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EFFECT OF STIMULATION OF THE P6 ANTIEMETIC POINT ON POSTOPERATIVE NAUSEA AND VOMITING

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SUMMARY

The antiemetic action of stimulation of the P6 (Neiguan) acupuncture (ACP) point has been studied in women, premedicated with nalbuphine 10 mg, undergoing minor gynaecological operations under methohexitone–nitrous oxide–oxygen anaesthesia. Invasive ACP—manual or electrical at 10 Hz—applied for 5 min at the time of administration of the premedication markedly reduced the incidence of vomiting and nausea in the first 6 h after operation, compared with untreated controls. This did not occur with stimulation of a "dummy" ACP point outside the recognized ACP meridians. Non-invasive methods (stimulation via a conducting stud or by pressure) were equally as effective as invasive ACP during the early postoperative period. However, both these non-invasive approaches were less effective than invasive ACP in the 1–6 h postoperative period, although each was as effective as two standard antiemetics (cyclizine 50 mg, metoclopramide 10 mg). In view of the total absence of any side effects in more than 500 ACP procedures, the clinical applications of this finding are worthy of further study.

On a visit to mainland China [1] the senior author observed women in an antenatal clinic being instructed to press a point on the right forearm as a preventative against morning sickness. An antiemetic point, P6 (or Pe 6)—so called because it is the sixth point on the pericardial meridian—is mentioned in English language text books on acupuncture [2–4], but with no evidence to show its efficacy. The Belfast Department of Anaesthetics had previous experience of studying antiemetics under clinical conditions using "opioid premedication-postoperative sickness" as a model [5–7], and it was decided to test the efficacy of stimulation of P6 under these circumstances.

This paper reports the findings of our study which took more than 5 years to complete and involved more than 500 patients. Some of the findings have been published previously, either in the form of preliminary reports [1, 8, 9] or as abstracts of work presented at scientific meetings [10–20]. An attempt is made here to put the various parts of this work into perspective. During the early part of the study, which involved invasive acupuncture (ACP), Fry reported beneficial antiemetic effects from pressure on the P6 point in the postoperative period [21] and this and another non-invasive approach have been included in the programme.

The study evolved gradually as results became available, and eventually covered a much wider field than was envisaged originally. This pattern of progress is reviewed before describing the method in detail. It should be noted that the objective was to see if acupuncture, or a modification of the ACP technique, had any antiemetic action; there was no attempt to explain how it worked. It included a limited comparison of the relative efficacy of ACP and clinical doses of three commonly used antiemetics.

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Course of study

This began with an "open" comparison of the incidence of perioperative sickness in two comparable groups, each of 25 women, having the same premedication, anaesthesia and operative procedures. One group had manual ACP needling at P6 point for 5 min at the time of administration of the premedication (meptazinol 100 mg); the other had the premedication only. Those having ACP had a lower incidence of sickness compared with the controls, the difference being significant during the first 1 h after operation [10]. More important, it showed that a model which had been used in other antiemetic studies [5–7] could be adapted to a study of P6 ACP. When presented at a scientific meeting, this work was criticized for lack of a "dummy ACP" group to exclude the psychological effect of the procedure. It also showed an unacceptably high incidence of sickness with this premedication, a feature not anticipated when the study was started.

In the next study, the premedication was nalbuphine 10 mg, which provided an acceptable degree of sedation for most patients. This second study incorporated the use of a dummy point (outside the accepted ACP meridian) near the right elbow. In random order, patients had either P6 ACP, "dummy ACP" or no treatment. There were 25 patients in each group [1], but the P6 and control groups were later increased to 31 [11]. Ethics Committee approval limited the dummy group to 25 patients.

A limited study was carried out with pethidine 75–100 mg [12]. This was chosen as a more widely used premedicant than nalbuphine: P6 ACP and control subjects with this premedication were interspersed at random in the latter part of the nalbupine–manual ACP study. The results of this are not presented here as they add no additional data to the nalbuphine study. Thereafter, nalbuphine 10 mg was the only premedication used. As preoperative sickness is uncommon with this drug, observations were limited to the postoperative period.

In all subsequent studies further "control" and P6 manual ACP subjects were included at random to a total of 56 in each series, with additional dummy ACP studies to a total of 30.

The application of a DC electrical stimulus (electro ACP: ACPe) to the ACP needle was next studied. An open comparison of various frequencies, ranging from 2.5 to 1000 Hz, for varying times (5–15 min), showed which were the most promising (10 Hz, 5 min) and in random order this was compared with manual ACP and with two antiemetics given i.m.—cyclizine 50 mg and metoclopramide 10 mg. Initially, droperidol 2.5 mg was included in this comparison, but it was withdrawn after a high frequency of restlessness necessitated "breaking the key" and revealing this as the causative drug [8, 15].

Non-invasive methods of applying a stimulus to the P6 point were studied next. The first of these was the use of a conductive "stud" applied to the forearm (ACPs). An initial open study showed three frequencies and duration of stimulus which merited investigation and each of these was studied in 31 patients, with further control and manual ACP subjects [19]. There was some overlap between this and the previous study.

The final study involved "Sea bands", a commerically-available stud in an elasticated band which easily fitted the forearm. This is referred to as "Acupressure" (ACPx). This was applied before administration of the premedication and patients were asked to press it for 5 min each hour before and after operation. In the first 25 patients the recovery ward staff reminded the patients in the postoperative period [20], while in the last 20 a research nurse was available to follow the patients and encourage them to press the stud.

Antiemetic point

There are several points to which antiemetic activity is ascribed, but only P6 was used in this study [17]. This is commonly termed "Neiguan" (inner pass), but is referred to also as Nei-kuan or HC6 on the Arm Absolute Yin (heart constrictor) meridian [4].

Neiguan is situated two "Chinese inches" proximal to the distal wrist crease, a Chinese inch (Cun) being the width of the intraphalyngeal joint of the thumb [3, 17]. It lies approximately 1 cm deep to the skin between the tendons of flexor-carpi radialis and palmaris longus.

Stimulation of P6

In invasive ACP a fine (24–28 swg) 3–4 cm needle is inserted (without local anaesthesia) to a depth of approximately 1 cm. Verification of correct position is obtained by the occurrence of a non-anatomically distributed sensation (chi) over the whole hand. The occurrence of paraesthesiae along the course of the median nerve indicates the

the needle is too deep. This sense of heaviness or pressure, which occurs in about 85% of patients, persists throughout the period of stimulation.

Stimulation can be performed by manual rotation of the needle (ACPm) or it can be connected to a battery-operated DC square wave stimulator (Shackman JR-863-4 or Meridian), with the neutral lead held in the other hand, attached to an indifferent point or attached to the other limb (ACPe).

Non-invasive electro stimulation of P6 was made via a gold plated rare earth cobalt magnet conducting stud (ACPs) embedded in a rubber casing. Three frequencies were evaluated: unilateral 5 Hz, bilateral 2.5 Hz, bilateral 10 Hz, each applied for 5 min. The application for 5 min of pressure via a band and stud (ACPx) completed the study [20].

The right hand was used until the last part of the study, when a retrospective analysis of data suggested that best results were obtained by use of the dominant hand [22]. This was not considered to be important, as only 7% of a hospital population said they were left-handed.

PATIENTS AND METHODS

The study, which was approved by the University Medical Ethics Research Committee, was carried out in women (16–50 yr, 45–80 kg) scheduled for minor gynaecological operations under general anaesthesia. Premedication was with nalbuphine 10 mg given i.m. by the anaesthetist 60–90 min before operation. Atropine was not given. ACP, in one form or other, was applied at the same time as the premedication. Anaesthesia was induced with methohexitone 1.6 mg kg^{-1} and continued with nitrous oxide in oxygen and intermittent doses of the barbiturate as required. No volatile agents or i.v. opioids were used.

The nature of the study was explained to the patient and verbal permission for inclusion obtained before administration of the premedication. All were told that the study was designed to reduce side effects and improve the efficacy of the premedication; nausea and vomiting were not mentioned at this stage, but a full description of the study objectives were given at the time of the last postoperative visit.

Patients were visited at 1 h and 6 h after operation by a person who was unaware of the preoperative treatment. At both times, observations included the occurrence of vomiting (V) including vomiting with nausea or retching, or nausea (N) alone.

TABLE I. *Basis for pooling data from two successive control (no treatment) and three ACP series. V = vomiting ± nausea or retching; N = nausea alone*

			Time after operation (h)								
			0–1			1–6			0–6		
		n	V	N	—	V	N	—	V	N	—
Controls	a	25	3	12	10	3	12	10	6	11	8
	b	31	3	14	14	5	14	12	8	13	10
Total		56	6	26	24	8	26	22	14	24	18
ACP Manual	a	25	3	3	19	0	3	22	3	3	19
	b	31	4	3	24	0	3	28	4	3	24
ACP Electro		31	1	1	29	2	3	26	4	2	25
Total		87	8	7	72	2	9	76	11	8	68

TABLE II. *Mean (SEM) duration of anaesthesia in the various series of patients*

Series	*n*	Duration (min)
Control (no ACP)	56	8.71 (0.41)
P6 acupuncture (ACPm and ACPe)	87	10.11 (0.49)
P6 studs (ACPs)	93	9.48 (0.25)
P6 Sea bands (ACPx)	51	9.49 (0.48)
"Dummy" acupuncture	30	9.71 (0.56)

Statistical comparisons were made with χ^2 test (df = 2, except in three comparisons when N and V figures were combined).

Of the six authors one (J.W.D.) participated in all parts of the study and three (G.G., K.T.J.F., A.G.A.L.) for the greater part of it. The others were each involved for at least 1 year. As far as was possible, at least two of the authors were involved with each individual patient, but on occasions the anaesthetic was given by another member of the academic staff.

Presentation of findings

As this was a continuing study, a number of "control" and P6 ACP (manual or electro) observations were made with each successive variation in procedure. Thus an early paper refers to 25 "control" patients [1] and a later paper to 31 [8]. This review is based on total observations in each series, irrespective of when they were made. Examples of comparability of successive studies are given in table I. Similarity of results was found also with successive ACPs and ACPx studies and justified the pooling.

Comparability of series has also to be considered. The patients were all women and drawn from a limited age and weight range. However, the duration of anaesthesia may affect markedly the incidence of sickness, particularly with short duration administration of nitrous oxide–oxygen [23] and in the operations involved in this study [5]. The mean duration of anaesthesia was comparable in all six groups (table II) and also within the various series (total number of patients 317). An additional 62 patients received the antiemetics and the average duration of their anaesthesia was within the same range as for the other studies.

RESULTS

Preanaesthetic sedation was adequate in almost all patients and only two of more than 500 patients approached refused to take part in the study. Anaesthesia was satisfactory throughout and no patient complained of side effects from the acupuncture or its modifications.

The pooled data in the five series are given in table III.

TABLE III. *Incidence of sickness at the time of observation noted in the postoperative period in women premedicated with nalbuphine 10 mg and the treatments indicated. V = vomiting ± nausea or retching; N = nausea alone*

		Time after operation (h)								
		0–1			1–6			0–6		
	n	V	N	—	V	N	—	V	N	—
Controls	56	6	26	24	8	26	22	14	24	18
Invasive ACP (P6)	87	8	7	72	3	8	76	11	8	68
Dummy ACP	30	4	9	17	2	12	16	7	13	10
Non-invasive ACPs	93	12	7	74	14	18	61	18	16	59
Non-invasive ACPx	51	3	1	47	7	14	30	7	15	29

At all times of observation invasive acupuncture (ACPm and ACPe) was followed by a significantly lower incidence of sickness than the control group ($\chi^2 = 29.9$ (0–1 h), 34.2 (1–6 h), 32.2 (0–6 h); df = 2; $P < 0.001$). This benefit was not produced by dummy ACP (0–6 h; $\chi^2 = 0.32$; df = 2; $P = 0.98$). The 87 patients having P6 ACP had less postoperative sickness than the 30 having dummy ACP ($\chi^2 = 10.2$ (0–1 h), 16.2 (1–6 h), 22.9 (0–6 h); df = 2; $P < 0.006$–0.001).

The pooled data from the 93 patients having ACPs showed significantly less sickness than the control group ($\chi^2 = 31.2$ (0–1 h), 13.0 (1–6 h), 15.7 (0–6 h); df = 2; $P < 0.001$). With ACPx a significant difference from the control group was found only in the first 1 h after operation ($\chi^2 = 31.4$; df = 2; $P < 0.001$).

All four acupuncture treatments, both invasive (ACPm and ACPe) and non-invasive (ACPs and ACPx) were of similar efficacy in reducing sickness during the first 1 h after operation. However, invasive ACP was followed by less sickness in the 1–6 h period than either ACPs ($\chi^2 = 11.11$; df = 1; $P < 0.01$) or ACPx ($\chi^2 = 14.7$; df = 1; $P < 0.01$). This was shown by the lesser overall (0–6 h) efficacy of these non-invasive approaches.

Figure 1 presents graphically the findings in the various groups and in those patients receiving either cyclizine 50 mg or metoclopramide 10 mg. Their efficacy was similar to that of the non-invasive methods described: equally effective to invasive ACP in the first 1 h after operation, but significantly less effective ($P < 0.025$) in the 1–6 h period. No side effects were noted with the antiemetics.

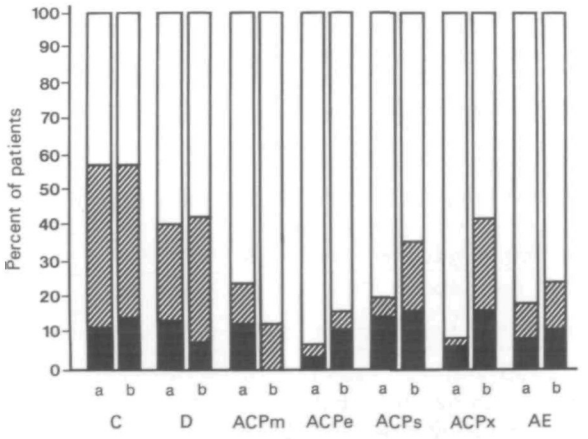

FIG. 1. Percentage incidence of postoperative vomiting (including nausea and vomiting and retching; black columns) and nausea (cross-hatched columns) in groups of patients premedicated with nalbuphine 10 mg and treated with stimulation of the P6 acupuncture point: ACPm = manual ACP; ACPe = electro ACP; ACPs = indirect stimulation via a conducting stud; ACPx = acupressure (Sea bands). C = Control; D = data for stimulation of a "dummy" ACP point; AE = patients premedicated with standard antiemetics (cyclizine 50 mg and metoclopramide 10 mg). a = 0–1 h; b = 1–6 h.

DISCUSSION

The pooling of data from various studies may be criticized [24], but the setting of all the studies was standardized (standard patient population, similar type of operation, duration of anaesthesia

and anaesthetic technique). The temporal dispersion of the different parts of the study was not great; with the exception of the initial comparisons, the other parts were performed in parallel and control cases were included in each facet. There were no "within group" changes as the study progressed. The limited number of patients subjected to "sham acupuncture" may be criticized, but in our opinion ethical consideration did not allow persistence with a technique which we had shown to be ineffective.

These observations show that, under appropriate conditions, stimulation of the acupuncture point P6 had an effective antiemetic action, not shared by stimulation of a sham ACP point. In this action P6 ACP was as effective as cyclizine 50 mg or metoclopramide 10 mg. Invasive needling of P6, with either manual or electrical stimulation, had a more prolonged antiemetic action than transcutaneous stimulation (electrical or manual), but nevertheless the latter was of clinical value and more acceptable to some patients than needling. The brevity of action of acupuncture antiemesis, demonstrated here and elsewhere [25] was contrary to experience with its use in other fields where administrations are carried out usually at intervals of several days [26].

With the exeption of the work of Fry [21], who used acupressure, there were no other comparable studies until recently. However, a New Zealand study, using an opioid-based anaesthetic technique, failed to demonstrate any antiemetic action from P6 ACP carried out during anaesthesia [27]. A similar study from Belfast with ACP given during anaesthesia showed ACP to be less effective as an antiemetic than droperidol [28, 29]. This suggests that, despite the failure of ACP at a point other than P6 to have a demonstrable antiemetic action, there may be a strong psychological element in acupuncture antiemesis. However, more recent work demonstrates that the timing of ACP in relation to the administration of the emetic studies is important. Using the same naluphine-operation model as in these studies, Dundee and Ghaly [30] failed to demonstrate antiemetic activity when the ACP was carried out immediately before induction or during anaesthesia. Thus it would appear that, to be effective as an antiemetic, ACP must be applied before the emetic stimulus [31]. This agrees with our studies in oncology when we found that P6 ACP was effective as an antiemetic only when it was given before chemotherapy [25].

Nalbuphine is not a commonly used premedicant; it is similar to morphine in the time course of its emetic effects, with most nausea and vomiting occurring in the postoperative period. It differs from meptazinol and pethidine which have an earlier onset of emetic effect, with frequent preoperative sickness. P6 ACP was effective as an antiemetic with all three drugs, suggesting that the antiemetic action is manifest soon after its administration. In other studies we have confirmed that, when a prolonged antiemetic action is required, as after cisplatin, then clearly an invasive technique would be superior to the use of studs or bands [32].

The sedative effect of nalbuphine 10 mg was so satisfactory that any minor additional soporific effect of ACP would not have been detected. We cannot comment on this aspect of ACP therapy as it was not studied. In this and other studies, we have carried out more than 1000 administrations with no side effects.

Mann [26] considered that "the only thing of importance in acupuncture is to stimulate the right place, the nature of the stimulus being of secondary importance". While this may apply to relief of pain and needling of trigger points, our findings with ACPs and ACPm show that it does not apply to the prevention of opioid-related postoperative sickness. A stimulus of 10 Hz applied for 5 min was an effective antiemetic; prolonging the period of stimulation to 15 min or increasing the stimulus to 100 Hz reduced its efficacy [8]. Nevertheless, our findings with stimulation of a dummy point in this study and in patients with sickness induced by cancer chemotherapy [25, 33] and in other fields show that careful attention should be paid to the point of stimulation.

Almost all the research work on the mode of action of ACP is related to its use in pain [34]. We can offer no explanation for our findings: the endorphin explanation for the analgesia induced by ACP [35–40] is unlikely to apply here, as opioid activity is associated with vomiting rather than antiemesis.

Prevention of nausea and vomiting is not listed among the generally accepted use of acupuncture [3], nor does it appear in the W.H.O. list of indications for its use. Our findings are sufficiently impressive to encourage others to explore this in more detail. It is 5 years since our first studies were presented and more than 4 years since the first publication, and we still await others to take

up the challenge of confirming or refuting our findings. It is difficult to envisage the eventual use of ACP antiemesis in clinical practice. Under the conditions of this study it is as effective as the commonly used antiemetics; moreover we found it to be completely devoid of side effects. While much postoperative sickness may be prevented by avoiding the use of opioids, this simple remedy cannot be applied to all drug-induced emesis. One such situation is cancer chemotherapy and it is in this or similar fields that acupuncture may prove valuable as a non-toxic antiemetic.

The report of the British Medical Association Board of Science and Education on Alternative Therapy comments that techniques such as acupuncture should, where possible, be subjected to modern methods of study [41]. One criticism of research in this field is the small number of patients involved [42, 43]. This paper is an attempt to answer both these points. It has been suggested that acupuncture should not be used therapeutically as a single entity, but only as part of the total alternative approach to medicine [44]. Our studies suggest that this is fallacious [45]; we should look at the best aspects of Chinese medicine and study them as an adjuvant to (or complement to) Western medicine, and not as an alternative therapy.

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