

Monitoring of Neuromuscular Blockade at the P6 Acupuncture Point Reduces the Incidence of Postoperative Nausea and Vomiting

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Background: **Electrical stimulation of the P6 acupuncture point reduces the incidence of postoperative nausea and vomiting (PONV). Neuromuscular blockade during general anesthesia can be monitored with electrical peripheral nerve stimulation at the wrist. The authors tested the effect of neuromuscular monitoring over the P6 acupuncture point on the reduction of PONV.**

Methods: **In this prospective, double-blinded, randomized control trial, the authors investigated, with institutional review board approval and informed consent, 220 women undergoing elective laparoscopic surgery anesthetized with fentanyl, sevoflurane, and rocuronium. During anesthesia, neuromuscular blockade was monitored by a conventional nerve stimulator at a frequency of 1 Hz over the ulnar nerve (n = 110, control group) or over the median nerve (n = 110, P6 group) stimulating at the P6 acupuncture point at the same time. The authors evaluated the incidence of nausea and vomiting during the first 24 h.**

Results: **No differences in demographic and morphometric data were found between both groups. The 24-h incidence of PONV was 45% in the P6 acupuncture group *versus* 61% in the control group ($P = 0.022$). Nausea decreased from 56% in the control group to 40% in the P6 group ($P = 0.022$), but emesis decreased only from 28% to 23% ($P = 0.439$). Nausea decreased substantially during the first 6 h of the observation period ($P = 0.009$). Fewer subjects in the acupuncture group required ondansetron as rescue therapy (27% *vs.* 39%; $P = 0.086$).**

Conclusion: **Intraoperative P6 acupuncture point stimulation with a conventional nerve stimulator during surgery significantly reduced the incidence of PONV over 24 h. The efficacy of P6 stimulation is similar to that of commonly used antiemetic drugs in the prevention of PONV.**

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VARIOUS antiemetic drugs reduce but do not eliminate postoperative nausea and vomiting (PONV).[1,2] There is no completely effective therapy,[3,4] and even newly investigated drugs do not abolish PONV.[5] The PONV-reducing effects of acupuncture and its different approaches, such as needle acupuncture, electroacupuncture, and acupressure, are well described and were recently reviewed.[6,7]

The P6 or Neiguan acupuncture point is located 2 Chinese inches (cun units) proximal to the distal skin crease of the wrist, in the anterior ante brachial region on the ulnar side of the tendon of the flexor carpi radialis.[8,9]

Stimulation of the P6 acupuncture point in adult women undergoing gynecologic laparoscopic surgery showed a marked reduction of PONV incidence.[10,11] Transcutaneous electrical stimulation of the P6 acupuncture point reduced nausea but not vomiting after laparoscopic cholecystectomy, which is associated with a high risk of PONV.[12–14] In contrast, a recently published placebo-controlled study showed that P6 acupuncture reduced vomiting but not nausea.[15]

Monitoring of neuromuscular blockade is standard in modern anesthesia. Supramaximal electrical stimulation of a peripheral motor nerve tests the muscular response.[16,17] The easily accessible peripheral nerves at the wrist are commonly used during anesthesia. Our study was triggered by the idea that a constant electrical stimulus over the median nerve at the region of the well-known P6 acupuncture point might have an advantageous effect on PONV while measuring the neuromuscular blockade at the same time.

Therefore, we proposed this double-blinded randomized controlled trial evaluating the effects of electrical stimulation of the P6 acupuncture point at the dominant wrist using a conventional neuromuscular stimulation device for the evaluation of muscle relaxation during general anesthesia on the incidence of PONV. Our hypothesis was to test that stimulation of the P6 acupuncture point with a conventional nerve stimulator decreases the incidence of PONV.

Materials and Methods

With institutional review board approval (Ethik Kommission der Gemeinde Wien, Vienna, Austria, and Kantonale Ethik Komission, Bern, Switzerland) and informed consent, a total of 220 women with American Society of Anesthesiologists physical status I–III and aged 18–80

yr, who were scheduled to undergo elective gynecology and abdominal laparoscopic surgery of more than 1 h in duration, participated in the study.

We excluded pregnant and breast-feeding women and patients with eating disorders, obesity (body max index >35 kg/m^2), severe renal or liver malfunction, central nervous system injury, vertebrobasilar artery insufficiency, vestibular disease, cytostatic therapy, and preoperative vomiting or antiemetic therapy.

Randomization to the Study Group and Nerve/Acupuncture Stimulation

After induction of anesthesia, patients were assigned to one of two groups using a set of computer-generated random numbers. The assignments were kept in sealed, sequentially numbered envelopes until used, and the envelope numbers with the assignment were recorded. Patients and PONV evaluators were not informed of the group assignments. The attending anesthesiologist could not be blinded to the group assignment, but he or she was not involved with the PONV assessment.

The two groups were as follows:

Control group–ulnaris group: The pregelled silver–silver chloride electrodes (diameter 0.5 cm) were placed over the ulnar nerve. The distal electrode was placed approximately 1 cm proximal to the point at which the proximal flexion crease of the wrist crosses the radial side of the tendon to the flexor carpi ulnaris muscle at the volar side of the wrist. The proximal electrode was placed approximately 3 cm proximal to the distal electrode and was the positive electrode electrical stimulation elicited thumb adduction.[16]

Treatment group–P6 acupuncture group: The same electrodes as described above were used to stimulate the median nerve at the P6 acupuncture point, also known as Master of the Heart 6.[6] This point is on the antebrachial region of the forearm, 2 cun (equivalent to the width of the interphalangeal of the thumb of the patient) proximal to the anterior crease of the wrist, between the tendons of the palmaris longus and flexor carpi radialis muscles (or one sixth of the distance between the distal wrist crease and the cubital crease). The first electrode was placed between the two tendons 1 cm proximal to the P6 point. The second electrode was placed 2 cm distal to the P6 point. This second electrode acts as a skin surface electrode to allow electrical current through the P6 acupuncture point, the point most commonly used for treatment of PONV.[7] Because most authors recommend the patient's dominant hand for stimulation,[12] we assessed handedness in the preoperative interview. The only difference between both groups was where the electrodes were placed.

Anesthetic Management

The anesthetic management was standardized. After overnight fasting, patients were premedicated with 1 mg lormetazepam, 1 h before surgery. Anesthesia was induced with sodium thiopental (3–5 mg/kg), fentanyl (1–3 μg/kg), and rocuronium (1 mg/kg). Anesthesia subsequently was maintained with sevoflurane (1.2–1.8%). Thirty percent oxygen in nitrogen, no nitrous oxide, was used, and fentanyl, adjusted by the attending anesthesiologist with the goal of maintaining arterial blood pressure within 20% of preinduction values.

During surgery, additional rocuronium was administered as necessary to allow surgical relaxation maintaining mechanical twitches below 10% in response to supramaximal stimulation of the stimulated nerve at the wrist of the dominant arm. A commercially available neuromuscular transmission monitor (TOFwatch S; Organon Teknika, Boxtel, The Netherlands) based on the measurement of acceleration using a piezoelectrical transducer with integrated nerve stimulator was used for the nerve stimulation. The piezoelectric ceramic wafer was placed at the volar side of the thumb. We placed and fixed the hand on an armrest to assure free movement of the thumb. Before the first administration of muscle relaxant, supramaximal stimulation was applied to define the 100% twitch height. That means no neuromuscular blockade at all. Single-twitch stimulation with 1 Hz (over 0.2 ms, at a constant current of 50 mA)[6,17] was applied for both groups in each patient throughout maintenance of anesthesia. Meticulous effort was made to assure that movement of the thumb was not impeded.

After intubation of the trachea, both lungs were mechanically ventilated to maintain end-tidal carbon dioxide tension between 35 and 40 mmHg, and oxygen was administered as necessary to maintain oxyhemoglobin saturation at 95% in all patients.

At the end of the operation, neuromuscular relaxation was reversed by the use of a single dose of 0.4 mg glycopyrrolate and 2.5 mg neostigmine intravenously until 100% of twitch height was reached. Patients were extubated after clinical signs of full recovery and restoration of normal respiratory function.

Rescue treatment for PONV, using ondansetron (4 mg intravenous), was given if two or more episodes of vomiting occurred or if persistent nausea was reported with a repetition after 2 h. All patients had patient-controlled analgesia postoperatively.

Measurements

Demographic and morphometric data as well as historic factors that may influence PONV (*e.g.*, PONV history, smoking history) were collected preoperatively from the patients' records and by interviewing them during the consenting procedure.[18] Intraoperative and postoperative data were first averaged for each patient and then averaged for each group. Antiemetic rescue

medication (ondansetron) and postoperative analgesics were recorded over 24 h. Pain was evaluated with a continuous visual analog scale (1 = no pain to 10 = unbearable pain) in the postanesthesia care unit.

From arrival at the postoperative care unit and arrival at their wards, patients were evaluated for nausea and vomiting by a blinded investigator who was not aware of the patients' group assignments at the following intervals while awake: 0–2 h in the postanesthesia care unit and 2–6 h (as early PONV), 6–12 h, and 12–24 h (as late PONV) according to recommendations for the study of PONV.[18–21]

As a primary endpoint, we defined PONV as the presence of nausea and/or vomiting throughout the observation period. Nausea is the desire to vomit without the presence of expulsive muscular movements and was evaluated categorically as yes or no. Vomiting is the active expulsion of gastric content, and retching and was defined as an active attempt to vomit without expulsion of gastric contents. Retching and vomiting were summarized under emetic episodes and reported as vomiting. Repeated episodes occurring within 2 min were considered the same episode.[22]

During the 24-h observation period, the PONV evaluators observed possible side effects of transcutaneous electrical stimulation, such as local irritation, redness, contact dermatitis, or muscle ache from continuing stimulation.

Statistics

We based our sample size calculation on the PONV incidence in our previous study,[23] where we found an incidence of PONV in the control group of 44% and a reduction of 50% to the treatment group. We defined this relative reduction of 50% of PONV as a clinically relevant target of antiemetic prophylaxis for PONV for our study. This indicated that including 216 patients would provide a 95% chance of identifying a statistically significant difference between the groups at a two-tailed α level of 0.05 (type I error) using a chi-square analysis. We aimed to include a total of 220 women in the study. An intention-to-treat analysis was performed.

Morphometric and parametric data as well as intraoperative and postoperative results were compared for interval data with a Student *t* test or for categorical data with a chi-square test. The number of patients with PONV in each group was analyzed using a chi-square test over the 24-h observation period as well as for the early (0–6 h) and late (6–24 h) postoperative period.

We considered our major outcomes to be statistically significant at $P < 0.05$. Data are presented as mean ± SD or as percentages. All statistical analyses were conducted using SAS 9.1 (SAS Institute Inc, Cary, NC) and with Primer of biostatistics 4.02 (for Windows 95; McGraw-Hill, New York, NY).

Results

Two hundred twenty patients were recruited for this study (n = 110 in each group) without any dropout over the observation period. Demographic and morphometric characteristics and factors likely to influence PONV were similar in the two groups (table 1). There also were no differences for the intraoperative and postoperative variables except PONV. No side effects were detected after using the electrical stimulation.

The visual analog scale results for pain recorded in the postoperative care unit over the first 2 h were comparable between the two groups (2.1 ± 1.7 for P6 *vs.* 1.9 ± 1.5 for the control group; $P = 0.41$). The need for opioids (piritramide) was similar between the P6 group and the control group for the first 6 h (6 ± 6 *vs.* 5 ± 5 mg; $P = 0.14$) and also for the late period (up to 24 h) (1 ± 5 *vs.* 1 ± 2 mg; $P = 0.19$). The treatment with nonsteroidal antirheumatic medication was comparable for the first 6 h (38% *vs.* 50%; $P = 0.078$), as well as for the late period (37% *vs.* 48%; $P = 0.13$). The difference of 13% over the 24-h observation period was not significant (55% *vs.* 68%; $P = 0.051$).

There was a significant difference between both groups for the primary endpoint, experiencing postoperative nausea and vomiting (both combined) over the 24-h observation period (table 2). If we split up postoperative nausea and vomiting, nausea but not vomiting was significantly lower in the P6 acupuncture group (40% *vs.* 56%; $P = 0.022$).

During the early postoperative period (0–6 h), combined PONV and nausea was highly significantly different (33% *vs.* 51%; $P = 0.009$), whereas no difference was found for the late postoperative period (6–24 h; table 2). That means the number needed to treat is 6 to prevent PONV over 24 h and less than 5 for early PONV prevention.

Furthermore, the need for rescue therapy treatment with ondansetron showed a decrease (27% *vs.* 39%; $P = 0.086$) of 12%, which was observed for the 24-h period, for the early period (25% *vs.* 36%; $P = 0.109$), and no difference in the late period.

Discussion

Transcutaneous electrical nerve stimulation to assess neuromuscular blockade is standard and well established under general anesthesia during surgery. Transcutaneous electrical stimulation of the P6 acupuncture point has been shown effective for the prevention of PONV.[24,25] The results of our study showed for the first time that the combined unilateral stimulation of the P6 acupuncture point while measuring neuromuscular blockade reduces PONV overall in the early period after surgery.

Despite advances in anesthesia and the introduction of new narcotics, anesthetics, and constantly new developed antiemetics, particularly the 5-hydroxytryptamines,

Table 1. Demographic, Morphometric, Intraoperative, and Postoperative Data

	P6 Acupuncture Group, N. Medianus (n = 110)	Control Group, N. Ulnaris (n = 110)	*P* Value
Age, yr	46 ± 14	45 ± 15	0.68
Weight, kg	74 ± 19	74 ± 15	0.93
Height, cm	165 ± 10	165 ± 7	0.41
History of PONV	33 (30)	31 (28)	0.88
History of motion sickness	28 (25)	35 (32)	0.37
Smoker	42 (38)	30 (27)	0.11
Risk of PONV			
40%	37 (34)	35 (32)	0.88
60%	43 (39)	47 (43)	0.68
80%	22 (20)	25 (23)	0.77
ASA physical status			0.70
I	76 (69)	74 (67)	
II	32 (29)	32 (29)	
III	2 (2)	4 (4)	
Handedness, right/left	102/8	97/13	0.36
Type of laparoscopic surgery			
Cholecystectomy	62 (56)	63 (57)	1.0
Gynecologic	48 (44)	47 (43)	1.0
Intraoperative fentanyl, μg	397 ± 139	396 ± 130	0.96
Intraoperative fluid intake, ml	1,398 ± 551	1,388 ± 571	0.89
Duration of anesthesia, min	118 ± 58	117 ± 61	0.86
Duration of surgery, min	81 ± 53	76 ± 54	0.42
Intraoperative MAP, mmHg	88 ± 14	86 ± 13	0.52
Intraoperative HR, beats/min	72 ± 12	74 ±13	0.20
Intraoperative F_{IO_2}	44 ± 10	46 ± 11	0.30
End-tidal sevoflurane concentration, %	1.7 ± 0.3	1.7 ± 0.3	0.47
End-tidal CO_2, mmHg	35 ± 7	34 ± 3	0.32
Intraoperative Sa_{O_2}, %	99 ± 1	99 ± 1	0.84
Duration at PACU, min	90 ± 45	88 ± 38	0.57
PACU MAP, mmHg	82 ± 13	84 ± 10	0.30
PACU HR, beats/min	72 ± 14	74 ± 13	0.26
PACU Sa_{O_2}, %	98 ± 5	99 ± 3	0.11

Data are presented as mean ± SD or n (%). No significant differences between the two groups, Student *t* test and chi-square test.

ASA = American Society of Anesthesiologists; CO_2 = carbon dioxide; F_{IO_2} = fraction of inspired oxygen; HR = heart rate; MAP = mean arterial pressure; PACU = postanesthesia care unit; PONV = postoperative nausea and vomiting; Sa_{O_2} = oxygen saturation.

the incidence of nausea and vomiting remains between 20% and 70%.[19,26–28] The relative reduction of PONV by 25% in our study is comparable to the effect of well-established drug treatments.[4,5] On the other hand, we found that P6 acupuncture point stimulation with a standard neuromuscular blockade monitor has a more profound effect on the incidence of postoperative nausea than on postoperative vomiting.

Postoperative nausea and vomiting is not only an unpleasant sequela for patients after anesthesia and opera-

Table 2. Incidence of Postoperative Nausea and Vomiting

	P6 Acupuncture Group, N. Medianus (n = 110)	Control Group, N. Ulnaris (n = 110)	*P* Value
Early PONV, 0–6 h	39 (35; 26–44)	62 (56; 47–65)	**0.003**
Nausea	36 (33; 23–41)	56 (51; 42–60)	**0.009**
Emesis	18 (16; 9–23)	28 (25; 17–34)	0.136
Late PONV, 6–24 h	21 (19; 11–26)	22 (20; 13–27)	1.000
Nausea	19 (17; 10–24)	19 (17; 10–24)	1.000
Emesis	9 (8; 6–19)	14 (13; 10–24)	0.378
Overall PONV, 0–24 h	49 (45; 35–54)	67 (61; 52–70)	**0.022**
Nausea	44 (40; 31–49)	62 (56; 47–65)	**0.022**
Emesis	25 (23; 14–30)	31 (28; 20–37)	0.439
Ondansetron rescue			
Early phase, 0–6 h	28 (25; 17–33)	40 (36; 27–45)	0.109
Late phase, 6–24 h	4 (4; 0–7)	5 (5; 0–8)	0.856
Over 24 h postoperative	30 (27; 19–36)	43 (39; 30–48)	0.086

Data are presented as n (%; 95% confidence interval). Statistics: chi-square test.

PONV = postoperative nausea and vomiting.

tion. The psychological impact of previous nausea and vomiting experience is well known as a potent trigger for PONV.[29] This "minor" postoperative complication may result in delayed discharge and unplanned hospitalization after ambulatory surgery, including increase of cost.[22,30]

Gan *et al.*[31] showed that electrical stimulation of the acupuncture point reduced overall early PONV and nausea. It is not surprising that in our study, the transcutaneous electrical stimulation of the P6 acupuncture point while monitoring neuromuscular blockade during surgery reduced PONV in the early postoperative period. On the other hand, it is surprising that this effect reduced the incidence of PONV significantly over 24 h. We defined PONV *a priori* as our primary outcome and presented that significant difference. However, in the separate analysis of nausea and vomiting, we found that nausea was the real factor that contributed to the reduction of PONV, which is in accord with the described effect of the P6 acupuncture point.

An advantage of our researched method to reduce PONV is its ease of application. Anesthesiologists are used to placing electrodes to monitor neuromuscular blockade, and the P6 acupuncture point is well described and easy to find even for non–acupuncture-trained physicians. This method is safe and without any complication or side effects, as we showed in the study when we looked meticulously at possible side effects of stimulation. These findings are in accord with the current literature, which does not report any case reports or reviews that continuing stimulation of the median nerve causes nerve damage. Because we did not use needles for the acupuncture stimulation, patients had no sequelae such as infection or tissue damage from needles.

One limitation of our study is that we included only women. Reasons for that were study design and logistic considerations, but the results of our study will apply also for men because there is no report that women react differently from men to stimulation of the P6 acupuncture point. Another limitation was the use of the single-twitch mode to monitor neuromuscular blockade. That is different from the broad use of the train-of-four mode usually used during surgery. With this study, we proved that neuromuscular monitoring over the P6 acupuncture point can reduce PONV. We are sure that other methods of nerve stimulation are able to provide a similar effect, but that has to be proven in the future.

We found a nonsignificant difference in smokers (11%; $P = 0.11$), with a higher rate in the P6 acupuncture group. At our given number of 220 study participants, only a difference of 15% could reach significance.

We also did not perform a formal cost-effectiveness analysis, but the acupuncture stimulation does not augment costs during anesthesia because the electrodes used for the neuromuscular monitoring are used for the acupuncture stimulation. But the resulting antiemetic effect is similar to that provided by standard costly antiemetic drugs.

The combined use of acupuncture stimulation and drugs as a multimodal prophylactic regimen is promising based on Coloma *et al.*,[11] but that has to be proven in the future for our tested antiemetic strategy as well as applications in other settings such as children or with the use of nonvolatile anesthetics.

Conclusion

Intraoperative transcutaneous electrical stimulation of the P6 acupuncture point with a conventional nerve stimulator to monitor neuromuscular blockade significantly reduced the incidence of PONV over 24 h. The major reduction factor is the effect of acupuncture stimulation on early nausea (in the first 6 h after surgery). The number needed to treat is 5 for early PONV and 6 for 24-h PONV. These observed antiemetic effects of acupuncture are similar to those previously reported for antiemetic drugs. This combination of intraoperative transcutaneous electrical stimulation of the P6 acupuncture point with monitoring neuromuscular blockade is simple and easy to perform, without any danger to the patient.

Because this technique can be used in virtually all patients undergoing general anesthetic, without purchasing additional equipment and with no additional cost, it is an excellent addition to our current concepts of the multimodal management of PONV and has the potential for changing clinical practice.

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