group were 59.6% and 31.1% (P <0.05). There was no significant difference in the incidence of PONV at 0-2 h in the two groups (P >0.05). Compared with the control group, the incidence of PONV within 2-6 h, 6-24 h, and 24 h after operation were significantly less in TAES group (P <0.05). Compared with the control group, the level of PONV were significantly less in TAES group (P <0.05). Fourteen patients in the control group and 5 patients in the TAES group received rescue antiemetic (p<0.05). Table 2 showed the incidence of PONV in two groups of patients in different stages and rescue antiemetics in two groups. Compared with the control group, there were 14 cases of nausea and vomiting after operation in group TAES, which was significantly, lower than 28 cases in control group.

The severity of PONV experienced by the patients in the TAES group was significant less than those of control group (P < 0.05). The results are presented in table 3.

Variable	Control group (n=47)	TEAS group (n=45)	χ^2 value	P value
After surgery 0-2 h	5 (10.6)	6 (13.3)	0.159	0.69
After surgery 2-6 h	20 (42.6)	10* (22.2)	4.432	0.038
After surgery 6-24 h	15 (31.9)	6* (13.3)	4.506	0.034
Within 24 h	28 (59.6)	14* (31.1)	7.507	0.006
rescue antiemetics	14 (29.8)	5* (11.1)	4.893	0.027

Table 2: Comparison of the incidence of PONV in two groups of patients in different stages and rescue antiemetics in two group [n(%)].

Variable	The classification				
	Grade 0	Grade I	Grade II	Grade III	Grade IV
Control group (n=47)	19(40.4)	8(17.0)	12(25.5)	6(12.8)	2(4.3)
TEAS group (n=45)*	31(68.9)*	3(6.7)*	9(20.0)*	2(4.4)*	0(0)*

Table 3: Comparison of the classification of the two group patients with postoperative nausea and vomiting after 24 h operation [n(%)].

*P<0.05(Z=-2.691).

The serum concentration of plasma motilin was significantly decreased at T3 in TAES group ($P < 0.05$). The results are presented in table 4. The concentration of plasma motilin (MTL) in two groups was significantly higher than that before operation, and the difference was statistically significant ($P < 0.05$). The plasma MTL concentration in the control group at 12 h after operation was significantly higher than that before the operation, and the difference was statistically significant ($P < 0.05$). Compared with the control group, the concentration of MTL in plasma of group TAES at 12 h after operation was significantly decreased, the difference was statistically significant ($P < 0.05$).

Time	TAES group	Control group	T value	P value
T1	167.1±23.8	163.2±25.8	0.35	0.73
T2	212.7±23.7*	219.6±24.9*	0.63	0.54
T3	180.0±14.6	206.5±18.9*	3.49	0.003*
T4	168.0±21.8	169.4±25.4	0.13	0.89

Table 4: Comparison of two group in MTL ($\bar{x}\pm s$, pg/ml).

Discussion

PONV occurs mainly at 24 h after surgery, but a few patients can last for several days. There are many factors affecting PONV, including surgical factors, anesthesia methods, patient factors and other factors. Postoperative nausea and vomiting in patients with Department of Neurosurgery will increase the intracranial pressure, affect the cerebral perfusion pressure, serious damage to the nervous system, but also increase the risk of aspiration, intracranial recurrent bleeding, is not conducive to postoperative rehabilitation [14]. Although there is a variety of alone or combined medication, but the incidence has not changed significantly in the incidence of PONV.

Nilsson I and others reported that the incidence of PONV in Department of neurosurgery was close to 80% and there was no significant difference in the incidence of PONV between tentorial and supratentorial tumors [11,14-16]. In our study, all the craniotomy and tumor resection were included in the study, and no supratentorial

tumor and supratentorial tumor were compared. As a widespread complementary therapy, acupuncture appears to be effective in the treatment of many symptoms and/or disorders, partly by regulating the functions of the autonomic nervous system and neuroendocrine system, especially in improving postoperative pain relief and reducing postoperative side effects [17,18]. TEAS are an acupuncture-like technique that may produce effects similar to those elicited by acupuncture or EA treatment [19]. In our study, it was found that there was no significant difference in the incidence of PONV between two groups after 0-2 H. However, the incidence of PONV in group TAES was significantly lower than that in the control group at the three time points of 2-6 h, 6-24 h and 24 h, and the incidence of nausea and vomiting in group was significantly lower than that in the control group, and the number of rescue antiemetics required was lower in the TAES group than in the control group.

A large number of clinical studies have shown that Transcutaneous Electrical Acupoint Stimulation (TAES) at Neiguan or Zusanli can effectively prevent the occurrence of PONV [9-15]. As a high-risk group of PONV, the incidence of PONV can be reduced after TAES treatment in craniotomy patients. However, the effect of combined stimulation of Neiguan point and Zusanli point on the incidence of PONV has not been reported. In our study, we combined multi acupoint therapy. The results showed the incidence of PONV in group TAES was significantly lower than that in the control group at the three time points of 2-6 h, 6-24 h and 24 h, and the incidence of nausea and vomiting in group was significantly lower than that in the control group. From our point of view, a long duration of acupoint stimulation will increase patients' discomfort and pain, especially for those in the acupuncture group. However, if the stimulation time is too short, the therapeutic effect of acupuncture on PONV will be uncertain.

Craniotomy patients as a high-risk group of PONV may be related to direct surgical stimulation injury. Study found that increased intracranial pressure directly or indirectly affects the limbic system of the thalamus and medulla oblongata, and stimulates the vagus nerve system, so that the parasympathetic excitation, thus contributing to the secretion of MTL [20]. At the same time, elevated intracranial pressure can also directly stimulate the hypothalamus, brain stem, cerebellum, pituitary pheochromocytoma, make it secrete abnormal, leading to a large number of MTL secretion, and the center through the integration of signals, further promote the secretion of MTL in the peripheral gastrointestinal tract. Excessive MTL acts on receptors in the central and gastrointestinal tract, resulting in gastrointestinal spasm and increased stress. In our study, immediately after the plasma MTL concentration was significantly increased compared with before operation after operation in the two groups, TAES group at 12 h after the operation is restored to the preoperative level, but the control group at postoperative MTL compared with preoperative plasma concentration of 12 h and TAES group in the same period was significantly higher after 24 h plasma MTL of two groups were recovered to the preoperative level. The incidence of PONV and the degree of nausea and vomiting were decreased in group TAES, which might be related to the dynamic changes of plasma MTL concentration. The sample size in this study was relatively small, and the single-center design is another limitation. Selection bias may have resulted in discrepancies in the measurement indicators. Thus, further studies with several centers and a larger sample size are needed to thoroughly evaluate the efficacy of TEAS in perioperative pain relief, patient recovery, lung protection and prognosis improvement.

In conclusion, TEAS is a noninvasive and non-pharmacological modality for perioperative analgesi and acupuncture point stimulation is easy to learn, economical and practical, has been proved to effectively reduce the occurrence of PONV, reduce postoperative medication, thereby reducing the adverse reactions of drugs. Combination with Neiguan and Zusanli acupoint stimulation in craniotomy surgery, based on the use of conventional doses of azasetron, PONV can further reduce the incidence and severity of nausea.

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