ORIGINAL RESEARCH

Comparing the Antiemetic Effects of Ondansetron and Metoclopramide in Patients with Minor Head Trauma

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Abstract

Introduction: Nausea and vomiting are the most common complications after minor head trauma that increases the risk of intracranial pressure rising. Therefore, the present study was aimed to compare the antiemetic effects of metoclopramide and ondansetron in the treatment of post-traumatic nausea and vomiting. **Methods:** The study was a controlled, randomized, double blind clinical trial, which was conducted in the first 6 months of 2014 in emergency department Al-Zahra and Kashani Hospitals in Isfahan, Iran. The patients with minor head trauma associated with nausea and vomiting were randomly divided into 2 groups: treatment with metoclopramide (10mg/2ml, slow injection) and treatment with ondansetron (4mg/2ml, slow injection). The comparison between the 2 groups was done regarding antiemetic efficacy and side effects using SPSS 21 statistical software. **Results:** 120 patients with minor head trauma were distributed and studied into two groups of 60 patients (mean age 35.6±14.1 years; 50.0% male). Administration of both ondansetron and metoclopramide significantly reduced the severity of nausea (P<0.001). Changes in the severity of nausea in both groups before and after the treatment revealed that nausea had been decreased significantly in both groups (P < 0.001). The incidence of fatigue (p=0.44), headache (p=0.58) and dystonia (p=0.06) had no significant difference in the two groups but the incidence of drowsiness and anxiety in the metoclopramide group was significantly higher (P < 0.001). **Conclusion:** The present study indicated that the treatment effectiveness of ondansetron and metoclopramide are similar. However, incidence of drowsiness and anxiety in the metoclopramide was considerably higher. Since these complications can have adverse effects on the treatment of patients with brain injury, it is suggested that it may be better to use ondansetron in these patients.

Key words: Head injuries, closed; nausea; vomiting; multiple trauma

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Introduction:

In general, brain injury can occur due to sudden and severe head strike to a hard object, which can be mild, moderate or severe (1). The main causes of head injury include traffic accidents, falling from heights, physical violence, accidents at work, inside home accidents and during exercise incidents. However, the most important cause of head trauma in Iranian population is traffic accident (2). Among the warning signs of head trauma are nausea, vomiting, dizziness, headache, blurred vision, and loss of balance, difficulty in sleeping, memory problems, tinnitus and fatigue (3). Nausea and vomiting are the most common complications after minor head trauma that in addition to severe harassment of patients increases the risk of aspiration and intracranial pressure rising. Ondansetron and metoclopramide are two available antiemetic agents in the emergency department. Ondansetron is a serotonin 5-HT3 receptor antagonist, which connects to the peripheral and central receptors of serotonin (1). This drug is mostly used in nausea and vomiting after chemotherapy and surgery (2). It does not have any effect on dopamine receptors thus; it does not have extra pyramidal effect (3). Its maximum effect is in intravenous administration right after the injection. This drug has a half-life of 2-7 hours and is metabolized in the liver where it changes into Glucuronide and sulfate which is inactive. Its most common side effects include headaches, fatigue, diarrhea, constipation, dizziness and anxiety. The recommended dose for the treatment of nausea and vomiting is 4-8 milligrams (4, 5). Metoclopramide as an old antiemetic is mostly used in high doses, before chemotherapy and for

nausea and vomiting caused by various reasons (6-8). This drug blocks the dopamine receptors on the peripheral and central dopamine receptors and increases the movement of the upper gastrointestinal tract without increasing secretion (9, 10). Its intravenous absorption takes about 3 minutes and the peak of its effect is about 15 minute. This drug is metabolized in the liver and its half-life is approximately 4-5 hours (11). Its most common side effects include dystonia > 10%, fatigue, drowsiness, and flushing. Based on the above-mentioned reasons, the present study was aimed to compare the antiemetic effects of metoclopramide and ondansetron in the treatment of post head trauma nausea and vomiting.

Methods:

Study design and setting

The study was a controlled, randomized, double blind clinical trial, which was conducted in the first 6 months of 2014 in Al-Zahra and Kashani Hospitals in Isfahan, Iran. The present study was supervised and accepted by the ethics committee of Isfahan University of Medical Sciences. All the participants have consciously signed a written consent before entering the study. The study was registered in Iranian registry of clinical trial (IRCT number: IRCT2015043012072N6).

Participants

The studied population included patients with minor head trauma associated with nausea and vomiting who were referred to the emergency department .Minor head trauma has been considered as GCS 14-15. The patients older than 15 years old, with minor head trauma, nausea and vomiting, and a triage level of 3 or higher based on emergency severity score were included. The exclusion criteria were considered as follow: hemodynamic instability; pregnancy/lactation; any neurologic deficit; restless leg syndrome; alcohol usage; consumption of any antiemetic drugs during the 8 hours prior to admission; previous administration of intravenous fluids; motion/vertigo related nausea and vomiting; chemotherapy or radiotherapy; inability to complete and understand study explanations or outcome measures; finally allergy or previous adverse reactions to metoclopramide or ondansetron; and lack of data regarding demographic data and the severity of nausea and vomiting based on the visual analog scale (VAS). The qualified patients then entered the study using convenience sampling. Permuted-block randomization was done with a bock size of 6.

Intervention

The patients were randomly divided into 2 groups: treatment with metoclopramide (10mg/2ml, slow injection) and treatment with ondansetron (4mg/2ml, slow injection). Preparing the drugs was done by an independent pharmacologist in a sterilized manner. For the study to be double –blind, the drugs were packed in nameless syringes, and in numbered, dark packs and only the main researcher knew about the drug content. The drugs were kept in a fridge in the emergency department. The patients and the other researchers were blind to the drug content and the treatment group. Drug information and treatment group of the patients would only be revealed if the patients showed extrapyramidal side effects of the drugs, which did not happen in this study. Drug administration and patient assessment was done by emergency medicine residents. 20 minutes post drug administration, nausea level was measured again. If the severity of nausea had not decreased at least by 20 mm compared to the rate before the treatment intervention, a rescue dose (4mg ondansetron) would be prescribed for the patient.

Measurements

Nausea severity was measured using self-rated visual analogue scale (VAS) before and 20 minutes after the intervention. VAS was a standard 100 mm (mm) method on which the left side indicated no nausea and the right side was an indicator of the worst nausea possible. Using this scale for assessing nausea severity was accepted in previous studies. According to these studies the minimum difference in nausea severity counted as clinically significant, was set at 20 mm. Nausea severity was divided into 3 levels: severe nausea (VAS > 70 mm), moderate nausea (50 mm < VAS <70 mm) and mild nausea (VAS < 50 mm).

Outcomes

The primary outcome was defined as mean nausea severity according to VAS in the twentieth minute post drug administration. Secondary outcomes included needing a rescue dose and side effects of the drugs.

Statistical analysis

Population sample size for each group was determined based on comparing mean nausea severity between the 2 treatment groups. Based on previous studies (12), mean and standard deviation of nausea severity reduction before and after ondansetron administration was 40 mm and 24 mm respectively. Based on this, by considering $\alpha = 0.05$ and 90% power ($\beta = 0.1$), the sample size of 43 patients in each group was sufficient. Finally, 60 patients were included in each group. The data were analyzed using SPSS 21.0. Nausea severity was expressed as mean and standard deviation. To compare the 2 groups, t-test was used and for comparing the effects of the drug before and after administration, paired t-test was used. The drug side effect was also expressed as frequency and percentage. The comparison between the 2 groups was done using the chi square, the Fisher exact, or Mann-Whitney U test. In all the analyses, $p < 0.05$ was defined as the level of significance.

Results:

Finally, 120 patients with minor head trauma were distributed and studied into two groups of 60 patients (mean age 35.6 ± 14.1 years; 50.0% male). Mean age of metoclopramide and ondansetron treated groups were

Table 1: Distribution of clinical signs in the two groups

Variable	Metoclopramide N (%)	Ondansetron N (%)	P
Age (Mean ± SD)	36.1 ± 14.0	35.0 ± 14.2	0.69
Gender			
Male	27 (45.0)	33 (55.0)	0.27
Female	33 (55.0)	27 (45.0)	
Headache			
Yes	30 (50.0)	33 (55.0)	0.58
No	30 (50.0)	27 (45.0)	
Drowsiness			
Yes	26 (43.3)	8 (13.3)	<0.001
No	34 (56.7)	52 (86.7)	
Fatigue			
Yes	23 (38.3)	19 (31.7)	0.44
No	37 (61.7)	41 (68.3)	
Anxiety			
Yes	37 (61.7)	11 (18.3)	<0.001
No	23 (38.3)	49 (81.7)	
Dystonia			
Yes	5 (8.3)	0 (0.0)	0.057
No	55 (91.7)	60 (100.0)	

36.1 ± 14.0 and 35.0 ± 14.2 years, respectively (p = 0.69). The sex distribution in ondansetron (45.0% male) and metoclopramide groups (55.0% male) had no significant difference. Administration of both ondansetron and metoclopramide significantly reduced the severity of nausea (P < 0.001).

The average score of nausea severity before the injection of ondansetron and metoclopramide in the groups were 89.3±12.5 and 85.3 ± 14.9, respectively (p = 0.11). After intervention, nausea in the two groups were 32.3 ± 14.8 and 36. 5 ± 17.8, respectively (p = 0.17) (Figure 1). Before intervention 51 patients (85.0%) of the ondansetron group and 47 patients (78.3%) of the metoclopramide group had severe nausea (VAS > 70 mm) (p = 0.35). After intervention only 2 patients (3.3%) of the ondansetron treated and 5 patients (8.3%) of the metoclopramide treated group had severe nausea (p = 0.16). However, changes in the severity of nausea in both groups before and after the treatment revealed that nausea had been decreased significantly in both groups (P < 0.001) (Figure 2). The incidence of fatigue (p = 0.44), headache (p=0.58) and dystonia (p = 0.06) had no significant difference in the two groups but the incidence of drowsiness and anxiety in the metoclopramide group was significantly higher (P < 0.001) (Table 1). 2 (1.7%) patients needed the rescue dose which were in the metoclopramide treated group (p = 0.50).

Discussion:

The present study showed that the antiemetic effect of ondansetron and metoclopramide in patients with minor head trauma is the same. The frequency of severe nausea in the ondansetron group reduced from 85% to 3.3% while in the metoclopramide group, reduced from 78.3% to 8.3%. The incidence of drowsiness and anxiety were significantly lower in the ondansetron treated patients.

The antiemetic effects of ondansetron and metoclopramide have been compared in various studies, the results of which are in line with the current study. For instance, a study by Pitts et al. reveals that the effectiveness of ondansetron and metoclopramide compared to the placebo, show no significant difference in decreasing nausea and vomiting in the patients admitted to the emergency department (13). Also Egerton-Warburton et al. expressed in their study that the antiemetic effects of ondansetron and metoclopramide were no different compared to the placebo (14). In addition, Barrett et al. and Al-Ansari et al. have reported similar results (12, 15). In the present study, mean pain relief was 48.8 mm in the metoclopramide group and 57.0 mm in the ondansetron ones which was significantly different from the results of the mentioned studies. In this regard, Egerton-Warburton et al. showed that administering 4mg ondansetron and 20mg metoclopramide resulted in a 27 mm and 28 mm decrease in nausea severity, respectively (2). These levels in the Barrett et al. study was 40 mm for ondansetron and 32 mm for metoclopramide (15). Concerning the drugs' side effects, Patanwala et al. propose in their review study that due to safety, ondansetron is a better choice for the first line of treatment for decreasing nausea and vomiting in the patients admitted to the emergency department (16). The present study also showed that compared to metoclopramide, ondansetron administration, showed less side effects. In addition, in a study by Egerton-Warburton et al. 6 patients showed side effects in the group treated with metoclopramide,

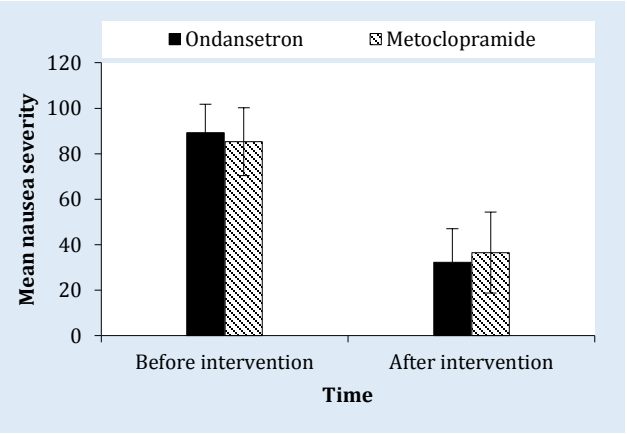

Figure 1: Mean changes of nausea severity before and after intervention in the 2 groups

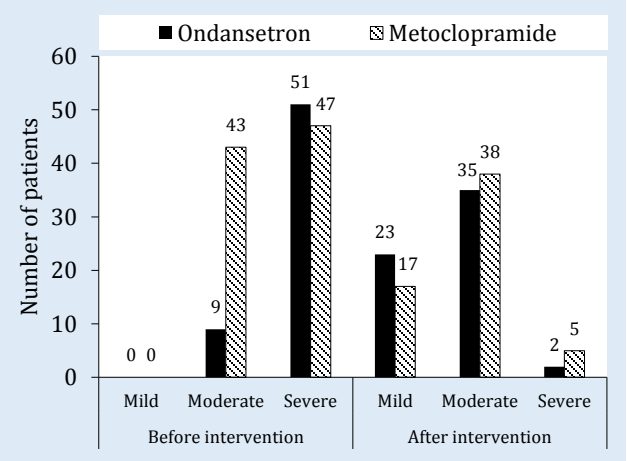

Figure 2: Frequency of nausea before and after treatment in both groups

whereas only 2 showed side effects in the group treated with ondansetron (14). A shortcoming in the present study was the lack of a placebo group. If such a group was studied, an assessment of the placebo effect would have been possible. In addition, since convenience sampling was used, selection bias is possible.

Conclusion:

The present study indicated that the treatment effectiveness of ondansetron and metoclopramide are similar. However, incidence of drowsiness and anxiety in the metoclopramide was considerably higher. Since these complications can have adverse effects on the treatment of patients with brain injury, it is suggested that it may be better to use ondansetron in these patients.

Findings.

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Conflict of interest:

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All authors passed four criteria for authorship contribution based on recommendations of the International Committee of Medical Journal Editors.

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