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Perception of Bodily Sensation as a Predictor of Treatment Response to Acupuncture for Postoperative Nausea and Vomiting Prophylaxis

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ABSTRACT

Objectives: Conditions associated with the response to acupuncture treatment remain widely elusive. This study aimed to identify predictors of treatment response in patients undergoing acupuncture treatment for prevention of postoperative nausea and vomiting (PONV). An intervention-specific questionnaire was developed to assess perception of bodily sensations (PBS) in patients undergoing acupuncture treatment.

Design: Exploratory study in addition to an observer-blinded randomized controlled trial.

Settings/location: The departments of anesthesiology and of gynecology, University of Heidelberg, Germany.

Subjects: Two hundred and twenty (220) female patients scheduled for breast or gynecologic surgery.

Interventions: True acupuncture on point P6 (Neiguan) or placebo/sham acupuncture on a virtual point 1 cm proximal and lateral to P6.

Outcome measures: Of 220 female patients scheduled for breast or gynecologic surgery who were included in the trial, 202 completed the newly developed PBS questionnaire before the intervention. The main outcome was incidence of PONV in relationship with PBS and the kind of acupuncture applied. Logistic regression analyses were performed to identify predictors of treatment response for those receiving surgery ($n = 195$).

Results: High PBS predicted low treatment response in patients receiving breast surgery (odds ratio [OR] = 1.6; $p = 0.039$ for each 10-point increase). The PBS questionnaire showed good item difficulty, internal consistency, and divergent validity. Treatment response in patients receiving gynecologic surgery was predicted by the kind of acupuncture applied (OR = 0.4; $p = 0.027$), whereas PBS played no role in this group.

Conclusions: The incidence of PONV after breast surgery seems to be influenced by some psychological mechanisms. In this group of patients, acupuncture might be more effective in patients who have low PBS.

INTRODUCTION

The effectiveness of acupuncture is often a controversial subject (NIH Consensus Conference, 1998). Experimental studies have been able to show physiological mechanisms of acupuncture (Das et al., 1984; Li et al., 2001; Middlekauff et al., 2002; Takeshige et al., 1992). However, clinical studies have shown negative as well as positive results. Meta-analyses have been unable to show clear results in favor of acupuncture (Ernst et al., 1998; Linde et al., 2000; Melchart et al., 2001). According to the 1997 National Institutes of Health (NIH) conference on acupuncture, the best evidence of the efficacy of acupuncture exists in adult postoperative nausea and vomiting (PONV) and in dental pain (NIH Consensus Conference, 1998). Recent reviews have confirmed the effectiveness of P6 stimulation in preventing

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PONV (Lee and Done, 1999; Vickers, 1996). But even in this very well-studied condition, the mechanisms of action are not clear.

Studies concerning placebo-effects (Streitberger and Kleinhenz, 1998) and other psychologic mechanisms (Choi and Tweed, 1996) have faced problems with methodology, but did not consider other important aspects of acupuncture therapy, such as taking into account the necessity of individual treatment according to the rules of Traditional Chinese Medicine (TCM) (Linde et al., 2000). Additionally, there exists the problem of nonresponders to acupuncture treatment. Relations between treatment response and pain processing in the periaqueductal gray have been shown in experimental studies with rats (Lee et al., 2002; Tang et al., 1997). In a clinical study, patients with psychogenic pain seemed to respond less than those with nociceptive pain (Carlsson and Sjolund, 1994; Lee et al., 2002). In addition, psychologic aspects related to the theory of cognitive orientation have been shown to be important for treatment response (Kreitler et al., 1987).

According to the experience of experts on acupuncture, different types of patients have different responses to acupuncture. These responses are thought to be related to aspects of body image and perception of bodily sensations (Mann, 1992). Up to now, there has been no clinical evidence of this relationship.

Therefore, the primary aim of this study was to investigate if perception of bodily sensations (PBS) can predict the response to acupuncture therapy. For this purpose, it was necessary to develop an acupuncture-specific questionnaire for assessment of PBS. In order to evaluate this postulated relationship, patients of a randomized controlled trial for testing the antiemetic efficacy of acupuncture (Streitberger et al., 2004) received this questionnaire.

Due to time constraints during the ongoing study, it was necessary to develop this questionnaire within a period of 2 months. Therefore, we used the experiences of about 20 teachers of acupuncture and literature findings as the basis for 10 questions about PBS. As there seems to be some relationship between mood disorders and increased awareness of bodily sensation (Mechanic, 1972; Rief et al., 1998) we also measured levels of depression and anxiety with the Hospital Anxiety and Depression Scale, to evaluate possible confounding with the PBS.

MATERIALS AND METHODS

Subjects

The study was conducted between January and August 2002 at the Department of Anesthesiology, in cooperation with the Department of Gynecology, University of Heidelberg.

Women assigned to gynecologic or breast surgery were asked whether they were willing to participate in the randomized controlled trial, including additional questionnaires about perception of bodily sensations (PBS). Sample selection, methods, and results of the randomized trial are described in detail elsewhere (Streitberger et al., 2004).

Inclusion criteria included women aged between 18 and 80 years, without exercise-limiting diseases according to ASA [American Society of Anesthesiologists] classification I and II, scheduled for gynecologic or breast surgery with general anesthesia, and having given signed written informed consent. Exclusion criteria included acupuncture treatment during the past 6 months; pregnancy; nausea or vomiting during the past 24 hours; a history of lymphedema of the upper limbs; eczematous skin changes at the location of the acupuncture point P6; or coagulopathy.

The study protocol was approved by the Ethics Committee of the University of Heidelberg.

After inclusion in the study, the patients received the PBS questionnaire in addition to the baseline investigation. They were asked to fill in the questionnaire before surgery. External randomization was stratified by type of surgery (gynecologic or breast) to ensure balance between groups. Patients were randomized into 4 groups, receiving either acupuncture or placebo/sham acupuncture at point P6 either before or after induction of anesthesia.

Twenty minutes before induction of anesthesia, patients allocated to the acupuncture group were prepared for study treatment by marking the acupuncture point P6 on both forearms with a plastic ring covered by a bandage. A sham point was marked 1 cm proximal and 1 cm lateral of P6 on both forearms of the patients allocated to the placebo group. Patients in the acupuncture group received acupuncture through the bandage and plastic ring with a 0.32 × 30 mm stainless steel needle (Asia Med, Munich, Germany). The needles were inserted by a trained medical doctor until a dull needle sensation (*deqi*) occurred, or to ~1 cm deep if patients were already anesthetized. In the control group, patients received sham acupuncture with a blunted, telescopic placebo needle designed by the senior author and manufactured by Asia Med. This placebo needle simulates an acupuncture procedure without penetrating the skin (Streitberger and Kleinhenz, 1998). The efficiency of this method for blinding acupuncture treatment has been shown in various studies (Kleinhenz et al., 1999; Streitberger et al., 2003; White et al., 2003).

Measures

A blinded observer at the ward evaluated outcome 24 hours postoperatively. The primary outcome measure of the trial was postoperative nausea and vomiting (PONV) occurring within 24 hours after surgery. The patients were asked if they experienced nausea and vomiting, including time of first occurrence. Secondary outcome criteria included early occurrence of PONV requiring additional antiemetic drugs in the recovery room, administered by the medical team.

The patients filled in the Hospital Anxiety and Depression Scale (HADS) and the PBS questionnaires prior to surgery and the acupuncture trial.

The HADS is a screening instrument for anxiety and depression in non-psychiatric patients. It measures disease-related psychological distress by means of a depression and anxiety index (Zigmond and Snaith, 1983). It is sensitive to changes both during the course of disease and in response to psychotherapeutic and psychopharmacological intervention. HADS scores predict psychosocial and possibly also physical outcomes (Hermann, 1997).

Development of the PBS questionnaire

Based on statements of teachers of the German Acupuncture Society (DÄGfA) and findings in the literature (Mann, 1992), 10 items were formulated for the PBS questionnaire. It was hypothesized that a high perception of bodily sensation would predict a greater treatment response. The final questionnaire was discussed with 2 independent acupuncturists, who approved the items of the questionnaire as being relevant with regard to important perceptions of bodily sensations in patients undergoing acupuncture. The patients' level of agreement to the 10 items was measured on a 6-point scale, ranging from 1 = not true to 6 = completely true. The agreement of the acupuncturists to the final version of the questionnaire was valued as a reference to the content validity of the questionnaire.

Statistical analysis

Baseline data were compared descriptively. The intention-to-treat analysis of the primary outcome variable of the trial was carried out using the stratified Mantel-Henszel test. Secondary outcome variables were analyzed in the form of a descriptive comparison using Fisher's exact test for categorical variables, the mean score test for ordered categorical variables, and the Mann-Whitney U test for continuous variables (Streitburger et al., 2004).

For psychometric analysis of the PBS questionnaire, intervention subjects as well as controls were included. Up to 2 missing values were input by interpolation. Patients with >2 missing values on the questionnaire were excluded from our analysis. Psychometric properties assessed by this newly developed questionnaire were measured at the start of this study and include descriptive statistics for each item and the sum score. In addition, item difficulty, internal consistency (Crohnbach's coefficient α) as a measure of reliability, and divergent validity (measured as a correlation with both the anxiety and the depression subscales of the HADS) were investigated. As no gold standard measure for PBS in patients undergoing acupuncture was available, the assessment of criterion validity was not possible. A bodily sensations sum score was calculated by adding the values of the 10 items.

The association between PBS, anxiety, depression, the kind of acupuncture applied (predictor variables) and PONV (dependent variable) was calculated by univariate logistic regression analyses according to the intention-to-treat principle. Odds ratios were calculated for each 10-point increase in the PBS questionnaire and for each 5-point increase in the HADS. The interaction between the kind of acupuncture applied and the PBS was calculated by multivariate logistic regression including the variables "kind of acupuncture," "PBS," and "kind of acupuncture × PBS."

Further analysis of the PBS questionnaire was carried out using an exploratory strategy based on primary and secondary outcome analysis, as the patients with gynecologic surgery seem to have better responses to acupuncture than those with breast surgery (Streitberger et al., 2004).

RESULTS

Baseline characteristics

Between January and August 2002, 325 women requiring gynecologic or breast surgery were asked to participate in the study, of whom 67 did not fulfil the inclusion criteria, and 38 denied consent. Of the 220 randomized patients, 8 did not undergo surgery and 1 patient withdrew consent after randomization. One hundred and nine (109) patients were assigned to the acupuncture group, and 111 to the placebo/sham group. Of the 211 patients, 18 did not receive the allocated treatment due to organizational reasons. Baseline characteristics, including incidence of risk factors for PONV, revealed no relevant differences between the two groups (Table 1).

Outcomes

Results of the randomized controlled trial showed in the intention-to treat analysis an incidence of PONV within 24 hours of 50.9% in the placebo group and of 43.4% in the acupuncture group, but this difference was not statistically significant ($p = 0.27$). The differences were more pronounced for patients receiving gynecologic surgery ($p = 0.07$) than for those receiving breast surgery ($p = 0.86$). Concerning the short-term follow-up of the whole group in the recovery room there was a nearly significant reduction in PONV in those receiving true acupuncture ($p = 0.06$) (Streitburger et al., 2004).

Two hundred and five (205) patients completed the questionnaire. Because of organizational reasons, 15 questionnaires were missed. Ten (10) questionnaires had 1 missing value and 1 questionnaire had 2 missing values. Three questionnaires with 5, 7, and 9 missing values were excluded from the analysis.

The mean sum score ± standard deviation (SD) of the PBS questionnaire was 37.5 ± 9.8 ($n = 202$; range 10–60). Mean scores of the 10 items ranged from 2.6 (item 6) to 5.1 (item 2), corresponding to item difficulties varying from 0.43 to 0.85. Internal consistency was $r_\alpha = 0.80$, and di-

TABLE 1. PATIENT CHARACTERISTICS

	Acupuncture (n = *105*)	*Sham/placebo* (n = *106*)
Mean age, years (range)	44.3 ± 13.4 (range, 18.3–79.4)	46.5 ± 13.4 (range 22.4–74.5)
Mean weight, kg (range)	67.4 ± 12.1 (range, 49.0–120.0)	67.4 ± 13.0 (range 41.0–108.8)
Smoker	33 (31.4%)	36 (34.0%)
Non-smoker	72	70
Previous history of smoking	11 (10.5%)	9 (8.5%)
Never smoked	61 (58.1%)	61 (57.5%)
Menopause	38 (36.2%)	44 (41.5%)
History of motion sickness	33 (31.4%)	39 (36.8%)
History of migraine	31 (29.5%)	33 (31.3%)
History of cardiovascular disease	23 (21.9%)	25 (23.6%)
History of gastrointestinal disease	16 (15.2%)	7 (6.6%)
Previous surgery	97 (92.4%)	94 (88.7%)
History of PONV		
Nausea	41 (39.0%)	38 (36.2%); $n = 105$
Vomiting	34 (33.3%)	38 (36.2%); $n = 105$
Anxiety concerning		
Result of surgery	63 (53.8%)	62 (55.5%)
PONV	33 (30.6%)	36 (32.4%)
Awareness during surgery	41 (38.0%)	33 (29.7%)
Not awakening	54 (50.0%)	45 (40.5%)
Postoperative pain	47 (43.5%)	34 (30.6%)
Breast surgery	62	62
Without lymph node dissection	33	23
With lymph node dissection	13	7
Plastic	14	20
Other	2	5
Gynecologic surgery		
Laparoscopy	45	46
Laparotomy	24	20
Other	11	14
	10	12
Questionnaires		
Depression	5.17 ± 3.74; $n = 101$	4.64 ± 3.88; $n = 99$
Anxiety	7.86 ± 3.98; $n = 99$	7.86 ± 4.33; $n = 98$
PBS, sum score	37.64 ± 9.05; $n = 101$	37.28 ± 10.51; $n = 101$

PONV, postoperative nausea and vomiting; PBS, perception of bodily sensation.

vergent validity with respect to the depression scale of the HADS was $r = 0.21$, while it was $r = 0.30$ for the anxiety scale of the HADS (Table 2).

For analyzing the relationship between treatment response on acupuncture and psychologic variables, univariate logistic regression analysis was performed according to the intention-to-treat principle, including all patients who received surgery ($n = 195$) and filled in the questionnaire completely.

The univariate logistic regression analysis showed no significant impact of PBS on PONV in the recovery room (OR 1.3; 95% confidence interval [CI] 0.96–1.78; $p = 0.09$) and within 24 hours (OR 1.3; CI 0.98–1.77; $p = 0.07$). As the differences between sham and true acupuncture concerning the incidence of PONV were more pronounced for gynecologic surgery in the main study, we performed an exploratory analysis of the two subgroups in this trial. According to this, the univariate logistic regression analysis indicates a predictive value of PBS in both short- ($p = 0.04$) and long-term ($p = 0.04$) outcomes for those receiving breast surgery, but not for gynecologic surgery (Table 3).

The logistic regression analysis show no significant interaction between the kind of acupuncture applied and PBS in patients with breast surgery, thus pointing to PBS as an independent predictor. Those patients with a low score in the PBS questionnaire showed a lower incidence of PONV (OR 1.6 for each 10-unit increase).

Remarkably, these associations do not show up in those patients receiving gynecologic surgery. In those patients the kind of acupuncture applied is a significant predictor of PONV ($p = 0.04$). Additionally, preoperative depression significantly predicts treatment response in the recovery

TABLE 2. PERCEPTION OF BODILY SENSATION (PBS) QUESTIONNAIRE AND CORRELATION BETWEEN ANXIETY AND DEPRESSION

Items on a 6-point range (1 = not true; 6 = completely true)	n	*Mean ± SD*	*Anxiety (corr)*	*Depression (corr)*
1. I notice small changes in my body very precisely	201	4.03 ± 1.51	0.04	0.00
2. I notice immediately when a piece of clothing is uncomfortable	202	5.14 ± 1.24	0.03	0.03
3. My body reacts very sensitively when challenged	202	3.26 ± 1.69	0.31*	0.16**
4. I notice immediately when something is not quite right with me	202	4.36 ± 1.46	0.16*	0.02
5. I notice very early when I'm getting sick	199	4.05 ± 1.55	0.17**	0.05
6. I often feel that something itches or feels too tight	199	2.56 ± 1.76	0.19*	0.18*
7. I take off all jewelery and my watch as soon as I get home	200	2.91 ± 2.10	0.11	0.16**
8. I think a lot about my body	202	3.30 ± 1.73	0.25*	0.19*
9. I think a lot about my health	201	3.75 ± 1.67	0.29*	0.24*
10. I take all symptoms seriously	201	4.10 ± 1.50	0.12	0.11
PBS sum score (range, 10–60)	202	37.46 ± 9.78	0.30*	0.21*

*$p < 0.04$.
**$p < 0.05$.

room in this group (OR 2.78 per each 5-point increase). There was no interaction between acupuncture and PBS in those receiving gynecologic surgery.

DISCUSSION

The study has shown no significant impact of PBS on the main treatment outcome for the entire group. However, an exploratory analysis reveals a complex relationship between the efficacy of acupuncture and PBS in patients receiving breast surgery. The interaction between PBS and acupuncture treatment did not reach significance. This means that PBS as a predictor seems to be independent of the kind of acupuncture applied. One reason for this result could be that the size of the study is possibly too small to detect a probable interaction.

However, patients with higher PBS had a lower treatment response in this group. This result does not conform to the initial hypothesis of a positive relation between PBS and treatment response. One explanation might be that treatment response could be affected by some tendency for somatization. Noticeably, certain questions (e.g., questions 3, 6, 8, 10) of the PBS questionnaire are similar to some cognitive aspects of somatization as described by Rief et al. (1998). In their study, the perception of minor autonomic body sensations (e.g., "I hate to be too hot or too cold") and the self-concept of being weak (e.g., "I am physically rather weak and sensitive") showed significant correlation with the somatization index. Kreitler et al. (1987) have shown the influence of cognitive aspects such as goals, norms, and beliefs about oneself and general beliefs on treatment response, but these were not associated with some kind of PBS. With respect to those findings, it should be taken into consideration that the patients with higher PBS could have a higher emotional or cognitive intolerance to bodily reactions such as nausea.

Interestingly, these relationships could not be found in the group receiving gynecologic surgery. In this group there

TABLE 3. PREDICTORS OF POSTOPERATIVE NAUSEA AND VOMITING (PONV) FOR BREAST SURGERY AND GYNECOLOGIC SURGERY

	PONV in recovery roomPONV within 24 hours					
	OR	*95% CI*	p	*OR*	*95% CI*	p
Breast surgery (n = 115)						
Kind of acupuncture (true/sham)	0.75	0.32–1.73	0.50	1.09	0.52–2.30	0.82
PBS (10-point increase)	**1.63**	**1.02–2.58**	**0.04**	**1.55**	**1.03–2.33**	**0.04**
Anxiety (5-point increase)	0.91	0.39–2.12	0.83	1.70	0.79–3.66	0.18
Depression (5-point increase)	0.58	0.25–1.38	0.22	1.16	0.54–2.49	0.70
Interaction between acupuncture and PBS	1.69	0.61–4.69	0.32	1.98	0.80–4.87	0.14
Gynecologic surgery (n = 80)						
Kind of acupuncture (true/sham)	**0.36**	**0.15–0.89**	**0.03**	0.42	0.17–1.06	0.07
PBS (10-point increase)	1.17	0.74–1.84	0.51	1.15	0.72–1.83	0.56
Anxiety (5-point increase)	0.89	0.37–2.16	0.80	1.24	0.50–3.07	0.64
Depression (5-point increase)	2.27	0.91–5.63	0.08	**2.78**	**1.07–7.24**	**0.04**
Interaction between acupuncture and PBS	1.09	0.42–2.82	0.85	0.78	0.29–2.08	0.62

OR, odds ratio; CI, confidence interval; PBS, perception of bodily sensation.
Significant results are bolded.

was a clear tendency towards treatment response within the recovery room depending on the kind of acupuncture applied, sham or true, as we pointed out elsewhere (Streitburger et al., 2004). There seems to be a dominant effect of acupuncture itself, perhaps strongly mediated by some physiologic mechanisms, so that the PBS plays no role.

The relation between PBS and treatment outcome of patients with breast surgery could reveal another mechanism of efficacy of acupuncture. For example, treatment response seems to be related to increases in vagal tone during therapy, as pointed out by Chambers and Allen, who showed the influence of acupuncture on depressive disorders parallel to the responsiveness of the autonomic nervous system (Allen et al., 1998; Chambers and Allen, 2002). It could be speculated that there may also be some connection between reduced responsiveness of the autonomic nervous system and high PBS.

Further investigation is needed, to explain the interaction between efficacy of acupuncture, the autonomous nervous system, and the psychologic aspects mentioned above. This could also lead to a differentiated understanding of the efficacy of acupuncture as a part of transcultural medicine, where some aspects of efficacy in connection with the influence on the autonomic nervous system have also been shown over time (Bernardi et al., 2001; Chambers and Allen, 2002; Lehrer et al., 1999).

There are some other limitations in our study. Given the lack of questionnaires that measure body sensations specifically in patients undergoing acupuncture, it was necessary to develop a new body sensations questionnaire before the beginning of this study. Because of time constraints, we were not able to perform an extensive qualitative study. The baseline assessment of this study was used to assess psychometric properties of the questionnaire, and also to predict responses to therapy. Optimally, the validation of the questionnaire and its use to predict treatment outcome should have been done in independent studies. However, this was not possible here, and future studies might evaluate the validity and utility of the questionnaire as a self-administered measure of body sensations in patients undergoing acupuncture. Still to be done are evaluations of retest reliability and validity of the questionnaire.

However, the newly developed body sensation questionnaire proved to have reasonable item difficulty and internal consistency. Content validity was approved by experienced acupuncturists, and the fair correlation with both depression and anxiety indicate that the bodily sensation questionnaire measures a construct that is relatively independent from anxiety and depression. Thus, the bodily sensations questionnaire might serve as a preliminary measure to assess relevant body sensations in patients undergoing acupuncture.

As a result of these limitations, particularly as the results are based on exploratory findings, further prospective studies are necessary to evaluate the impact of bodily awareness on treatment response in acupuncture.

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