Is ondansetron a less effective antiemetic against moderately emetic as compared with highly emetic chemotherapy?

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The severity of sickness in the first 5 days after cancer chemotherapy was compared in patients who had or had not received ondansetron 8 mg three times daily. Patients were divided into those having highly emetic chemotherapy, irrespective of gender and women having moderately emetic drugs. Ondansetron appeared to be more effective in the former group.

Keywords ondansetron cancer chemotherapy emesis

Introduction

The concomitant use of the 5-HT₃ receptor antagonist ondansetron has reduced the incidence of sickness with cancer chemotherapy to the extent that it is no longer a major clinical problem (Editorial, 1991). When investigating the complementary antiemetic effect of ondansetron and stimulation of the P6 acupuncture point we formed the impression that ondansetron was less effective with moderately emetic chemotherapy, such as cyclophosphamide, 5-fluorouracil, adriamycin than with the highly emetic drugs such as cisplatin. Once the use of ondansetron had been established, it would have been unethical to omit it for the sake of investigation. We here report a comparison of the severity and incidence of sickness in a series of patients studied before the introduction of ondansetron, who had no antiemetics with their first course of chemotherapy and patients having similar chemotherapy with ondansetron at their first treatment. The data for the two series were collected consecutively, with one investigator common to both series.

Method

Patients

All were adults who were divided into two groups.

1. Men or women having highly emetic chemotherapy or high doses of moderately emetic drugs (HE), with (44) or without (63) ondansetron. The majority of these were hospitalised for 4–5 days and were visited daily.
2. Women (ME/F) having normal doses of moderately emetic chemotherapy; 24 of these had ondansetron while 102 did not. The majority were outpatients, who attended hospital every 3 weeks. The frequency

and severity of sickness was noted at their next hospital visit.

Drugs

The grouping of drugs into highly emetic or moderately emetic followed the universally accepted classification (Priestman, 1989).

Ondansetron

The dose was 8 mg by mouth given three times daily. All patients had a single dose given 1 h before the chemotherapy; in hospitalised patients this was administered intravenously but it was taken by mouth in outpatients. Treatment was continued for 4–5 days in all patients.

Sickness

This was graded on a simple four point scale in both series which embraces the frequency, severity and duration of both nausea and vomiting. Details have been described elsewhere (Dundee *et al.*, 1990). As a means of quantifying the relative degree of sickness in each series a numerical value was assigned to each grade. 0: nil, 1: slight, 2: moderate, 3: marked. These values were not subjected to statistical analysis. The χ^2 test was used in all other comparisons.

Results

Figure 1 gives the degree of sickness in all four groups. No patient who received ondansetron in either series had severe persistent vomiting.

Figure 1 Incidence of sickness following highly emetic chemotherapy (HE) in both men and women and with moderately emetic chemotherapy in women (ME/F) with or without ondansetron 8 mg three times daily. Severity of sickness: ■ marked; ▨ moderate; ▩ slight; □ nil.

Table 1 Relative degree of sickness in different series, based on a four point scale grading frequency and severity

Series	HE		ME/F	
	-	+	-	+
Mean score	2.27	0.62	1.61	0.88
% reduction with ondansetron	83		45	

In the absence of ondansetron there was significantly ($\chi^2 = 40.3$ df = 3 $P < 0.0001$) more sickness in the HE as compared with the ME/F group (Figure 1). With ondansetron the trend was reversed and sickness was slightly but not significantly ($\chi^2 = 2.33$, df = 2, $P = 0.4$) less after highly emetic chemotherapy.

With ondansetron there was significantly less sickness after chemotherapy in both groups ($\chi^2 = 49.3$, df = 3, $P < 0.0001$ for the HE group, $\chi^2 = 15.0$, df = 3, $P = 0.002$ for the ME/F group) (Table 1). Assigning a numerical score to the severity of sickness shows that, in the doses used, ondansetron appears to be more effective as an antiemetic with emetic chemotherapy than with moderately emetic drugs.

Discussion

These findings are open to various interpretations. Outpatients may not be able to recall the extent of their sickness when questioned after 3 weeks, particularly if it has not been severe. This would however apply to all patients in the ME/F group irrespective of whether they had ondansetron or not. Factors, other than the emetic effects of the chemotherapy, which are not amenable to relief by ondansetron, may account for the residual sickness, which was similar in both the HE and ME/F groups. Patients in the ME/F group would be more ambulatory than those in the HE series and this may have contributed to the sickness in the former.

Finally ondansetron may *per se* be a less effective antiemetic with moderately, as compared with highly emetic cytotoxic drugs. This study, as executed describes rather than explains the phenomenon.

These findings are important considering the cost of ondansetron (Editorial, 1991) when oncologists may have to reserve its use for those in most need.

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