

## Short communication

# A pilot study of metoclopramide, dexamethasone, diphenhydramine and acupuncture in women treated with cisplatin\*

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**Summary.** A total of 26 women who submitted to cisplatin chemotherapy received as antiemetic treatment a combination of metoclopramide, dexamethasone and diphenhydramine. Acupuncture according to traditional Chinese medicine was also carried out. The results were compared with those obtained in a similar group of women with cancer, who were treated in the same setting with the same antiemetic combination but without additional acupuncture. Acupuncture was shown to increase complete protection from nausea and to decrease the intensity and duration of nausea and vomiting. However, the difficulties of performing acupuncture routinely in daily practice are a hindrance to its wider use.

## Introduction

Preliminary data suggest that acupuncture could reduce emesis induced by cisplatin (CDDP) chemotherapy in cancer patients [1], but the evidence is meagre; the use of acupuncture should be further explored. We therefore conducted a study to verify whether the addition of acupuncture to a standard antiemetic treatment could improve drug efficacy in a group of patients who were at high risk of experiencing emesis from CDDP chemotherapy despite the administration of appropriate antiemetic treatment [3].

## Patients and methods

From April 1988 to January 1989, all consecutive women who were hospitalized in the Medical Oncology Division of Perugia and who submitted to CDDP combination chemotherapy at doses of  $\geq 50$  mg/m<sup>2</sup> were entered in the study. Criteria for exclusion were a Karnofsky performance status of  $<60$ , contraindications to antiemetic drugs used,

the presence of nausea and vomiting from other causes, cerebral metastases and contemporary use of narcotics and/or CNS sedatives.

After giving their informed consent, all patients received the same antiemetic treatment: metoclopramide (3 mg/kg i.v. 30 min before CDDP and 1.5 h afterward) plus dexamethasone (20 mg i.v.) and diphenhydramine (50 mg i.v.), both given 30 min before CDDP. Acupuncture according to traditional Chinese medicine was also carried out. A needle was placed in the 6MC (pericardium meridian) point (the so-called great point in vomiting) during the infusion of CDDP (20 min) and then replaced by a needle for permanent use, which was removed 24 h after CDDP administration. If nausea occurred, patients were instructed to press the needle gently until the symptom subsided.

Efficacy assessment of antiemetic treatment was based on the overall count of the vomiting episodes, the duration of vomiting episodes, the intensity of nausea and its duration. Complete protection was defined as the absence of vomiting, nausea or both. The duration of vomiting episodes was calculated as the time between the beginning of CDDP infusion and the last episode of emesis. Evaluation of the intensity of nausea was monitored at 2, 4, 6, 8 and 24 h after chemotherapy and was carried out on the basis of a score system. The score was calculated by the attending personnel and was determined after questioning of the patient according to the following scale: 0, no nausea; 1, slight nausea; 2, moderate nausea; and 3, severe nausea. The duration of nausea was calculated as the total number of minutes during which the patient mentioned feeling nauseated over the 24-h period. Side effects were also assessed in detail by general questioning and monitoring of the patient at the above-mentioned intervals.

## Results

A total of 26 consecutive women (22 without previous chemotherapy experience) with a mean age of 55 years (range, 36–74 years) who had received CDDP chemotherapy (mean dose, 69.9 mg/m<sup>2</sup>; range, 50–120 mg/m<sup>2</sup>) were studied. CDDP was combined in 12 women with doxorubicin plus cyclophosphamide, in 8 patients with VP16, in 3 subjects with mitomycin, vindesine and bleomycin and in 2 women with 5-fluorouracil; 1 patient received CDDP alone.

The results obtained in patients treated with acupuncture were compared with those obtained in a similar group of women treated in the same setting with the same antiemetic combination but without additional acupuncture

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**Table 1.** Effect of acupuncture added to antiemetic therapy<sup>a</sup> in CDDP-treated women

	Acupuncture	No additional treatment
Number of patients	26	51
Complete protection from vomiting (%)	57.7 (CI 39–77)	49.0 (CI 35–63)
Mean number of vomiting episodes	1.7	3.2
Duration of vomiting (min)	160	249
Complete protection from nausea (%)	88.5 (CI 77–100)	66.7 (CI 54–80)
Mean maximal score of nausea	0.2	0.6
Duration of nausea (min)	29	113
Complete protection from nausea and vomiting (%)	53.8 (CI 35–73)	41.2 (CI 28–55)

<sup>a</sup> Metoclopramide + dexamethasone + diphenhydramine  
CI = 95% confidence interval

(see Table 1). There was no difference between the two groups in complete protection from both nausea and vomiting and from vomiting alone. However, complete protection from nausea, the mean number of vomiting episodes, the mean maximal score of nausea and the duration of nausea and vomiting were clearly reduced by the addition of acupuncture.

There were no side effects due to acupuncture. Slight sedation (57.7% of patients), diarrhea (11.5%) and extrapyramidal reactions (7.7%; one case of akathisia and one of trismus) were mentioned and were ascribed to antiemetic drugs.

## Discussion

Complete protection from both nausea and vomiting in women subjected to CDDP chemotherapy at doses of  $\geq 50$  mg/m<sup>2</sup> remains less than satisfactory [2, 3]. Acupuncture used in addition to a standard antiemetic treatment could be a non-toxic and inexpensive treatment that might be useful; however, unfortunately, the results obtained in our study are not as good as those reported by the only other study published to date [1]. Reasons for these differences are not clear but could possibly be related to differences in the technique used (manual vs electroacupuncture) or the population studied or, in particular, to the higher dose of CDDP used in our patients. The fact that we compared the results of our pilot study to "historic" controls should not be considered a major pitfall, because all patients studied were very similar for all factors that can influence nausea and vomiting (i.e., age and dose of

CDDP), were treated with the same antiemetic combination in the same setting of administration and were evaluated in the same way.

Our data therefore provide further evidence that acupuncture can increase complete protection from nausea and can decrease the intensity and duration of nausea and vomiting. If the difficulties of performing acupuncture routinely in a busy ward are considered, however, it is doubtful that this practice could become a standard antiemetic treatment.

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## References

1. Dundee JW, Ghaly RG, Fitzpatrick KTJ, Lynch GA, Abram WP (1987) Acupuncture to prevent cisplatin-associated vomiting. *Lancet* I: 1083
2. Roila F, Tonato M, Basurto C, Bella M, Passalacqua R, Morsia D, Di Costanzo F, Donati D, Ballatori E, Tognoni G, Franzosi MG, Del Favero A (1987) Antiemetic activity of high doses of metoclopramide combined with methylprednisolone versus metoclopramide alone in cisplatin-treated cancer patients: a randomized double-blind trial of the Italian Oncology Group for Clinical Research. *J Clin Oncol* 5: 141–149
3. Roila F, Tonato M, Basurto C, Picciafuoco M, Bracarda S, Donati D, Malacarne P, Monici L, Di Costanzo F, Patoia L, Ballatori E, Tognoni G, Del Favero A (1989) Protection from nausea and vomiting in cisplatin-treated patients: high-dose metoclopramide combined with methylprednisolone versus metoclopramide combined with dexamethasone and diphenhydramine: A study of the Italian Oncology Group for Clinical Research. *J Clin Oncol* 7: 1693–1700