Acupuncture prophylaxis of cancer chemotherapy-induced sickness

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Summary

In a multi-facet study we evaluated the efficacy of P6 electroacupuncture (10 Hz applied for 5 min) as an antiemetic in patients receiving a variety of cancer chemotherapy drugs. The study involved 130 (15 in an open pilot study, 10 in a randomized placebo controlled crossover study and 105 in a definitive study) patients who had a history of distressing sickness after previous treatment, and who, on the basis of a previous survey, would be expected to have a 96% chance of this with subsequent therapy. Sickness was either completely absent or reduced considerably in 97% of patients and no side effects were encountered. The limited crossover study, using a 'dummy' acupuncture (ACP) point showed that the beneficial effects were limited to the P6 point. Logistic and ethical considerations excluded the possibility of carrying out a larger placebo-controlled study. While in our hands P6 ACP was an effective antiemetic in patients having cancer chemotherapy, because of the time involved and the brevity of the action (8 h) an alternative approach to electro-ACP is required before this technique is adopted clinically.

Introduction

Despite advances in the treatment of malignancy, many patients cannot tolerate the sickness which follows effective chemotherapy[1]. The relative ineffectiveness of tolerable doses of available antiemetics is shown by the multiplicity of publications on the subject[2-5]. Cisplatin sickness can be mitigated by an intensive five-drug regimen involving high doses (1 mg/kg) metoclopramide, with diphenhydramine, dexamethasone, diazepam and thiethylperazine[6,7], although at the expense of marked sedation, while encouraging results have been reported with less complicated regimens all including dexamethasone and metoclopramide[8-10].

As a result of our experience in reducing postoperative sickness with P6 acupuncture (ACP), manual or electric[11-14] and the complete absence of side effects from this technique it was felt that there could be a place for this in patients having cancer chemotherapy. It has been stated[15] that 'the treatment of chemotherapy-induced nausea and vomiting is often approached without enthusiasm by the oncology team, partly because of the lack of effectiveness of some of the more widely used antiemetics and also because the oncologist's first priority is to treat the cancer'. We here report a study carried out at our local radiotherapy centre where radiotherapists and anaesthetists collaborated in evaluating the potential use of ACP in preventing post-chemotherapy sickness. The general plan of the study, which involved 130 patients, was approved by the University medical ethical research committee.

Incidence of sickness

To assess the extent of the problem, in the local population, over a period of one month, 71 consecutive adult outpatients of both sexes were questioned. These were under the care of five consultant oncologists and there was a wide spectrum of both types of tumour and treatments. They were asked about emetic symptoms following their treatments: when they started? How long they lasted? How severe were they? Did they disturb sleep? Could they eat meals normally? The antiemetics used and their effectiveness were also noted.

Of these patients, 54 (76%) had distressing emetic symptoms (vomiting on several occasions, troublesome nausea for at least 8 hours and often thoughts of stopping treatment because of sickness) following chemotherapy, of whom 52 (96%) complained of further distressing sickness after subsequent treatment. Sickness usually started within 2-3 hours of the treatment, but in some it was delayed for 6-8 hours; in many patients the problem persisted for 4-5 days. In our survey mitozantrone, used in the treatment of breast carcinoma, was associated with the lowest incidence of emetic side effects, while cisplatin, used in the treatment of testicular neoplasms, was always followed by sickness. It appears that if a patient is sick after chemotherapy, this sickness is likely to accompany a subsequent administration and tolerance does not appear to develop to the emetic side effects of cancer chemotherapy agents.

Problems of acupuncture studies

The British Medical Association[16] report on alternative therapy points out that 'new and unconventional techniques should be evaluated with the same scientific methods as have been applied to therapeutic methods now known', but agrees that 'for many therapies a formal trial would be quite inappropriate'. From experience gained in this work the situation with ACP and cancer chemotherapy sickness appears to lie between these extremes. Patients have a serious complaint and the dosage and nature of the chemotherapy should not be affected by the antiemetic. Furthermore, until the efficacy of ACP was established in this group of patients it was not justifiable to stop currently used antiemetics (usually metoclopramide and prednisolone). 'Anticipatory' sickness occurs in

●Dr Lynch has died since this paper was written.

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some patients, based either on previous experience or on hearsay from others[1,17,18] and this points to the need of using a placebo which, in this situation, is a 'dummy' point outside the accepted ACP meridians[12]. The problems of getting informed consent for such a procedure, which on the basis of antiemetic studies in other fields was unlikely to be beneficial for the patient, was overcome by adopting the scheme described by Zelen[19]: patients requiring repeated ACP were told that while P6 was our standard treatment if they were agreeable, we would like to try another point on one occasion but revert to P6 if this was not successful, in other words, we wished to know which of two ACP points would be best for them.

One cannot get informed consent for ACP from chemotherapy patients without explaining the objective of the study thus giving them expectations of a beneficial outcome. A large no-treatment group is ethically unacceptable. Even when the person doing the follow-up does not know whether P6 or 'dummy' ACP points were used, patients often show the site of the needle and a completely 'double blind' study proved impossible.

However, the criteria for assessing benefit can be standardized. Counting the number of emetic episodes[20,21] is impractical in outpatients and more difficult than a comparison by the patient of the severity of sequelae before and after the test treatment: here the benefit of ACP can readily be graded.

The majority of patients attending an oncology outpatient department are for repeat treatments and those who had previous experience of emetic symptoms were more than willing to participate in a study. Those attending for the first time present problems, as the mention of antiemetics often suggests that they are likely to have problems with sickness. An unrewarding study of ACP in these patients is reported elsewhere[22].

Pilot study

As this was a new field for the use of ACP it was necessary to do a small open pilot study. This was carried out in 15 patients who had been very sick after a previous course of chemotherapy and to whom the objectives of the study were clearly explained. The antiemetics given with the previous dose of chemotherapy were continued. ACP (q.v.) was given immediately before or shortly after chemotherapy and patients were seen either on the evening of treatment or on the next morning.

In Table 1, a good result refers to complete or almost complete absence of symptoms over a period of 8 hours, when these had previously been troublesome. The inpatients received cisplatin, after which vomiting had previously been severe and persistent, whereas nausea was the main complaint of the outpatients. The severity and frequency of both was reduced by ACP. Most of the patients were enthusiastic about the outcome and requested further treatment, thus encouraging us to continue the study. Two outpatients stopped their antiemetic (metoclopramide) which they felt was causing excessive sedation.

Table 1. Results of open pilot study in which P6 electro ACP (10 Hz) was applied for 5 min after administration of chemotherapy. All patients had been sick from a previous course of therapy

	Number	Benefit Good	Poor
Outpatients	10	8	2
Inpatients	5	4	1
Total	15	12	3

Main study

Method

Following the pilot study the method of treatment was standardized. Outpatients with a history of troublesome nausea and/or vomiting following previous cancer chemotherapy, were referred to the anaesthetists by the oncologist. The nature of the investigation having been explained to the patient and a history of emetic symptoms taken, permission was sought from each patient to partake in the study. Following the results of a haematological test, to rule out leucopenia, the consenting patient had electro ACP administered at P6 point for 5 min, followed immediately by cancer chemotherapy.

The ACP was applied using a standard sterilized (or disposable) 32 swg ACP needle. It was inserted to a distance of approx. 10 mm at the P6 point[12] and a second needle inserted in a neutral point (with no known antiemetic properties). The P6 point (Neiguan) is located 2 'Chinese inches' (a Chinese inch 'cun' is approximately the width of the intra-phalangeal joint of the thumb) from the distal wrist crease and lies between the tendons of palmaris longus and flexor carpii radialis. Electrodes were attached from these needles (positive to P6 and negative to the neutral point) to a battery-operated Shackman JS 863-4 ACP machine. This has a variable frequency which was set to 10 Hz in all cases, and a variable power (DC) output from 0 to 60 mN. This was slowly increased until the patient could 'feel' the current in the needles, but never to a point where pain was experienced. The non-anatomically distributed sensation, known as Chi[12] was experienced by most patients, who found it to be pleasant. Stimulation was maintained for 5 min.

When emetic symptoms following chemotherapy had previously been limited to the day of treatment only, then the patient was asked to note the degree of sickness at this time following the chemotherapy and ACP. When the emetic symptoms persisted longer than the day of treatment or did not start or several hours after treatment the patients were visited at home on the evening and twice daily thereafter as necessary when the severity of sickness experienced since the previous visit was noted and ACP was repeated as necessary.

Inpatients admitted for treatment or persistent nausea and vomiting had the same explanation of the study and application of the ACP as for outpatients. All inpatients were seen twice daily and some participated in the cross-over study.

Crossover study

Since many inpatients required repeat ACP it was possible, with the explanation mentioned above, to use a 'dummy' point at the right elbow on one occasion and to revert immediately to P6 ACP if this proved ineffective. Ethical considerations required an analysis of data after 10 patients, following which the use of a dummy point was discontinued.

Grading findings

Patients were asked to grade their sickness on a four-point scale: A, worse than before; B, same as before; C, less than before; D, completely absent. On the basis of this data the effects of ACP were classed as very good (complete absence of symptoms), good (some benefit or benefit for a short period) or poor.

Results

The findings of the crossover study which have been presented elsewhere in detail[23] are summarized in Table 2 and show a marked improvement after P6, but not after 'dummy' ACP.

Table 3 shows very good results from acupuncture in all groups, with 63% of patients having complete absence of sickness for at least 8 hours and only 5% showing no benefit at all. The least satisfactory results occurred in those patients receiving cisplatin, but even in these only 3% failed to have some benefit from the ACP.

There were no side effects attributable to ACP and no patient 'dropped out' owing to this treatment.

Discussion

This study not only demonstrates the efficacy of P6 acupuncture as an antiemetic but also highlights some of the problems involved in studies of this type. Lewith[24] has criticized published ACP studies because of small numbers but this does not apply to the present work. We found that the criteria he set out for acceptable studies[25] could not be fully achieved in the clinical setting of cancer chemotherapy side effects. The local ethical committee's request for a preliminary open pilot study may have affected some of our early findings, but this insistence was understandable, as was their request to analyse the findings of the first 10 patients in the crossover study.

While one cannot offer a scientific explanation for the findings based on Western medical knowledge, it is difficult to ignore a success rate of 97% in a total 130 treated patients. In most of our patients the standard antiemetics (metoclopramide and prednisolone) were not stopped and it may well be that ACP, by means as yet unknown, adds another approach to the relief of vomiting. Unlike other multitherapy approaches, in our hands ACP carried no side effects.

The emotional-expectation-placebo aspect cannot be completely ruled out and despite the findings shown in Table 2, this may play an important aspect in the efficacy of ACP[26] as we believe it does in reducing the sickness of early pregnancy[27]. It is interesting to note that when ACP was used for disabling breathlessness, the subjective improvement was much greater than the objective results[28]. One may look on nausea as being subjective, yet in our postoperative studies, when the incidence of nausea alone and that of vomiting (with or without nausea) were both recorded the beneficial effects applied to both aspects of sickness[29]. Perhaps we are too concerned with the scientific aspects of the problem[30] rather than concentration on improving the quality of life for the patient[31] irrespective of how this is achieved.

Brevity of the emetic action of ACP, as practised by us, is a major problem. Patients often required repeat ACP on the evening of their treatment necessitating a home or hospital visit which was only possible because of availability of a full-time research worker. Furthermore ACP, as described here, is too time-consuming to offer any hope of being adopted as a routine. We are currently studying the use of acupressure and application of DC current to 'studs' placed on the P6 spot. If successful, either of these could be used by the patient at home.

In a situation where up to 20% of patients may stop potentially curative treatment because of side effects[32] ACP has proved an effective antiemetic in our hands and we would encourage others to see if these results can be reproduced. However, as recent

Table 2. Effects of P6 when compared with 'dummy' ACP on a randomized crossover study in 10 patients

	Effects of acupuncture		
ACP point	*Very good*	*Some benefit*	*No benefit*
P6	5	5	0
Dummy	0	1	9

Table 3. Effects of P6 electroacupuncture in 105 patients who were sick following a previous course of cancer chemotherapy

				Benefit		
n	*Sex*	*Malignancy*	*Chemotherapy*	*Very good*	*Good*	*Poor*
Inpatients						
29	M	Testes	Cisplatin Etoposide Bleomycin	16	12	1
5	F	Lymphoma	Cyclophosphamide Doxorubicin Vincristine ±Prednisolone	2	3	0
Outpatients						
28	F	Breast	Mitozantrone	19	9	0
36	F	Breast	Cyclophosphamide Methotrexate 5 Fluorouracil	27	6	3
7	M/F	Lymphoma	Cyclophosphamide Vincristine ±Doxorubicin ±Prednisolone	2	3	2

experience of ACP as a perioperative antiemetic has shown[33,34] one must appreciate that even minor changes in the protocol could affect the outcome, particularly if the ACP is applied some time after administration of the chemotherapy. In such studies one would suggest that recent views[35] on ethics of decision making should be considered.

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