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Short communication

A phase II antiemetic combination (COMD) for cisplatin-induced nausea and vomiting*

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Summary. Thirteen patients resistant to high-dose metoclopramide (≥5 emetic episodes in 24 h following chemotherapy) were treated in the subsequent course of CDDP chemotherapy with COMD (chlorpromazine, orphenadrine, metoclopramide, dexamethasone). A statistically significant reduction in the number of vomiting episodes was obtained, and 69% of patients showed a better acceptance of CDDP treatment. Subsequently, the same antiemetic combination was administered to 31 untreated patients receiving CDDP alone for the first time: 67.7% obtained complete protection from vomiting with minimal toxicity.

According to our experience, COMD is an efficacious and well-tolerated antiemetic combination in cisplatin-treated patients; however, further studies with larger numbers of patients are required to confirm these preliminary results.

Introduction

High-dose metoclopramide is the standard treatment for prevention of cisplatin (CDDP)-induced nausea and vomiting. About 60% of CDDP-treated patients, however, still have this troublesome side effect [1], and the optimal treatment of such resistant cases has not yet been identified. As the use of a combination of antiemetic drugs seems to offer a certain prospect of efficacy [2–7], we designed an intensive four-drug parenteral antiemetic regimen for use in patients who were resistant to high-dose metoclopramide.

We report here the results obtained in these patients and our experience with use of the same regimen in untreated patients undergoing CDDP chemotherapy for the first time.

Materials and methods

Thirteen patients considered resistant (≥5 emetic episodes in 24 h following chemotherapy) to high-dose metoclopramide (120 mg i. v. every 2 h ×4) were treated in the subsequent course of CDDP chemotherapy with the COMD antiemetic combination. Six patients were men and seven, women, their average age being 55.5 years (range 35–66); the average dose of CDDP administered as a single drug was 73.3 mg/m^2 (range 57.1–100).

The COMD combination was given according to the following schedule:

Chlorpromazine	25 mg
i. m. immediately before CDDP	
Orphenadrine	40 mg
i. m. immediately before CDDP	
Metoclopramide	1 mg/kg
i. v. 30 min before CDDP and every 2 h × 4	
Dexamethasone	20 mg
i. v. 30 min before CDDP	

The same antiemetic combination was administered to 31 previously untreated patients (16 men, 15 women; average age 53.9 years; range 31–71) who were undergoing chemotherapy for the first time and who were being treated with CDDP alone (average dose 69.4 mg/m^2; range 50–103 mg/m^2). Treatment efficacy was evaluated by monitoring the number of vomiting episodes and the in-

Table 1. Nausea and vomiting episodes in metoclopramide resistant and previously untreated patients

Resistant patients	Metoclopramide	COMD
Average no. of vomiting episodes	11	6.3 $P=0.003$[a]
Average score for maximal intensity of nausea	1.69	1.07 NS
Untreated patients	**No. of patients**	**%**
No emesis	21	67.7
Major antiemetic effect (≤2 emetic episodes)	6	19.3
Minor antiemetic effect (3–5 emetic episodes)	2	6.5
Failure (>5 emetic episodes)	2	6.5
No nausea	27	87.1
Slight nausea	3	9.7
Severe nausea	1	3.2

NS, not significant
[a] Wilcoxon's matched-pairs signed rank test

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tensity of nausea calculated according to the following score: 0 = no nausea; 1 = slight; 2 = moderate; 3 = severe nausea. Assessment of treatment efficacy and side effects was performed every 2 h after chemotherapy for the first 8 h and then at 24 h.

Results

Results of COMD treatment are shown in Table 1. COMD combination significantly reduced the number of vomiting episodes in metoclopramide-resistant patients. Nausea was also reduced but not significantly, probably because of the small number of patients. On the whole, acceptance of COMD treatment was better in 69% of cases (9 patients). Only three reported mild somnolence.

COMD treatment in untreated patients afforded complete protection in 67.7% of patients (95% confidence limits 51% and 84%). Treatment-related toxicity was also minimal in these untreated patients; 21 reported mild somnolence (67.7%), while 2 complained of diarrhea and 2 of dry mouth. No extrapyramidal reaction occurred. The percentage of patients with mild somnolence does not vary significantly between the emetics and nonemetics ($P < 0.28$ with Fisher's exact test).

Discussion

These results give evidence that COMD is an efficacious and well-tolerated antiemetic combination in patients treated with CDDP chemotherapy. Its use can be recommended in patients resistant to the usual high-dose MTC regimens. Whether it also represents a useful alternative as treatment of choice in all CDDP-treated patients cannot be decided without further investigation.

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