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THE NATURAL COURSE OF EMESIS AFTER CARBOPLATIN TREATMENT

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Abstract

Twenty-eight patients receiving their first cycle of carboplatin treatment (300–400 mg/m^2) entered a prospective study in which the natural course and intensity of postchemotherapy emesis was evaluated. Twenty-five patients (89%) experienced nausea at some time after carboplatin treatment and twenty-three patients (82%) vomited. The median number of emetic episodes was 13.5. In the 23 patients who experienced vomiting, the mean period of latency of vomiting (time from start of carboplatin administration to onset of vomiting) was 6.25 h. The period of maximum incidence of vomiting was between 8 and 12 h (71% of patients with vomiting). Between 6 and 14 h after the start of carboplatin treatment, more than 50% of patients were continuously vomiting. Vomiting declined significantly after 24 h. According to these data, carboplatin is a severely emetic drug. Prospective antiemetic trials are necessary in order to obtain antiemetic schedules which are able to increase the tolerance to carboplatin treatment.

Key words: Carboplatin, postchemotherapy emesis.

Carboplatin (cis-diammine-1,1-cyclobutanate-dicarboxylatoplatinum II), a second generation platinum drug, has been selected for clinical trials due to its antitumoral properties and toxicity spectrum. This drug apparently retains the same antitumoral activity as its parent compound, cisplatin, but shows less renal and emetic toxicity (1), thus resulting in a superior therapeutic index. Nevertheless, due to the fact that emesis is still one of the most frequent side effects of carboplatin, clinical trials will be necessary in the near future in order to obtain antiemetic programmes which increase the tolerance to the treatment.

This paper presents the results of a prospective study in which we analysed the intensity and chronology of emesis after carboplatin treatment, in order to obtain the necessary data to adequately design future antiemetic trials.

Material and Methods

Twenty-eight consecutive patients, receiving their first course of first-line or second-line chemotherapy with carboplatin, entered a prospective study in which the natural course of carboplatin-induced emesis was evaluated. The characteristics of the patients are shown in Table 1.

Patients included in the study had a Karnofsky index $\geqslant 70$ and did not present other causes of emesis (gastric disease, hypercalcemia, CNS metastasis, etc.). Patients with previous anticipatory nausea and vomiting were excluded from the study.

Chemotherapy was given in an outpatient setting with carboplatin in doses of 300 mg/m^2 for patients with previous chemotherapy or 400 mg/m^2 for patients without previous cytotoxic treatment. The total dose of carboplatin was diluted with 500 ml of a 5% dextrose solution and infused i.v. over an hour.

Most patients started treatment between 10 a.m. and 1 p.m. They did not receive other cytotoxic drugs or antiemetics during the first four weeks after chemotherapy administration, which was the period under study.

Patients received instructions how to daily fill out a special questionnaire on the evolution of the emesis, recording each episode of dry or ejective vomiting as well as the time it occurred during the four weeks after chemotherapy. Patients also recorded the maximum intensity of nausea according to the following ordered categoric scale: 0 (no nausea); 1 (slight nausea); 2 (mild nausea); 3 (severe nausea); 4 (nausea as severe as possible).

In order to characterize the natural course of carboplatin induced emesis the incidence and intensity of nausea and vomiting and the chronology of vomiting after chemotherapy were analysed.

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Table 1

Characteristics of the patients

Sex (n)	
Males	10
Females	18
Age (years)	
Median	59
Range	49–71
Prior postchemotherapy emesis (n)	
Yes	11
No	17
Tumors (n)	
Small cell lung cancer	10
Ovarian cancer	8
Breast cancer	10

Results

Incidence and intensity of nausea. Twenty-five patients (89%) experienced some degree of nausea after carboplatin treatment, while 3 patients (11%) did not. Table 2 shows the distribution of patients according to the maximum intensity of nausea experienced during the period under study. The mean score of the maximum intensity of nausea (±SD) was 1.9 ± 1.3.

Incidence and intensity of vomiting. Twenty-three patients (82%) experienced ejective or dry vomiting episodes after carboplatin. The distribution of patients according to the number of vomiting is shown in Table 3. The mean number of vomiting episodes (±SD) was 16 ± 15 and the median number of vomiting 13.5 (range 0–52).

Chronology of carboplatin induced vomiting. In the 23 patients who experienced vomiting, the mean period of latency (time from start of carboplatin treatment to onset of vomiting) ±SD was 6.25 ± 2.38 h. The minimum and maximum periods of latency of vomiting were 2.5 and 10.5 h respectively.

The chronological course of vomiting after carboplatin treatment is shown in Figs 1 and 2. Fig. 1 shows the percentage of patients who experienced vomiting during the previous 2 h over time after carboplatin treatment. Fig. 2 shows the mean number of vomiting episodes ± standard error of the mean recorded by patients during the previous 2 h over time after carboplatin treatment. The period of maximum incidence of vomiting was between 8 and 12 h after the start of carboplatin administration. During this period of time, 71% of patients were vomiting. Between 6 and 14 h, more than 50% of patients were continuously vomiting. Vomiting declined significantly after 24 h (36 h: 14%, and 48 h: 11% of patients with vomiting). Three patients (11%) continued to vomit 48 h after carboplatin treatment.

Table 2

Distribution of the patients according to the maximum intensity of nausea

Score	No. of patients (%)
0	3 (11)
1	11 (39)
2	5 (18)
3	4 (14)
4	5 (18)

Table 3

Distribution of the patients according to the number of vomiting episodes

No. of vomiting	No. of patients (%)
0	5 (18)
1–2	2 (7)
3–10	6 (21.5)
11–20	4 (14)
21–30	6 (21.5)
>30	5 (18)

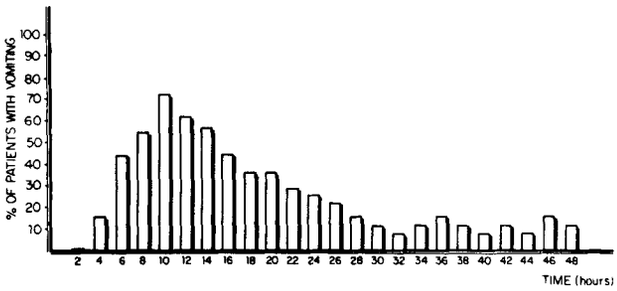

Fig. 1. Percentage of patients with vomiting during the previous 2 h over time after carboplatin administration.

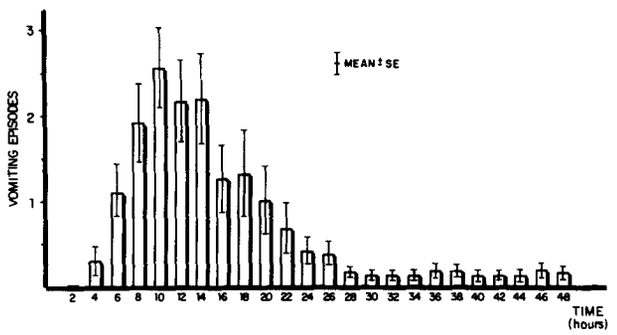

Fig. 2. Mean number of vomiting episodes (± standard error of the mean) reported by patients during the previous 2 h over time after carboplatin administration.

Discussion

This prospective study shows that carboplatin is able to induce severe emesis, since it caused nausea in 89% of patients and vomiting in 82%. Among the cytotoxic drugs,

only cisplatin and dacarbazine seem to possess an emetic capacity superior to carboplatin.

The emetic capacity of carboplatin shown in our study is apparently higher than that previously reported by the Toxicity Data Base of Bristol-Myers Company (2), which collected data on 710 patients from 23 different phase II or III trials in which carboplatin was used as an individual agent. According to this database, only 53% of patients under carboplatin treatment experienced vomiting, while an additional 25% suffered nausea without vomiting. This discrepancy is probably due to the usual tendency of these multicenter registers to collect preferably the most severe grades of toxicity, missing some cases of slight or mild toxicity. On the other hand, since our data are taken from a prospective study in which the incidence of emesis was specifically registered, they are probably more realistic.

The chronological course of carboplatin induced emesis resembles the course of emesis evidenced after high-dose cyclophosphamide (3) and FAC combination (5-fluorouracil, doxorubicin, cyclophosphamide) (4), but differs from that due to cisplatin (100 mg/m^2 in an 8-h infusion) (5). Cisplatin induced emesis begins more precociously (median period of latency of vomiting of 3.2 h) and usually finishes before the course of emesis after carboplatin treatment.

The data obtained from our study offer several practical suggestions. The incidence and intensity of carboplatin induced emesis, even though lower than those induced by cisplatin, are important enough to justify the use of a preventive antiemetic treatment in nearly all patients under treatment. Unfortunately, unlike cisplatin, we lack controlled trials which indicate the antiemetic or antiemetics of choice during carboplatin treatment. In the near future, controlled trials should be performed in order to study the activity against carboplatin induced emesis of conventional and new antiemetic drugs. According to our data, these trials should select antiemetic schedules which are able to ensure adequate serum levels of antiemetic drugs from the start of carboplatin administration until at least 24 h afterwards. In this way, the short-term programs of metoclopramide, which are usually recommended for the control of cisplatin induced emesis (6), would be inefficacious for the control of carboplatin induced emesis.

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