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Comparison of Efficacy of Ondansetron Versus Granisetron for the Control of Chemotherapy Induce Nausea and Vomiting

Dr.Dinkar N. Goswami

Associate Professor in Medicine GMERS Medical college Gandhinagar

ABSTRACT

Aim of Study *To compare the efficacy and safety of granisetron and ondansetron, for prevention of chemotherapy-induced emesis.*

PATIENTS AND METHODS *In a prospective randomized study, the efficacy and safety of granisetron and ondansetron were compared in 100 patients who received chemotherapy for carcinoma breast and ovary .Granisetron was administered as a single dose of 10 or 40 micrograms/ kg in group G . Ondansetron was administered in doses of 0.15 mg/kg in group O.The treatment groups were well-matched with respect to demographic data,complete response and side effects.*

RESULTS *For all evaluations, single doses of granisetron 10 or 40 micrograms/kg were as effective as three 0.15-mg/kg doses of ondansetron. Total control (no vomiting, no retching, no nausea, and no use of rescue) was attained by 88% of all patients who received granisetron 10 as compared to 72% of patients who receieved ondensetron .*

CONCLUSION *All three treatment regimens were well-tolerated. The results of this study indicate that a single dose of granisetron 10 or 40 micrograms/kg is more effective than ondansetron 0.15 mg/kg in the prevention of nausea and vomiting induced by chemotherapy.*

KEYWORDS :

Introduction

One of the most common and distressing symptoms after chemotherapy is nausea and vomiting.For the prevention of CINV several antiemetics of different pharmacological classes are available. A number of pharmacological agents (antihistamines, butyro-phenones, and dopamine receptor antagonists) have been tried for the prevention and treatment of chemotherapy induce nausea and vomiting but undesirable adverse effects such as excessive sedation, hypertension, dry mouth, dysphoria, hallucinations and extra pyramidal symptoms have been noted.[1] Currently, selective 5-hydroxytryptamine type 3 (5-HT3) receptor antagonists are frequently used for the prevention of chemotherapy induce nausea and vomiting because of their efficacy and fewer side-effects as compared with other antiemetics. [3,4] Granisetron produces irreversible block of the 5-HT3 receptors with half life of 5 to 8 hours.[5,6] We designed this prospective randomized study to assess and compare the antiemetic efficacy of ondensetron and granisetron to prevent chemotherapy induce nausea and vomiting

Mechanisms — A precise understanding of the mechanisms by which chemotherapy induces emesis remainsunclear. Two reviews summarize our current understanding of the pathophysiology of CINV. Higher central nervous system (CNS) centers located in structures in the limbic forebrain, such as the amygdala may be a source of some types of emetic stimuli. Some chemotherapy agents or their metabolites may interact directly or indirectly with receptors within the area postrema with subsequent activation of the vomiting center.

Substance P is released from sensory neurons following chemotherapy administration. Abundant NK1 receptors are found within the area postrema and the nucleus tractus solitarius, an important component of the anatomically indistinct emetic center.

Patient-related factors — A number of patient-related factors have been associated with an increased risk of CINV. These include the following:Emesis with prior chemotherapy increases the risk of CINV. Women have an increased risk of CINV compared with men.Younger patients are more susceptible to CINV than older patients.Patients with a significant history of alcohol consumption are less susceptible to CINV than those without such a history.Patients who experience acute emesis with chemotherapy are significantly more likely to have **delayed** emesis.Anticipatory emesis occurs in patients who have had poor control of either acute or delayed emesis with prior chemotherapy It has been suggested that a history of motion sickness may predispose to anticipatory emesis.

Method

After obtaining the institutional ethical committee approval and informed consent from every patient100 patients, aged 38-60 years, taken chemotherapy were randomly assigned to one of the two groups, containing fifty patients each. Patients who had gastrointestinal disease, had history of motion sickness and/ or PONV and those who had vomiting, retching, nausea before preceding the administration ofchemotherapy , taken antiemetic medication within last 24 hours were excluded from the study. Patients were randomly allocated into two groups (n=50each) to receive one of the following regimens: ondensetron 0.15 mg/kg in [group o] or granisetron 10 or 40 micrograms/kg [group G] (0.9% saline was added to make the desired volume).The study drugs were administered. All episodes of nausea, retching and vomiting were recorded for 0-24 hours hours s in ward. Complete response (free from emesis) was defined as no nausea and no vomiting and no need for any rescue medication. If there were two or more episodes of nausea and vomiting during 24 hours, rescue antiemetic (metoclopramide10 mg i.v.) was given. Data were analyzed using computer statistical software system Graph Pad. Comparisons between groups were performed by using student t test and Fisher's exact t test as appropriate. The results were expressed in mean±SD and number (%).

3. Results

The groups were comparable with respect to age, weight [Table 1]. The incidence of a complete response (no nausea and vomiting , no rescue medication) during 0-24 hours in was was 88% with granisetron. And 72 % with ondensetron. **Table 2:** Thus a complete response during 24 hour in the ward was significantly more in patients who had received granisetron. than in those who had received ondensetron

Table1: Patients characteristics (Mean± SD)

	Group o (n=25)	**Group G (n=25**
Age (years)	45.3 ± 5.23	46.1 ± 4.82
Weight (kg)	50.14 ± 6.32	52.23 ± 5.61

Table 2: Incidence of complete response during study

	ondansetron	granisetron
Nausea	72%	88%
Vomiting	74%	90%
Rescue Treatment	16 %	10%
Complete Response	72%	88%

Table 3: Incidence of adverse events and patient's satisfaction
Complications

	ondansetron	granisetron
Headache	6%	7%
Dizziness	4%	5%
Constipation	3%	3%
Myalgia	2%	2%
Patients Satisfaction	80%	96%

Discussion

The introduction of 5HT3 (serotonin) receptor antagonists in 1918 has heralded a major advance in treatment of CINV because of absence of adverse effects that were observed with commonly used antiemetic drugs. The 5HT3 receptor antagonists produce no sedation, no extra pyramidal symptoms or adverse effects on vital signs and do not interact with other anaesthetic agents. Dose of ondansetron hydrochloride and granisetron hydrochloride were based on body weight only in pediatric patients. However for standardization purposes their dose was based on body weight in our study in adults also. Hence, this study was conducted to compare the efficacy of ondansetron at a dose of 40-80µg/kg with granisetron Granisetron can be used in the dose of 40-80µg/kg for the treatment of cancer chemotherapy induced emesis .12 The dose of granisetron 2.5 mg (approximately 45µg /kg) for the control of CINV.

Delayed emesis — Emesis occurring more than 24 hours after chemotherapy is classified as delayed. It is best characterized following treatment with high-dose cisplatin. In the absence of antiemetic prophylaxis, delayed emesis after cisplatin peaks at approximately 48 to 72 hours after therapy, then gradually subsides over the next two to three days1. While the frequency and number of episodes of emesis may be less during the delayed period compared with acute emesis, the delayed form is less well controlled with current antiemetic medications. Delayed emesis occurs most frequently after cisplatin but can also occur following other agents, including carboplatin, cyclophosphamide, anthracyclines, and oxaliplatin .

Krzakowski *et al* compared the effectiveness of IV ondansetron 8mg in combination with IV dexamethasone 20mg with oral ondansetron 24mg in combination with oral dexamethasone 12mg in once daily regimens administered to patients receiving cisplatin 50mg/m2 or greater. Complete control of emesis was achieved in 85 per cent of patients in the oral group and 83 per cent in the IV group. No nausea was reported in 70 per cent of patients in the oral group and 68 per cent in the IV group.

Granisetron has a longer half-life than ondansetron and is claimed to be more effective in the prevention of delayed nausea and vomiting associated with chemotherapy,incidence of headache, dizziness and constipation between two groups. Thus both were devoid of clinically important side effects.The mean number of episodes of vomiting for patients treated with ondansetron was nearly always more than for those treated with granisetron.

Granisetron is a potent and highly selective 5-HT_3-receptor antagonist that has little or no affinity for other 5-HT receptors, or dopaminergic, adrenergic, benzodiazepine, histaminic, or opioid receptors. In contrast, other 5-HT_3-receptor antagonists have affinities for various receptor-binding sites. For example, Although not proven, the binding of these agents to additional receptor subtypes other than their target receptor may underlie the inferior adverse-event profile seen with ondansetron compared with granisetron].

The Italian Group for Antiemetic Research carried out a study comparing intravenous ondansetron 8mg versus granisetron 3mg. Dexamethasone was added to both treatments, 20mg by IV infusion 45 minutes before the cisplatin and 8mg IM twice a day on days 2 and 3 and 4mg twice a day on day 4. The group concluded from this study that ondansetron 8mg and granisetron 3mg combined with dexamethasone in this schedule showed similar efficacy and tolerability in the prevention of cisplatin-induced emesis. The incidence of acute emesis and nausea in the first 24 hours after chemotherapy is greater than 90 per cent in patients receiving highly emetogenic chemotherapy such as cisplatin, unless treated with antiemetic agents. Good control of these symptoms following chemotherapy is an important prognostic factor for later control of delayed emesis and nausea and of emesis and nausea experienced in subsequent cycles of chemotherapy. It is, therefore, important that emesis and nausea should be well controlled on the first cycle of chemotherapy, as this may have a significant effect on a patient's quality of life and willingness to complete the course of treatment. Furthermore, uncontrolled emesis frequently results in patients whose nutritional status is poor.

A further study comparing the efficacies of granisetron, ondansetron, and tropisetron in the control of delayed-onset nausea and vomiting in patients receiving moderate- or high-dose chemotherapy found similar efficacies among the three agents; complete response rates (no vomiting or retching) at 24–72 hours postchemotherapy were 55.5% in the granisetron-treated group, 48.5% in the ondansetron group, and 48.5% in the tropisetron group. Despite the clear efficacy of the setrons in the prevention of nausea and vomiting in the acute phase, delayed-onset emesis remains unresolved in many patients. combination of i.v. granisetron plus prednisolone plus metopimazine is also a highly effective antiemetic treatment in patients receiving moderately emetogenic chemotherapy in whom granisetron or prednisolone plus metopimazine has failed.

CONCLUSION.

One hundred patients who received chemotherapy for carcinoma breast were included in a prospective randomized control study to compare the efficacy of ondansetron(80µg/kg) with granisetron(20µg/kg) for the nausea and vomiting.. However the incidence of vomiting was much lower in both the groups and showed a decrease with time.. No significant side effect was noted in either of the groups. The results of this study indicate that a single dose of granisetron 10 or 40 micrograms/kg is more effective than ondansetron 0.15 mg/kg in the prevention of nausea and vomiting induced by chemotherapy.

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