Original Article

An investigation into the effect of gabapentin capsules on the reduction of nausea and vomiting after chemotherapy in cancerous patients under platinum-based treatment

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Abstract

Introduction and Objective: Chemotherapy-induced nausea and vomiting (CINV) is a condition that occur in most patients. This study aimed to investigate the effect of gabapentin capsules on the reduction of chemotherapy-induced nausea and vomiting in patients admitted in the hematological ward for adult patients with platinum-based treatment. **Materials and Methods:** The present study was a randomized clinical trial, which consisted of a control group and an experimental one. The study population consisted of 126 women and men with colonic and gastric cancer who were admitted to Ahwaz Shafa Hospital of adult hematology ward. Of these, 120 subjects were eligible to enter the study. Immediately after chemotherapy, gabapentin capsules were taken. Up to 72 hours later, nausea and vomiting were compared. Descriptive statistics was used to investigate the demographic characteristics. Paired *t*-test, independent *t*-test and ANOVA were used to compare the results. **Results:** The results showed that most of the patients had gastric cancer in the experimental (70%) and control group (66.66%). The results also showed that chemotherapy-induced nausea and vomiting in gabapentin recipient group was different from the placebo group. Accordingly, chemotherapy induced nausea and vomiting in gabapentin group was lower than the placebo group. **Conclusion:** Post-operative nausea and vomiting is an unpleasant experience. Today, the patients find it worse than pain, and they believe it is hard to afford the cost of treatment. Gabapentin seems to be a good drug for reducing nausea and vomiting.

Keywords: Cancer, chemotherapy, gabapentin, nausea, vomiting

Introduction

Chemotherapy-induced nausea and vomiting (CINV) is a common condition. Acute chemotherapy-induced vomiting reaches the maximum level at the first 5 to 6 hours after chemotherapy. Nausea and vomiting which occurs 24 hours after chemotherapy is called acute chemotherapy induced nausea and vomiting. Delayed chemotherapy-induced nausea and vomiting occurs after the first day until the end of the fifth day of the onset of chemotherapy.[1]

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Despite anti-nausea and vomiting treatments, the prevalence of chemotherapy induced nausea and vomiting (CINV) is high. Accordingly, the delayed and acute chemotherapy induced nausea and vomiting occur in low to moderate emetogenic diets (about 13%–32%) and in moderate to high emetogenic diets (about 36%–54%). The prevalence of delayed chemotherapy-induced nausea and vomiting immediately after the discharge and or at home, which is not reported, can even be higher than the reported level and is reported to be up to 75%.[2]

Nausea and vomiting are caused by impulses produced through the chemoreceptors, throat, gastrointestinal tract,

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and the brain cortex. Once the vomiting center in the medulla is stimulated, some signals are transmitted to the salivation center, abdominal muscle, respiratory system, and cranial nerves, most of which act through neurotransmitters containing serotonin, dopamine, acetylcholine, glucocorticoid, histamine, canabioid, opioid, and neurokine-1 (NK-1). The above routes are often associated with vomiting and do not justify nausea to a greater extent. The prevalence of nausea and its cause are not well defined.[3]

As mentioned earlier, chemotherapy-induced nausea and vomiting (CINV) is a common condition and affects the quality of life of the patients. Accordingly, about one-third of patients undergoing chemotherapy have reported that this condition has become a major fear for them to continue the chemotherapy. In addition to reducing the quality of life of patients, CINV leads to a delay in the subsequent chemotherapy courses, and it is sometimes associated with decreased dose of chemotherapy drugs. Most importantly, it can prevent the patient from collaborating with health providers in administering the next treatment.[1,4]

It is worth noting that CINV also imposes additional treatment costs. Shee *et al.* (2009) found that the CINV imposes an additional cost of 2,000–4,000 USD and increases the absenteeism in the workplace.[5]

Gabapentin is an analogue gamma-aminobutyric acid, initially approved by the American Food and Drug Administration in 1994 for the treatment of seizures. It has been approved for treating post-transplantation neurological pain and restless leg syndrome.[4]

The action mechanism of gabapentin in the treatment of neuropathic pain, which is most commonly used in clinical cases, is more likely based on the fact that Alpha 2/Delta Calcium Voltage Channels (VGCC) reduce the flow of neuronal calcium.[6-8] The only other approved drug that shares this mechanism of action is pregabalin.[9] The anti-nausea effects of gabapentin were first reported in 2003, which was associated with improvements in delayed chemotherapy induced nausea among 9 women with breast cancer.[10] Since then, several studies have reported the advantages of gabapentin in the treatment and prevention of chemotherapy or pregnancy induced nausea and vomiting.

Few studies have focused on the effects of gabapentin on CINV reduction. Given the effects of gabapentin on the reduction of nausea and vomiting following anesthesia and surgery, it can be used as an alternative therapy in order to control CINV. Owing to the increasing lifespan, prevalence of cancer and chemotherapy, CINV has become an issue of importance for health and treatment. Regarding the increase in cancer due to the aging of the communities and the acceptance of chemotherapy in cancer patients, the present study was aimed at comparing the effect of gabapentin and placebo in order to reduce the CINV.

Given the high prevalence of gastrointestinal cancers, the present study aimed to investigate the effect of gabapentin capsules on the reduction of chemotherapy induced nausea and vomiting in patients admitted to the adult hematology ward.

Materials and Methods

This is a randomized clinical trial with a control and experimental group, in which the effect of gabapentin capsules on the reduction of chemotherapy induced nausea and vomiting in patients admitted in the adult hematology ward was examined. The treatment was based on platinum. The independent variable of gabapentin capsule is the dependent variable of nausea and vomiting.

The sample size consisted of 120 women and men with colon, gastric, breast, neck, bladder, and ovarian cancer who were admitted to the adult hematology ward of Ahwaz Shafa Hospital.

Sampling method

The sampling method was "convenience sampling" in which the researcher selected the subjects with the help of nurses and hospital officials, using the research inclusion criteria.

Inclusion criteria

Patients undergoing chemotherapy.

Patients with moderate to high nausea and vomiting.

Exclusion criteria

Life expectancy <3 m, Creatinine 1.5 times higher than normal (Upper limit), Pregnancy or breastfeeding Inability to eat with gastrointestinal obstruction, history of seizure or epilepsy, sensitivity to gabapentin Severe disease along with cancer (cardiac, pulmonary, liver, etc.), Active stomach ulcer, Brain metastasis, Undergoing radiotherapy, Taking anti-nausea and vomiting drugs over the past 24 hours, Aminotransferases 2 times higher than normal (Upper limit).

Data analysis

Data was analyzed using SPSS (version 21) through ANOVA as well as T-test and Pearson correlation coefficient.

Findings

Table 1 shows the descriptive statistics of the patients' demographic characteristics. According to the results, the majority of patients in the experimental (61.66%) and control (53.33%) groups were female. Fisher test showed that there was no statistically significant difference between the two groups in terms of age and sex.

According to the results, there was no significant difference between the two groups in the number of vomiting in any of the days after chemotherapy [Figure 1].

Table 1: Frequency distribution of patients in the two groups (experimental and control)

Group	Experimental		Control		Total		Test results
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	
Sex							
Male	23	38.33	28	46.66	51	42.50	Pearson Chi-Square *P* Value=0.49
Female	37	61.66	32	53.33	69	57.50	
Total	60	100	60	100	120	100	

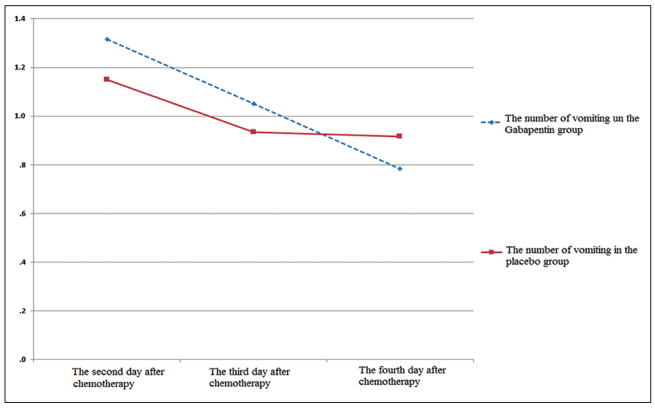

Figure 1: Number of vomiting in both gabapentin and placebo groups

The subjects were also studied in another way. In this study, patients were divided into two groups, one of which had nausea and the other did not suffer from nausea. There was no significant difference between the gabapentin recipients and placebo recipients [Table 2].

Table 2: Comparison of vomiting frequency, 3 days after chemotherapy

	Group	Mean	SD	*t*	*P*
The first day after chemotherapy	Gabapentin	1.06	0.75	1.104	0.272
	Placebo	1.15	0.86		
The second day after chemotherapy	Gabapentin	1.05	0.76	0.101	0.466
	Placebo	0.93	0.89		
The third day after chemotherapy	Gabapentin	0.78	0.80	0.224	0.348
	Placebo	0.91	0.74		

Discussion

The results showed that the chemotherapy-induced nausea and vomiting was not different between the gabapentin recipients and the placebo recipients. Accordingly, the rate of chemotherapy induced nausea and vomiting in the gabapentin recipients was not lower than the placebo recipients.

The present study does not agree well with other studies, particularly in reducing the nausea and vomiting by taking gabapentin,[11-16] while it is consistent with other studies in terms of the ineffectiveness of gabapentin in reducing nausea and vomiting.

The present study does not agree well with the study by Misra *et al.* Craniotomy surgery for intracranial tumors increases the rate of nausea and vomiting 55%–70%. It was also found that taking 600 mg gabapentin two hours before anesthesia causes the PNOV to decrease 24 hours later, compared to control group. It can be argued that even a lower dose of gabapentin showed that PNOV level were lower. In the present study, the day before chemotherapy, the total dose was 900 mg per day. This dosage remained constant for up to 72 hours after chemotherapy, while it did not agree well with the placebo group for up to 72 hours, given a decrase in the CINV in the gabapentin group.[14,17-20]

In the present study, the CR (complete response, no vomiting) was significantly improved in patients receiving gabapentin and the rate of nausea and vomiting did not significantly improve. Cruz *et al.* (2012) reported that the full response increased with *P* value = 0.04.[21]

The role of gabapentin in the prevention of CINV is less clear. Gattoso *et al.* reported the results of a study in which 9 patients underwent chemotherapy. The authors of the study stated that reducing the neurotransmitters may play an important role in preventing CINV. However, the actual mechanism of gabapentin as an anti-nausea drug is not yet known Animal studies have shown the role of environmental and central mechanisms in vomiting and have identified the relationship between Substance *P* and NK-1 receptors involved in the physiology of this condition. Although the exact mechanism of action of gabapentin (GABA) is unclear, some scientists have concluded that the gabapentin binding sites can be pre-and post-synaptic and be associated with NK-1 receptors.[22] The hypothesis shows that gabapentin is an interesting and promising factor for the evaluation of CINV. The fact that gabapentin had a positive effect on delayed CINV was also found in the study by Pacco *et al.* (2008) and Seark *et al.* (2007).[23,24]

Some studies have also suggested that gabapentin can have a greater effect on PNOV reduction in combination with other drugs. For example, Park *et al.* investigated the combination of romostrine and intravenous gabapentin in controlling nausea after gynecological laparoscopic surgery. Accordingly, 48 hours after surgery, the response to PONV was significantly higher in gabapentin and rhamostrone group than in the gabapentin and rhamosterone group ($P = 0.027$). It can be said that in this study, this limitation was controlled by researcher. Therefore, only one anti-nausea and vomiting drug has been used. It can also be used for CINV and gabapentin in combination with other drugs in future research.[25]

Although most studies have reported that gabapentin is capable of reducing the pain, it is believed that this drug plays an important role in reducing the pain after surgery. Therefore, it is not necessary to take anodynes. Accordingly, Pandie *et al.* found that gabapentin reducinges the pain, but the rate of nausea and vomiting is one of the side effects of this drug.

In the present study, owing to the fact that pain was not studied in the subjects, it is not possible to come to a definite conclusion. The effect of gabapentin on the reduction of CINV was investigated.[26] In a review study, Hu at al. found that gabapentin reduced the nausea, but did not show significant differences, suggesting that it is in good agreement with the present study.

In recent years, some studies have shown that gabapentin can be part of a multifactor approach to reduce or alleviate the pain. Moreover, the effect of this drug on PONV has also been shown. In a systematic review which included 16 studies, Hou *et al.* (2006) investigated the pain management by taking 1200 mg of gabapentin. It reduced the pain scores, the use of anodynes and vomiting during the first 24 days after surgery. In this case, the dose before the chemotherapy reduced the rate of nausea and vomiting. However, there is a significant difference between the intensity of the pain and the rate of nausea and vomiting.

Despite taking gabapentin, inconsistent results have also been reported in reducing the pain after surgery.[27,28] However, the efficacy of gabapentinin in reducing nausea and vomiting after surgery alone or in combination with drugs is well known. Although Harsted *et al.* (2009) suggested that less anti-nausea and vomiting oral drugs be used before chemotherapy because they believe that oral drugs make it possible to control nausea and vomiting.[29] But in the present study, using gabapentin oral therapy, it was found that nausea and vomiting can be controlled even up to 72 hours after chemotherapy.

It seems that gabapentin (up to 1200 mg per day) can relieve the pain to a great extent. In the present study, given that 300 mg of gabapentin per day was taken, it could not be of much help and nausea and vomiting continued up to 72 hours after chemotherapy.[30]

In a review study by Gattuso *et al.*, out of 33 randomized clinical trials, 12 were related to the effect of gabapentin on nausea and vomiting. These clinical trials, in the first place, showed that gabapentin could reduce PONV. They also indicated that gabapentin can reduce CINV. Moreover, it was shown that gabapentin can effectively reduce the risk of nausea and vomiting during pregnancy (hyperemesis gravidarum).

Conclusion

In the present study, it was found that gabapentin did not reduce the intensity of nausea and vomiting in patients with cancer after chemotherapy. Owing to its systematic nature, chemotherapy seems to cause a number of side effects, including diarrhea, low blood pressure, drowsiness, constipation, nausea, and vomiting. Among these side effects, nausea and vomiting are the most common, worst, and most prevalent side effects experienced by 70–80% of patients. Although few research has been carried out to reduce CINV using gabapentin, the results of this study indicate that gabapentin does not have the ability to control CINV completely. Since the use of gabapentin did not significantly reduce the intensity of nausea and vomiting after chemotherapy in this study, it can not be recommended to reduce CINV.

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Conflicts of interest

There are no conflicts of interest.

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