Chinese Journal of Cancer Research 8(1):60 –63, 1996.

GRANISETRON COMPARED WITH ONDANSETRON PLUS DEXAMETHASONE IN THE PREVENTION OF NAUSEA AND VOMITING INDUCED BY A INTENSELY EMETOGENIC CHEMOTHERAPY REGIMEN: A RANDOMIZED CROSS-OVER STUDY

Yu Ding 于丁 Deng Huabang 邓华邦 Fan Yuhua 范玉华 Fu Xiaoyu 付小玉
Ke Yuhua 柯玉华 Hu Yanping 胡艳萍 Zhou Yunhua 周运华 Yang Ling 杨玲

Hubei Cancer Hospital, Wuhan 430070

Fifty-two patients with chemotherapy comprise cisplatin, adriamycin and dacarbazine underwent antiemetic therapy form September 1994 to June 1995. The chemotherapy regimens include CAP-VDS, ACO, EP, CHOP, AMF and MFP. The dose of PDD was 60–70 mg/M^2, ADR was 40–50 mg/M^2 and DTIC was 300 mg/M^2. This study was the randomized, cross-over study, ruled out any differences between individual patients. Group A: Granisetron was given on the first day of chemotherapy, Granisetron 3 mg, Dexamethasone 10 mg i.v. at 30 minutes before chemotherapy; Group B: Ondansetron was given on the first and second days, Ondansetron 8 mg, Dexamethasone 10 mg i.v. at 30 minutes before chemo-therapy. The rates of complete control-free of vomiting were 80.8% and 82.7% in both groups respectively at 24 hours (P>0.05), 57.7% and 53.9% respectively (P>0.05) at second day, and 67.3% and 53.9% respectively (P<0.05) at third day. No difference was observed between both groups for the result of antiemetic control in seven days, the rate of overall control are 82.7% and 80.8% respectively (P>0.05). Adverse events with both antiemetic treatments were mild (essentially headache), the percentage of headache with ondansetron was 9.5% and granisetron 7.7%, constipation with ondansetron was 80.8% and granisetron 61.5%. Constipation: Granisetron, given as one i.v. 3 mg injection before chemotherapy plus dexamethasone, and ondansetron, given intravenously 8 mg injection before chemotherapy at the first 2 days plus dexamethasone are similar results on acute and dalayed chemotherapy-induced vomiting in patients receiving their intensely emetogenic regimen.

Key words: Antiemetics, Chemotherapy, Vomiting granisetron, Ondansetron, Dexamethasone.

Nausea and vomiting are often the first side effects of anti-cancer drugs, particularly with cisplatin, adriamycin and dacarbazine. Intensely emetogenic regimens are widely used in the treatment of a great variety of cancers, including breast cancer, lung cancer and malignant lymphomas et al.. Prevention of nausea and vomiting in patients receiving these regimens is very important since nausea and vomiting are among the most distressing side effects of chemotherapy occurring in patients not receiving antiemetic treatment.[1] Several studies have shown that 5-HT3 receptor antagonists are superior to other antiemetic treatments during the acute phase of emesis.[2,3] From September, 1994 to June, 1995, 52 patients with chemotherapy comprise cisplatin, adriamycin and dacarbazine underwent antiemetic therapy.

Accepted November 17, 1995

MATERIALS AND METHODS

Entry Criteria

All patients were in hospital. All chemotherapy regimens included cisplatin or/and adriamycin, dacarbazine. Patients with renal failure or marked hepatic dysfunction were excluded. Eligibility criteria included the absence of prechemotherapy vomit with brain metastasis and intestinal obstruction.

Patient Characteristics

Of the 52 patients, males 38, females 14, ages 24–69 with median 47 years, including 28 lung cancer, 14 malignant lymphomas, 4 breast cancer, 3 gastrointestinal cancer, 2 head and neck cancer, and 1 testicular cancer.

Chemotherapy Regimen

Chemotherapy regimens including CAP-VDS (CTX, ADR, PDD, VDS), ACO (ADR, CTX, VCR), EP (Vp-16, PDD), CHOP (CTX, ADR, VCR, PDN), AMF (ADR, MTX, 5FU), MFP (MMC, 5FU, PDD). The dose of PDD is 60–70 mg/M^2, ADR is 40–50 mg/M^2 and DTIC is 300 mg/M^2.

Method

The study was a randomized, crossover study, ruled out any differences between individual patients. Group A was given granisetron in the first chemotherapy cycle and ondansetron in the second. Group B received ondansetron first and granisetron second. Granisetron was given on the first day of chemotherapy; ondansetron was given on the first and second days. No other antiemetic was used up to seven days after chemotherapy. All patients received the same dosages of antiemetic: granisetron 3 mg, dexamethasone 10 mg i.v. at 30 minutes before chemotherapy; and ondansetron 8 mg, dexamethasone 10 mg i.v. at 30 minutes before chemotherapy.

Criteria

The criteria used to measure nausea and vomiting are follow: Nausea. 0: complete control – no nausea; I: mile – not affecting food intake and daily activities; II: medium – affecting food intake and daily activities; III–IV: failure – severe nausea, lying in bed. Vomiting. 0: complete control – free of vomiting; I: major control – 1 or 2 vomits per day, not affecting food intake and daily activities; II: minor control – 3 to 5 vomits per day; III–IV: failure – severe vomiting, lying in bed.

RESULTS

A total of 52 patients were randomized and completed the 2-way cross-over. Figure 1 shows the number of patient of vomiting in two groups of patients. Figure 2 shows the results of vomiting episodes (n=52) – complete and major response. Table 1 shows the results of vomiting episodes (n=52) in seven days.

Table 1. Results of vomiting episodes (n=52) in seven days

	CC	MaC	MiC	F	CC+MaC (%)
Ondansetron	22 (42.3)	21 (40.4)	6 (11.5)	3 (5.8)	43 (82.7)
Granisetron	23 (44.2)	19 (36.5)	7 (13.5)	3 (5.8)	42 (80.8)

The rates of complete control-free of vomiting were 80.0% and 82.7% in both groups respectively at 24 hours (P>0.05). They were 57.7% and 53.9% in both groups respectively (P>0.05) at second day, and 67.3% and 53.9% respectively (P<0.05) at third day. No difference was observed between both groups for the result of antiemetic control in seven days, the rate of overall control are 82.7% and 80.8% respectively (P>0.05).

Adverse events with both antiemetic treatments were mild (essentially headache), the absence of extrapyramidal effects and akathisia in the patients,

but adverse events occurring with the highest frequency in both groups at each cycle were constipation. The percentage of headache with ondansetron was 9.5% and granisetron 7.7%, constipation with ondansetron was 80.8% and granisetron 61.5%. Moreover constipation with ondansetron was 78.9% and granisetron 55.8% in patients of complete control-free of vomiting.

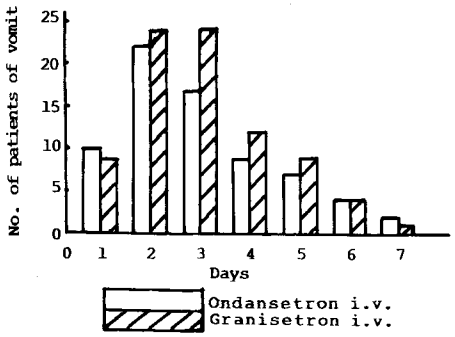

Fig. 1. Number of vomiting episodes in two groups of patients

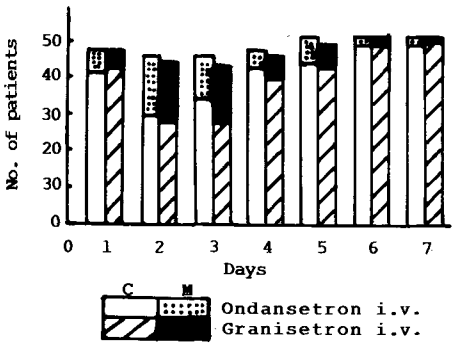

Fig. 2. Results of vomiting episodes (n=52) – complete and major response

DISCUSSION

A variety of safe and effective antiemetic agents that 5-HT3 receptor antagonist (like ganisetron, ondansetron and tropisetron) with dexamethasone have been identified and tested in cancer patients receiving chemotherapy.[4,5] 5-HT3 receptor antagonist are highly effective in preventing acute chemotherapy-induced nausea and vomiting.[6] Delayed emesis is a distinct clinical syndrome which occur more than 24 hours after administration of cytotoxic therapy, peaking at 48–72 hours and lasting for up to 7 days.[7] This study demonstrates that both granisetron and ondansetron plus dexamethasone are effective for the prophylaxis of emesis induced by 7-day fractionated cisplatin, adriamycin and dacarbazine regimens. Our results show that the rate of overall control in seven days are 82.7% and 80.8% respectively, and complete control-free of vomiting are 42.3% and 44.2% respectively in two groups.

Dexamethasone's efficacy against platinum-containing regimens was demonstrated by Aapro and Alberts,[8] who reported an 82% response against moderate doses of cisplatin. Allan, et al.[9] reported that the addition of dexamethasone to the 5-HT3 receptor antagonist ondansetron produced complete or major control in 69% of patients compared with 56% of that given ondansetron alone. Jones, et al.[10] reported that for control of emesis induced by moderately emetogenic non-platinum containing chemotherapy, dexamethasone has been shown to be superior to ondansetron (87% vs. 72%) for the control of delayed nausea on days 2–5. A similar result has been found in this trial.

In spite of the antiemetic treatment is safe and effective, the side effects were mile, but constipation was occurring with the highest frequency in this trial. We suggest that the addition of cathartic to the 5-HT3 receptor antagonist ondansetron and granisetron decrease the occurrence of constipation.

Conclusion: Granisetron, given as one i.v. 3 mg injection before chemotherapy plus dexamethasone, and ondansetron, given intravenously 8 mg injection before chemotherapy at first 2 days plus dexame-thasone are similar results on acute and delayed chemotherapy-induced vomiting in patients receiving their intensely emetogenic regimen.

REFERENCES

1. Buser K, Joss R, Piquet D, et al. A randomized double-blind comparison of oral oncansetron and placebo in the prophylaxis of CMF-induced nausea and vomiting. Proc Am Soc Clin Oncol 1990; 9:331.
2. Bonneterre J, Chevallier B, Metz R, et al. A randomized double-blind comparison of ondansetron and metoclopramide in the prophylaxis of emesis induced by cyclophosphamide, fluorouracile and

doxorubicin or epirubicin chemotherapy. J Clin Oncol 1990; 8:1063.

3. Kaasa S, Kvaloy J, Dicato MA, et al. A comparison of ondansetron with metoclopramide in the prophylaxis of chemotherapy-induced nausea and vomiting: a randomized double-blind study. Eur J Cancer 1990; 26:311.
4. Kris MG, Gralla RJ, Tyson LB, et al. Improved control of cisplatin-induced emesis with high-dose metoclopramide and with combinations of metoclopramide, dexamethasone, and diphemhydramine: results of consecutive trials in 255 patients. Cancer 1985; 55:527.
5. Kris MG, Tyson LB, Clark RA, et al. Oral ondansetron for the control of delayed emesis after cisplatin: report of a phase II study and a review of completed trials to manage delayed emesis. Cancer 1992; 70:1012.
6. Jantuen IT, Muhonen TT, Kataja W, et al. Teerenhovi 5-HT3 receptor antagonists in the prophylaxis of acute vomiting induced by moderately emetogenic chemotherapy–a randomised study. Eur J Cancer 1993; 29A:1669.
7. Kris MG, Gralla RJ, Clark RA, et al. Incidence, course and severity of delayed nausea and vomiting following the administration of high-dose cisplatin. J Clin Oncol 1985; 3:1379.
8. Aapro MS, Alberts DS. High-dose dexamethasone for prevention of cisplatin-induced vomiting. Cancer Chemother Pharmacol 1981; 7:11.
9. Allan SG, Farquhar DF, Harrison DJ, et al. Antiemetic efficacy of dexamethasone in combination for out-patients receiving cytotoxic chemotherapy. Cancer Chemother Pharmacol 1986; 18:86.
10. Jones A, Hill AS, Soukop M, et al. Comparison of dexamethasone and ondansetron in the prophylaxis of emesis induced by moderately emetogenic chemotherapy. Lancet 1991; 338:483.