http://www.pjbs.org

PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Pakistan Journal of Biological Sciences 11 (14): 1878-1880, 2008
ISSN 1028-8880

Effects of Gabapentin on Early Postoperative Pain, Nausea and Vomiting in Laparoscopic Surgery for Assisted Reproductive Technologies

Sussan Soltani Mohammadi and Mirsadegh Seyedi
Department of Anesthesiology and Intensive Care Medicine,
Tehran University of Medical Sciences, Tehran, Iran

Abstract: Prevention and treatment of postoperative pain, nausea and vomiting continues to be a major challenge in postoperative care. This study was designed to compare the effects of small dose of oral gabapentin with placebo as premedication on early postoperative pain, nausea and vomiting in patients undergoing ambulatory laparoscopic surgery for Assisted Reproductive Technologies (ART). Seventy women undergoing ambulatory laparoscopic surgery were randomly assigned to receive oral gabapentin 300 mg or placebo as premedication 1 h before surgery. Patients were anesthetized with the same anesthetic techniques. Duration of anesthesia, severity of postoperative pain and presence of Post Operative Nausea and Vomiting (PONV) were compared between the study groups. Demographic data and the duration of anesthesia were not statistically different between the study groups. There were significant differences in median VAS scores (25th-75th) measurements at all time points in the study groups ($p<0.05$). Ten patients (28%) in control and one patient (0.02%) in gabapentin group required additional IV analgesic that was statistically significant ($p = 0.012$). Two patients in gabapentin and nine patients in placebo group had nausea ($p = 0.022$). None of patients in gabapentin but four patients in placebo group had vomiting ($p = 0.114$). Administration of oral gabapentin 300 mg before ambulatory laparoscopic surgeries, decreased postoperative pain, analgesic requirement and nausea.

Key words: Gabapentin, laparoscopy, pain, postoperative, nausea and vomiting, postoperative

INTRODUCTION

Prevention and treatment of postoperative pain and complications such as Post Operative Nausea and Vomiting (PONV), continues to be a major challenge in postoperative care and plays an important role in the early mobilization and well-being of the surgical patient.

Opioid analgesics, with their well-known side-effects, continues to represent a cornerstone in postoperative pain control and testing new analgesics as well as combinations of analgesics in order to reduce the need for opioids, is a key area in acute pain research (Rose and Kam, 2002).

Gabapentin is an anticonvulsant that has anti-nociceptive and antihyperalgesic properties. In pain models it has shown anti-hyperalgesic properties, possibly by reducing central sensitization, a prerequisite for postoperative hyperalgesia. It binds the a^2d subunits of voltage dependent calcium ion channels and blocks the development of hyperalgesia and central sensitization (Goa and Sorkin, 1993; Eckhardt *et al*., 2000; Mathiesen *et al*., 2007).

After a single oral dose of 300 mg gabapentin, mean maximum plasma concentrations attained in 2-3 h. Absorption kinetics of gabapentin are dose dependent, possibly due to a saturable transport system. Bio-availability of a single 300 mg oral dose of gabapentin is 60% and decreases with increasing dose. Elimination of gabapentin is by renal clearance and is about 5-7 h after a single oral dose of 200 to 400 mg (Goa *et al*., 1993).

Recently an open clinical study demonstrated the anti-emetic effect of gabapentin in chemotherapy-induced acute (within 24 h) and delayed onset (2-5 days) of nausea and vomiting; Mitigation of tachykinin neurotransmitter activity by gabapentin has been postulated to play a role (Guttuso *et al*., 2003).

In the study by Pandey *et al*. (2006) on 250 patients scheduled for laparoscopic cholecystectomy, gabapentin as premedication effectively suppresses nausea and vomiting and post-operative rescue analgesic requirement (Pandey *et al*., 2006).

Surgery for Assisted Reproductive Technologies (ART) has developed in many countries and performed on an ambulatory basis. Since, the duration of surgery in

Corresponding Author: Sussan Soltani Mohammadi, Department of Anesthesiology, Dr. Shariati Hospital, Al-e-Ahmad High Way, North Kargar Street, 1411713135 Tehran, Iran
Tel: +98-21-22295296, +98-912-1226683 Fax: +98-21-88633039

these procedures is short, the main purpose of anesthesia for these operations, is shortening the recovery time by reducing the common complications such as nausea, vomiting and pain.

Therefore, we designed a placebo-controlled study to test the hypothesis that oral gabapentin 300 mg as premedication, would decrease postoperative pain, nausea and vomiting in these group of patients.

MATERIALS AND METHODS

This randomized clinical trial was performed in Dr. Shariati Hospital of Tehran University of Medical Sciences from August to December 2007. The study protocol conformed to the ethical guidelines of the 1989 Declaration of Helsinki.

After Institutional Ethics committee approval, each patient's informed consent was obtained separately. Seventy ASA I and II women aged 20-45 years, who were scheduled for outpatient laparoscopic surgery under general anesthesia for ART were included in this study. Patients with known allergy to any study drug and those receiving psychotropic drugs were excluded.

The patients were randomly assigned to receive either oral gabapentin 300 mg (n = 35) or placebo (n = 35) 1 h before surgery. Randomization was based on computer-generated codes that were concealed until interactions were assigned.

On arrival in the operating room, standard anesthesia monitors were placed. Patients preoxynated with oxygen (5 L min^{-1}) by mask with a port for monitoring expired CO_2 levels. All patients were premedicated with midazolam 1 mg IV (Amp 5 mg mL^{-1}, MIDAZOLEX®5, EXIIR-Iran) and fentanyl 2 μg kg^{-1} (Amp 10 mL, Fentanyl-Janssen™, Belgium).

Anesthesia was induced with propofol 2 mg kg^{-1} (Amp 20 mL, Dongkook Pharm. Co., Ltd.) and then maintained by 100 μg/kg/h propofol with oxygen.

Tracheal intubation was facilitated by succinylcholine 1.5 mg kg^{-1} (Vial 500 mg, BIOLOGICI Italia Lab™ -Italy) and atracurium was injected 0.03 mg kg^{-1} (Amp 10 mg mL^{-1} Mayne Pharma Plc™, UK) when it was necessary. At the end of the operation, the propofol infusion was discontinued and after reverse of muscle relaxant, trachea was extubated and patients were moved from the operating table to the transport stretcher before transfer to the step-down (Phase II) recovery unit. Duration of anesthesia, severity of postoperative pain and presence of PONV were recorded. Anesthesia time was calculated from the start of the propofol injection to tracheal extubation. Before leaving the operating room, fast-track eligibility (score > 9) was assessed using a standardized criteria unit by a blinded observer (Chung *et al*., 1995; Feeley and Macario, 2005).

Pain scores were recorded at emergence from anesthesia, 1st and 2nd h after operation by using a 10 cm linear visual analog scale (VAS), with 0 corresponding to no pain and 10 to the worst imaginable pain. Fentanyl was used as rescue postoperative analgesic and Ondansetron 4 mg IV as rescue medication for emesis.

Statistical analysis: A sample size of 35 patients in each group will be sufficient to detect a 30% difference of in the incidence of postoperative nausea and vomiting between the study groups assuming power of 90% and a significant level of 0.05. Statistical analysis was performed With SPSS package version 11.5. Normality of distribution was tested by Kolmogorov Smirnov test. Data were analyzed by Independent sample t-test, Mann-Whitney test, Chi-square or Fisher's exact test when appropriate. $p<0.05$ was considered statistically significant.

RESULTS

Demographic data and the duration of anesthesia were not statistically different between the study groups (Table 1) (independent sample t-test and Chi-square).

There were significant differences in median VAS scores (25th-75th) measurements at all time points in the study groups (Mann-Whitney test, $p<0.05$, Table 2).
Ten patients (28%) in control group and only one patient (0.02%) in gabapentin group required additional IV analgesic that was statistically significant (Chi-square, $p = 0.012$).

We used incidence of nausea and vomiting separately to present PONV, in the operating room before transferring to recovery (phase I) and during stay in

Table 1: Demographic and perioperative data in the study groups

Characteristics	Gabapentin group (n = 35)	Placebo group (n = 35)
Age (years)*	31.3±5.4	31.9±5.6
Weight (kg)*	69.6±9.7	70.3±10.8
ASA (I/II)†	26/9	24/11
Anesthesia time (min)*	46.7±9.9	44.2 ±9.7

*Values are expressed as means±SD, †ASA: American Society of Anesthesiologists

Table 2: Comparison the median (interquartile range) of VAS scores at emergence from anesthesia (VAS_0), first (VAS_1) and second (VAS_2) hour after operation between the study groups

Variables	Gabapentin group (n = 35)	Placebo group (n = 35)	p-value
VAS_0	1(0-2)	2(1-3)	0.007
VAS_1	3(1-3)	3(2-5)	0.007
VAS_2	3(2-3)	3(3-5)	0.002

recovery (phase II) (0 to 2 h postoperatively). Two patients in gabapentin and nine patients in placebo group had nausea (Chi-square, p = 0.022).

None of gabapentin group and four patients in placebo group had vomiting that was not statistically significant and Ondansetron 4 mg was used intravenously as rescue antiemetic (Fisher's exact test, p = 0.114).

Side effects related to the use of gabapentin were not found.

DISCUSSION

Although surgery for ART performed on an ambulatory basis and duration of surgery in these procedures is short, common complications such as nausea, vomiting and pain can delay recovery and increase discharge time. In this placebo controlled study we showed that oral administration of 300 mg gabapentin as premedication before surgery, decreased postoperative pain, analgesic requirement and nausea but not vomiting after ambulatory laparoscopic surgeries.

In a study by Pandey *et al.* (2006) 250 patients of ASA physical status I and II, scheduled for laparoscopic cholecystectomy were randomly assigned into two equal groups to receive 600 mg gabapentin or matching placebo two hours before surgery. They found that Incidence of post-operative nausea and vomiting within 24 h after laparoscopic cholecystectomy was significantly lower in gabapentin group (46/125) than in the placebo group (75/125) (37.8 vs 60%; p = 0.04). There was also significant decreased in fentanyl consumption in gabapentin group compared to placebo group (p = 0.01) (Pandey *et al.*, 2006).

These findings were correlated to present study except vomiting that was not statistically different between our groups. This may be related to the different type of surgery and dose of gabapentin.

In the study by Guttuso *et al.* (2003) oral gabapentin 300 mg twice daily was given for chemotherapy treatment in nine patients with breast cancer. Six of the nine reported at least a three-point improvement in peak delayed nausea (on an eight-point nausea scale) and three patients had complete resolution of nausea when taking gabapentin.

This study suggested that gabapentin was effective in reducing chemotherapy-induced nausea (Guttuso *et al.*, 2003).

In present study oral gabapentin 300 mg 1 h before surgery was effective in reducing postoperative nausea that was correlated to the study of (Guttuso *et al.*, 2003) but postoperative vomiting was not statistically different between the study groups. The lower incidence of post operative nausea in the gabapentin group may be due to a decrease in opioid-related side effect. Fentanyl requirement was lower in the gabapentin group (p = 0.012) and it was statistically significant.

The severity of postoperative pain and opioid consumption following different type of surgeries are variable and may affect on the incidence of PONV. So, further study may be required to see if gabapentin reduces the incidence of PONV when compared with placebo in patients undergoing non-painful procedures under general anesthesia.

REFERENCES

Chung, F., V.W. Chan and D.A. Ong, 1995. Post-anesthetic discharge scoring system for home readiness after ambulatory surgery. J. Clin. Anesth., 7: 500-506.

Eckhardt, K., S. Ammon and U. Hofman *et al.*, 2000. Gabapentin enhances the analgesic effect of morphine in healthy volunteers. Anesth. Analg., 91: 185-191.

Feeley, W.T. and A. Macario, 2005. The Post Anesthetic Care Unit. In: Miller's Anesthesia. Ronald, D.M. (Ed.). 6th Edn., Churchill Livingstone, Philadelphia, ISBN: 0-443-06618-3, pp: 2307-2727q.

Goa, K.L. and E.M. Sorkin, 1993. Gabapentin. A review of its pharmacological properties and clinical potential in epilepsy. Drugs, 46: 409-427.

Guttuso, T. Jr., J. Roscoe and J. Griggs, 2003. Effect of gabapentin on nausea induced by chemotherapy in patients with breast cancer. Lancet, 361: 1703-1705.

Mathiesen, O., S. Moiniche and J.B. Dahl, 2007. Gabapentin and postoperative pain: A qualitative and quantitative systematic review, with focus on procedure. BMC Anesthesiol., 7: 6-6.

Pandey, C.K., S. Priye, S.P. Ambesh, S. Singh, U. Singh and P.K. Singh, 2006. Prophylactic Gabapentin for prevention postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: A randomized double-blinded placebo-controlled study. J. Postgrad. Med., 52: 97-100.

Rose, M.A. and P.C. Kam, 2002. Gabapentin: Pharmacology and its use in pain management. Anaesthesia, 57: 451-562.