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ORIGINAL ARTICLE

The use of aprepitant and palonosetron in preventing chemotherapy-related nausea and vomiting inlung cancer patients

Shuxian Qu (✉), Zhendong Zheng (Co-first author), Zhaozhe Liu, Jianing Qiu, Xiaodong Xie (✉)

Department of Oncology, The General Hospital of Shenyang Military Region, Shenyang 110840, China

Abstract

Objective The aim of this study was to explore the clinical efficacy and toxicity of a combination aprepitant and palonosetron hydrochloride therapy in preventing chemotherapy-induced nausea and vomiting associated with a cisplatinum-based regimen in patients with lung cancer.

Methods Sixty-eight patients with lung cancer were randomly assigned to receive either aprepitant plus palonosetron hydrochloride (group A, n = 38) or tropisetron (group B, n = 30). Acute (0–24 h) and delayed (2–5 d) emetic episodes, nausea, vomiting, constipation, and dizziness were compared between the two groups in the five days following cisplatinum-based chemotherapy.

Results Group A had a higher complete control rate for both acute and delayed emetic episodes than Group B (36.8% vs. 13.3% and 31.6% vs. 13.3%, respectively; $P < 0.05$ for both). There was no significant difference in the constipation rate between the two groups.

Conclusion Aprepitant combined with palonosetron hydrochloride is active and well tolerated in both acute and delayed emetic episodes in patients with lung cancer treated by a cisplatinum-based regimen.

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Key words: aprepitant; palonosetron hydrochloride capsule; cisplatinum; tropisetron

Chemotherapy-induced nausea and vomiting (CINV) is a common and debilitating side effect of chemotherapy. Particularly high emetogenic chemotherapy drugs, such as cisplatin, can cause electrolyte imbalance, dehydration, and other complications [1]. CINV can also reduce the effects of chemotherapy, as well as patient compliance. The most common antiemetic drugs are the first generation 5-Hydroxytryptamine 3 (5-HT3) serotonin receptor antagonists [2–3]. However, these drugs have poor efficacy for the delayed nausea and vomiting frequently caused by cisplatin, because of their short half-lives. In this study, aprepitant and palonosetron capsules were administered to patients with lung cancer, receiving platinum-based chemotherapy from May 2015 to May 2016 to prevent chemotherapy-related nausea and vomiting, and the effects on CINV were examined.

Materials and methods

Patient information

The study included 68 patients, aged from 38 to 69 years, with a histopathological diagnosis of primary lung cancer. The patients were randomly divided into either an aprepitant and palonosetron group (Group A, n = 38) or a tropisetron group (Group B, n = 30), using prospective controlled study methods. All patients met the following inclusion criteria: Zubrod-ECOG-WHO score < 2, no brain metastases or gastrointestinal obstructions, no 5-HT3 receptor antagonist medication contraindications, no pregnant or breast-feeding women, and no indications preventing the administration of other antiemetic drugs. The two groups of patients had no statistically significant differences in baseline characteristics such as age, gender, chemotherapy, history of previous chemotherapy, or previous surgeries.

✉ Correspondence to: Shuxian Qu. Email: qushuxian2010@163.com; Xiaodong Xie. Email: doctor_xxd@163.com

Chemotherapy

Cisplatin (75 mg/m^2) was administered on the first day of a 21-day chemotherapy cycle. Other chemotherapeutic agents were provided according to the patient's normal regimen. Hydration was administered during chemotherapy to prevent renal toxicity.

Study drug

For Group A, patients received 125 mg aprepitant capsules (Novartis, USA) and intravenous injection of 0.25 mg palonosetron (Shandong Qilu Pharmaceutical Co., China) 30 min before chemotherapy. On days 2–4, patients took 80 mg aprepitant for oral.

For Group B, a 5 mg tropisetron sodium chloride injection (Shandong Qingfeng, China) was administered 30 min before chemotherapy, as well as on days 2 and 3. If vomiting occurred more than three times within a 24 h period, 5 mg dexamethasone was administered intravenously

Primary outcomes

Appetite, nausea, vomiting time, and severity of vomiting were recorded for five days following chemotherapy. Adverse reactions of the study drugs, such as headache, dry mouth, constipation, and facial flushing, were also recorded.

Evaluation criteria

All toxicities were graded using the Common Toxicity Criteria. Complete control (CR) rates (no emesis, no rescue) were analyzed for an acute (24 h after chemotherapy) and delayed (2–5 days after chemotherapy) period. Emetic episodes were scored on a scale of 0–III (0, CR); I, partial control (PR); II–III, invalid (SD)]. Remission was calculated as follows:

CR rate = complete response / total cases × 100%;

Effective control of acute vomiting rate = (number of cases + full control section controls the number of cases) / total cases × 100%.

Statistical analysis

SPSS v. 15.1 was used for statistical analysis. The Chi-square test was used for data comparison between groups. A P-value < 0.05 was considered to indicate statistical significance.

Results

Appetite

Appetite was similar between Group A and Group B (Table 1).

Table 1 The comparison of control of appetite

Time	Group (n)	Degree				CR (%)	χ^2	P
		0	I	II	III			
0–24 h	A (38)	5	20	8	5	13.2	0	1.000
	B (30)	4	16	6	4	13.3		
2–5 d	A (38)	10	13	13	2	26.3	4.454	0.035
	B (30)	2	14	12	2	6.7		

Table 2 The comparison of control of nausea

Time	Group (n)	Degree				CR (%)	χ^2	P
		0	I	II	III			
0–24 h	A (38)	13	17	5	3	34.2%	3.897	0.048
	B (30)	4	14	8	4	13.3%		
2–5 d	A (38)	12	14	11	1	31.6%	4.541	0.033
	B (30)	3	13	12	2	10.0%		

Table 3 The comparison of control of vomiting

Time	Group (n)	degree				CR (%)	χ^2	P
		0	I	II	III			
0–2 4h	A (38)	14	16	7	1	36.8	4.760	0.029
	B (30)	4	11	10	5	13.3		
2–5 d	A (38)	12	14	11	1	31.6	4.541	0.033
	B (30)	3	15	10	2	13.3		

Nausea

The control of acute and delayed nausea in Group A was better than in Group B (P < 0.05; Table 2).

Control of vomiting

The CR rate in Group A was 36.8% for the acute period and 31.6% for the delayed period. The CR rate in Group B was 13.3% for the acute period and 13.3% for the delayed period. Acute nausea and delayed vomiting were improved in Group A compared to Group B (P < 0.05; Table 3).

Adverse reactions

As shown in Table 4, the adverse reactions of the study drugs were similar between the two groups, namely, head heaviness, headache, fatigue, and dry mouth. Most patients had mild reactions. Some reactions may not have been specific to the study drugs, as it was difficult to distinguish from the effects of the chemotherapy. We observed no cases in Group A where chemotherapy was discontinued because of adverse reactions from the antiemetics.

Table 4 The comparison of adverse reaction

Adverse reaction	Group A (38)		Group B (30)	
	n	incidence (%)	*n*	incidence (%)
Dizzy	3	7.8	2	6.7
Thirst	5	13.2	4	13.3
Headache	4	10.5	3	10.0
Weak	3	7.8	2	6.7
Mild fever	1	2.6	0	0
Constipation	2	5.2	1	3.3
Anxiety	2	5.2	1	3.3
Diarrhea	1	2.6	1	3.3

Discussion

Nausea, vomiting, and other gastrointestinal symptoms are common adverse effects of chemotherapies used for lung cancer. Antagonists of 5-HT3 work by blocking the 5-HT receptors on the vagal afferent nerve endings of the gastrointestinal mucosa[2–4]. Palonosetron is a new 5-HT receptor antagonist, with a half-life of about 40 h and a strong affinity for the 5-HT3 receptor (more than 100 times greater than first-generation 5-HT receptor antagonists) [3–4]. There are a number of multi-center clinical studies demonstrating that palonosetron has a strong and long-lasting antiemetic effect [4–6]. In this study, palonosetron capsules in oral form had good absorption and bioavailability, with the maximum plasma levels being equal to intravenous administration.

Aprepitant is cited in the National Comprehensive Cancer Network guidelines as the first neurokinin-1 receptor antagonist to treat CINV [7]. Substance P is widely distributed in neuropeptide nerve fibers. When the nerve is stimulated, a large amount of substance P will be released and promote numerous biological processes by binding to NK-1. Aprepitant has a stronger affinity to NK-1 than to the 5-HT receptor [7–9]; thus, aprepitant combined with a 5-HT3 receptor antagonist should be able to prevent CINV better by acting on multiple targets.

Previous studies have shown that palonosetron can improve delayed nausea and vomiting control rate comparing to tropisetron, but not acute nausea or vomiting control rate [4]. In this study, the combination of palonosetron and aprepitant had an obvious advantage compared with the tropisetron group in efficiency and control rate in acute nausea, vomiting, and delayed emesis. This advantage resulted from the double antagonism of 5-HT receptors and substance P [9–10]. We observed a lower incidence of severe nausea and vomiting in the group that received the combination of aprepitant and palonosetron. No patients in the aprepitant and palonosetron group required a discontinuation of chemotherapy because of nausea, vomiting, and weight loss. However, the tropisetron group had three patients postpone chemotherapy for three days because of vomiting. We will need to increase the sample size in further studies to confirm this advantage of vomiting grade reduction.

There were no significant differences between the two groups in terms of adverse reactions to the study drugs. Group A had no severe adverse reactions resulting from the long half-life of palonosetron. This suggests a good security when aprepitant is combined with palonosetron. In short, the combination of aprepitant and palonosetron has a significant preventative effect against CINV after chemotherapy with cisplatin. This is a safe, economical, and effective treatment with good prospects for clinical application, particularly in controlling delayed emesis.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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