CLINICAL EXPERIENCE

Effect of Transcutaneous Electrical Acupoint Stimulation on Nausea and Vomiting Induced by Patient Controlled Intravenous Analgesia with Tramadol

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ABSTRACT **Objective:** To observe the effect of transcutaneous electrical acupoint stimulation (TEAS) on nausea and vomiting (N&V) induced by patient controlled intravenous analgesia (PCIA) with Tramadol. **Methods:** Sixty patients who were ready to receive scheduled operation for tumor in the head-neck region and post-operation PCIA, aged 39-65 years, with the physique grades Ⅰ-Ⅱ of ASA, were randomized into two groups, A and B, 30 in each group. The pre-operation medication, induction of analgesia and continuous anesthesia used in the two groups were the same. TEAS on bilateral Hegu (LI4) and Neiguan (PC6) points was intermittently applied to the patients in group A starting from 30 min before analgesia induction to 24 h after operation, and the incidence and score of nausea and vomiting, antiemetic used, visual analogue scores (VAS), and PCIA pressing times in 4 time segments (0-4, 4-8, 8-12 and 12-24 h after the operation was finished) were determined. The same management was applied to patients in Group B, with sham TEAS for control. **Results:** The incidence and degree of N&V, as well as the number of patients who needed remedial antiemetic in Group A were less than those in Group B. The VAS score and PCIA pressing time were lower in Group A than those in Group B in the corresponding time segments respectively. **Conclusion:** TEAS could prevent N&V induced by PCIA with Tramadol.

KEY WORDS transcutaneous electrical acupoint stimulation, patient controlled intravenous analgesia, Tramadol, nausea and vomiting

Tramadol is a kind of drug for central analgesia, with apparent anesthesia effect but no marked respiratory inhibitory effect, which rarely produces adverse reactions such as dependence and resistance, and so is widely used, in clinical practice for intravenous analgesia. However, the symptoms of nausea and vomiting (N&V) induced by Tramadol in the anesthesia process have turned the drug into a thorny problem. Various antiemetics have been applied to solve the problem but proved to have only limited action with many adverse reactions.

Transcutaneous electrical acupoint stimulation (TEAS) is considered as a safe and effective non-drug treatment without any toxic-adverse reaction for preventing and treating post-operation problems[1]. This study is aimed at exploring the effect of TEAS on N&V shown in the process of PCIA with Tramadol.

METHODS

Criterion for Inclusion

Included were patients ready to receive scheduled operation of tumor at the head-neck region and post-operation patient controlled intravenous analgesia (PCIA) with Tramadol, aged 39-65 years, with their physical condition of grades Ⅰ-Ⅱ according to the classification by the standard set by the American Society of Anesthesiologists (ASA).

Criterion for Exclusion

Excluded were patients who matched any single one of the following items: hypertension, vascular diseases of the heart and/or brain, history of motion sickness, alcoholism, drug abuse, serious dysfunction of the liver and/or kidney, having received chemotherapeutic agents within 24 h after operation or antiemetics within 24 h before operation, complicated with pregnancy, women in the menstrual stage, having received treatment with acupuncture apparatus, and showing symptoms of

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vomiting or retching 24 h before the operation.

General Materials

The sixty patients fitting the criteria of inclusion and enrolled were in-patients selected from the Tumor Hospital Affiliated to Harbin Medical University from October 2005 to May 2006. They were randomly assigned to two groups according to the time of their hospitalization using a randomizing number table.

The 30 patients in Group A were 17 males and 13 females, with mean age of 54.7 ± 10.2 years, body weight (BW) of 63.6 ± 10.8 kg, and their operation time (OT) lasting for 146.8 ± 70.8 min; the 30 patients in Group B were 16 males and 14 females, with mean age of 53.6 ± 9.5 years, BW of 64.3 ± 8.4 kg, and OT of 150.8 ± 80.3 min. The two groups were not different significantly in general condition (P>0.05, Table 1).

Table 1. Comparison of General Materials ($\bar{x} \pm s$)

Group	Case	Sex (M/F)	Age (Year)	BW (kg)	OT (min)
A	30	17/13	54.7 ± 10.2	63.6 ± 10.8	146.8 ± 70.8
B	30	16/14	53.6 ± 9.5	64.3 ± 8.4	150.8 ± 80.3

Anesthesia

The following method was applied to all the patients enrolled: Premedication: Midazolam 0.1 mg/kg by intramuscular injection.

Induction for general anesthesia: Midazolam 0.1-0.15 mg/kg, Fentanyl 3-5 μg/kg, vecuronium bromide 0.1 mg/kg, and Propofol 1-2 mg/kg.

Endotracheal intubation was performed to conduct general anesthesia with inhalation of 0.5%-2% isoflurane by mechanical ventilation (TV=8-10 mL/kg, RR=12 times/min), and vecuronium bromide was injected intermittently for maintenance. Normal saline or 6% medium molecular hydroxyethyl starch 10-15 mL/kg each hour was infused to maintain the liquid balance to crystal/colloid ratio as 1:1.

Routine monitoring on noninvasive blood pressure (BP), ECG, peripheral blood oxygen saturation (SpO_2) and end-expiratory partial pressure of CO_2 ($P_{ET}CO_2$) were carried out all through the operational period.

Post-operation Analgesia

PCIA with Tramadol was applied to both groups by pre-medication of loading dose Tramadol 75-100 mg via intravenous injection before ending the operation, and analgesic compound liquid, consisting of 100 mL of normal saline and 1 000 mg of Tramadol, 2 mL/h was given through a sustaining pump with a single injecting volume of 1 mL and locking time of 15 min. Supplemental Tramadol (50-100 mg) might be given when the analgesia proved to be insufficient.

To patients in Group A, TEAS was applied in the following way: LH-202 Han's acupoint stimulator was used with the electrodes stuck on the respective points before anesthesia, one pair on bilateral Hegu (LI4) points and the other pair on bilateral Neiguan (PC6) points. Electro-stimulation was started 30 min before starting the operation, with the parameters of stimulation as 2/100 Hz sparse-dense wave, 6 sec as a cycle, with output of 2 Hz and 100 Hz alternately each for 3 sec; the width of wave used was 0.6 ms for 2 Hz and 0.2 ms for 100 Hz, with the strength between 8-10 mA, i.e., adjusted according to the endurance of patients, which would be increased to 20-30 mA during operation. Within 24 h after the operation was completed with the patients back at the ward and PCIA started, 30 min of TEAS was given in the first 2-4 h, then once more every 3 h, 3 times in total.

As for patients in Group B, the electrodes were stuck to the respective points the same way as that for Group A, but no galvanizing was given, i.e., it was sham-TEAS that was done to them.

Monitoring Indexes

The post-operation condition of the occurrence of N&V and effect of analgesia were monitored in 4 time segments, i.e., 0-4 (T1), 4-8 (T2), 8-12 (T3) and 12-24 (T4) h after the operation ended.

For the condition of N&V, the incidence of occurrence was observed and scored according to the following rules: none was scored as 0; nausea alone as 1; vomiting 1-2 times in 30 min as 2 and over 3 times as 3. If nausea was persistent or the vomiting or retching was sustained for more than 10 min, Ondansetron might be administered for relief, and the condition of the use of antiemetics was recorded.

For analgesia effect evaluation, the pressing time PCIA and the visual analogue score (VAS, 0-10 scores for scoring pain from none to unendurable) were used as the indexes.

Statistical Analysis

All data were managed with SPSS 10.0 Software, the measurement data were expressed by mean ± standard deviation ($\bar{x} \pm s$); inter-group comparison was conducted with variance analysis; the enumeration data were analyzed with Chi-square test; $P<0.05$ was regarded as having significance.

RESULTS

Comparison of Condition of Nausea and Vomiting

As shown in Table 2, the incidence and scores of N&V in Group A was significantly lower than that in Group B in all the 4 time segments ($P<0.05$ or $P<0.01$).

In the 24 h after operation, 14 patients in Group B experienced vomiting and needed to be treated with intravenous administration (the occurrence rate being 47%), while this condition only showed in 5 patients of Group A with the occurrence rate being 17%; comparison between the two groups showed significant difference ($P<0.01$).

Table 2. Scores of N&V in Various Time Segments

Group	Case	Score	Scores of N&V (Case)			
			T1	T2	T3	T4
A	30	1	0	2	3	0
		2	2	1	2	0
		3	0	0	0	0
B	30	1	12**	8*	6*	3*
		2	8**	2	2	0
		3	2*	0	0	0

Notes: *$P < 0.05$ **$P < 0.01$, compared with Group A

Comparison on Effect of Analgesia

As shown in Table 3, the VAS scores at T1-3, and the PCIA pressing times at T1-4 in Group A were lower than those in Group B at the corresponding time segments respectively (all $P<0.05$).

Table 3. Comparison of VAS Score and PCIA Pressing Times (n=30,$\bar{x} \pm s$)

Group	Case	Time	VAS (Score)	PCIA (Times)
A	30	T1	1.84 ± 0.79*	1.13 ± 0.36*
		T2	2.05 ± 0.07*	1.15 ± 0.32*
		T3	2.13 ± 0.05*	1.18 ± 0.47*
		T4	2.03 ± 0.78	1.05 ± 0.40*
B	30	T1	3.25 ± 1.06	1.55 ± 0.24
		T2	3.14 ± 1.28	1.60 ± 0.48
		T3	2.95 ± 0.17	1.45 ± 0.60
		T4	2.27 ± 0.89	1.38 ± 0.36

Note: *$P < 0.05$, compared with Group B

DISCUSSION

It has been found that there are abundant receptors of dopamine, toadstool, serotonin, histamine and opium in the vomiting-related center, and all the activators of these receptors have nausea-inducing action to various degrees. Tramadol plays its analgesic effect by way of stimulating the μ receptor of the opioid and inhibiting the reuptake of monoaminergic substances, like 5-HT and noradrenalin, in the central nervous system (CNS). Its adverse effect of N&V has been proved by studies on its characteristics and clinical observation[2].

To prevent the adverse reaction to Tramadol, drug therapy with Droperidol, Metoclopramide and Ondansetron has often been used, but its effect is limited; the efficacy has been evaluated by some researches as 25%. Moreover, all these drugs have various degrees of adverse reactions[3]. For example, the occurrence of QT interval prolongation has been found when Droperidol and Ondansetron are used in the post-operation period to treat N&V[4]; some researchers hold that Ondansetron could weaken the analgesic effect of Tramadol, since it is an antagonist of the 5-HT_3 receptor, and one of the main mechanisms of Tramadol for analgesia is exactly its inhibition on 5-HT reuptake and promotion of 5-HT_3 release[5]. Therefore, researchers have been trying to seek a way of treatment that is effective but without causing toxic and adverse reactions to solve the problem.

Acupuncture has been proved to be capable of effectively preventing post-operational N&V[6,7], and puncturing Neiguan point is considered to have an efficacy equivalent to Ondansetron in treating N&V[7]. TEAS, a therapeutic approach that possesses the essential nature identical to acupuncture[8], could also attain the same effect as acupuncture in N&V prevention[9]. In this study, TEAS was used in coordination with PCIA and Tramadol to observe the effect on N&V in the analgesic process, and results showed that the incidence and degree of N&V in patients treated by it were significantly lower than in those treated by PCIA alone ($P<0.05$ or $P<0.01$), illustrating that it has a quite apparent N&V preventive action.

The mechanism of the preventive action of TEAS is still not clear, but the possible causes could be the following: It possesses certain analgesic effect due to the release of intrinsic opioid peptides in the CNS. Since electric stimulation with low frequency (2 Hz) could release endorphin and enkephalin and that with high frequency (100 Hz) could release dynorphin, the alternative stimulation of low and high frequency

would cause the release of the three opioid peptides simultaneously to produce a general analgesic action[8]. TEAS was proved to have a leading analgesic effect that could relieve post-operation pain. The Hegu point is one of the acupoints with the strongest analgesic effect; the Neiguan point is also an acupoint with analgesic effect[10]. In this study, alternating high-low frequency electric stimulation at the Hegu and Neiguan points was used to bring their analgesic effects into full play. The results showed that the requirement of post-operation analgesics in the treated group was significantly less than that in the control group, and at the same time, the VAS score in the former was lower than in the latter. Post-operation N&V could also be alleviated by analgesia[11].

The combined use of TEAS and PCIA helps reduce the dosage of opioid drugs used in the post-operation period, which would greatly reduce the adverse reaction to opioid drugs and thus decreasing the incidence of N&V.

Puncturing the Neiguan itself might have a direct action in relieving vomiting. A study has proved[12] that the incidence of post-operation N&V could be reduced by finger pressing, manual puncturing, electric stimulating or TEAS at the Neiguan point, which may act by way of stimulation to mediate the release of endorphin in the cerebral spinal fluid to induce an antiemetic effect. Moreover, acupuncture could also induce serotonin to promote transformation of transportation[13].

In sum, results of our observation have displayed that TEAS has a definite preventive effect on N&V induced by PCIA with Tramadol, showing in comparison with other approaches specificities of being safe, low cost and without adverse effects. Therefore, it could be taken as a way of treatment for preventing N&V during PCIA with Tramadol.

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