Egyptian Journal of Anaesthesia xxx (2016) xxx–xxx

HOSTED BY

ELSEVIER

Contents lists available at ScienceDirect

Egyptian Journal of Anaesthesia

journal homepage: www.sciencedirect.com

Randomized controlled trial of two oral regimens of gabapentin versus placebo in patients for Cesarean section under spinal anesthesia regarding postoperative pain, sedation, nausea and vomiting

Mohamed Hafez El Saied Hafez [a], Mona Hossam El Din Abdelhamid [a,*], Maha Mahammed Ismail Youssef [a], Iman Kasban Hussien Abdelrahim [b]

[a] Department of Anesthesia, ICU and Pain Management, Cairo University, Egypt
[b] The commission of public teaching hospital, National institute of Hepatology and Gastroenterology, Cairo, Egypt

ARTICLE INFO

Article history:
Received 17 July 2016
Revised 22 October 2016
Accepted 23 October 2016
Available online xxxx

Keywords:
Cesarean section
Spinal anesthesia
Gabapentin
Postoperative pain
Sedation
Nausea and vomiting

ABSTRACT

Background and aim: Pain after Cesarean delivery parturients is the most common postoperative complaint, and gabapentin has been shown to reduce acute postoperative pain but with little experience in parturient.

Methods: After approval from the ethical committee in Kasr Al Aini University Hospital, forty-five consenting women aging 20–40 yrs old ASA physical status I or II, with uncomplicated pregnancies scheduled to undergo elective Cesarean section delivery under spinal anesthesia were randomly allocated into three equal groups who received 600 mg gabapentin G600, 900 mg gabapentin G900, and control group GC. The study medication was given orally one hour before the anticipated time of the surgical incision, and data measured include, the time of first rescue of analgesia, the total duration of analgesia, the incidence of post-operative nausea and vomiting (PONV), the level of sedation, and the Neonatal APGAR score at 1 and 5 min.

Results: The time for first rescue of analgesia was comparatively shorter in patients of group GC as compared to G600 and G900 groups (P value = 0.001). Total analgesic requirement of pethidine in first 24 h was significantly lower in groups G600 and G900 as compared to group GC (P value = 0.000) and we found that there was statistically significant increase in the sedation scores of the patients in the G900 group as compared to GC group and G600 group. By comparing the presence of nausea and vomiting in the two gabapentin groups with the control group as a reference value, and with each other in the post-operative periods, we found that there was statistically significant decrease in the nausea score in the G900 group as compared to groups G600 and GC with p value (0.06 and 0.4) respectively.

Conclusion: Gabapentin 900 mg was more effective than 600 mg in reducing post Cesarean section pain, opioid consumption, nausea, and vomiting.

1. Introduction

Postoperative pain, nausea and vomiting (PONV) continues to be one of the most common and unpleasant complications after surgery especially obstetric surgeries [1].

The traditional pain treatment with opioids alone is nowadays not adequate any more. To optimize pain treatment and postoperative outcome, new analgesics and new combination of already existing analgesics are searched for [2].

Gabapentin is a drug with chemical structure that mimics that of the neurotransmitter GABA (gamma amino butyric acid) and acts on the same brain receptors. However, the mode of action is not fully understood. Among other mechanisms like decrease in the synthesis of the neurotransmitter glutamate, gabapentin acts by binding to the $\alpha 2\delta$ subunit of voltage-dependent ca2+ channels. It has introduced as antiepileptic drug but proved to be effective in controlling neuropathic pain [3].

Recently, gabapentin has been used to reduce pre-operative anxiety, acute postoperative pain, postoperative opioid requirements and postoperative nausea, vomiting and delirium [4].

The efficacy and safety of preoperative oral Gabapentin on pain and opioids consumption were studied in patients undergoing a

Peer review under responsibility of Egyptian Society of Anesthesiologists.
* Corresponding author.
E-mail address: monahossam29@yahoo.com (M.H.E.D. Abdelhamid).

http://dx.doi.org/10.1016/j.egja.2016.10.010
1110-1849/

Please cite this article in press as: Hafez MHES et al. Randomized controlled trial of two oral regimens of gabapentin versus placebo in patients for Cesarean section under spinal anesthesia regarding postoperative pain, sedation, nausea and vomiting. Egypt J Anaesth (2016), http://dx.doi.org/10.1016/j.egja.2016.10.010

variety of surgical procedures [5] as total abdominal hysterectomy [6], vaginal hysterectomy [7], thoracotomy [8], and spine surgeries [9] but conclusions about optimal dose and duration of treatment cannot be made because of heterogeneity of the trials.

Because gabapentin seems to prevent acute nociceptive and inflammatory pain and might reduce postoperative pain, there were two previous studies previously tried gabapentin for post Cesarean section delivery pain as that have compared gabapentin (600 mg with either 300 mg or placebo), but the results were controversial [10]. The present randomized double-blind controlled study was designed to compare the efficacy of two different doses (600 mg and 900 mg) of oral gabapentin premedication on the postoperative duration of analgesia (whether gabapentin reduces the postoperative need for additional pain treatment), PONV, and postoperative side effects after elective Cesarean delivery under spinal anesthesia. We aimed at identifying the dose with the best effect and the least side effects.

2. Patients and methods

This study was conducted in Kasr Al Ainy Medical Hospital, faculty of medicine Cairo University, from April 2015 to March 2016. After approval of the hospital ethical committee and after obtaining a written informed consent, a total of 45 consecutive women aging 20–40 yrs old ASA physical status I or II, with uncomplicated pregnancies at term (>37 completed weeks) scheduled to undergo elective Cesarean section delivery under spinal anesthesia were included in this prospective, randomized double blinded clinical trial of two oral doses of gabapentin. However, patients with contraindication to neuro axial anesthesia, patients known to be epileptic or on antiepileptic medications, patient with kidney or liver function impairment, patients known alcoholic or IV drug users, pregnancies with any obstetric complications as hypertension, oligohydramnios, polyhydramnios, antepartum hemorrhage, a psychiatric disorder, or inability to communicate effectively were excluded from the study.

Study group allocation into three groups (15 patients each) was generated by a computer-generated random number table and was sealed in opaque envelopes that were opened by an anesthetist not involved in the intra- or postoperative care of the parturient.

- **G_C** (n = 15): control group received three placebo capsules which are empty capsules similar to those of gabapentin 300 mg.
- **G_{600}** (n = 15): gabapentin 600 mg group received two capsules of gabapentin 300 mg and third empty one similar to gabapentin.
- **G_{900}** (n = 15): gabapentin 900 mg group received three capsules of gabapentin 300 mg.

The study medication was given by mouth with a sip of water one hour before the anticipated time of the surgical incision.

The medication was administered by the anesthetist, who also performed the subsequent assessment.

The investigator was blinded to group assignment until all women had been recruited and assessments were completed.

No other premedication was given at this time.

Preoperative evaluation for all groups included a detailed history, physical examination and investigations (hemoglobin level, platelet count, random blood glucose, serum creatinine, liver function tests, prothrombin time (PT) and international normalized ratio (INR)). (All patients were instructed in the use of numerical rating scale by the investigator.)

Preparation of the drugs for spinal anesthesia: Lidocaine 2% (Xylocaine), Bupivacaine (heavy marcaine), and fentanyl, spinal needles, Sterilized towels and gauze, povidone iodine for sterilization, Syringes and adhesive tape, appropriate sizes of tracheal tubes, laryngoscopes with long and short blades, oxygen source and Disposable face mask were prepared for any possible intervention. Also Atropine 1 mg/ml, diluted with saline to a concentration of 0.1 mg/ml, and Ephedrine hydrochloride (Ephedrine) 30 mg/ml, diluted with saline to concentration of 3 mg/ml. And general anesthetics as standby for any complications.

- On arrival to the operating room all patients were continually monitored by automated noninvasive blood pressure monitoring (NIBP), pulse oximetry and 5 leads electrocardiography (ECG).
- Pre induction baseline reading for patient's hemodynamic state (mean blood pressure (MBP), heart rate (HR) and saturation (spo2)) was recorded for all groups.
- An 18 G intravenous cannula was inserted in an appropriate vein and a preload of 10 ml/kg Ringer's lactate was started, along with antibiotic prophylaxis.
- Then the parturient was supported to be in the sitting position for preparation for the administration of the spinal anesthesia. Complete aseptic precautions including sterilization with povidone iodine and draping were performed. The L4/L5 intervertebral space was located. Using a size 22 G hypodermic needle, the skin overlying the intervertebral space identified was anaesthetized with 3 mL of 2% lidocaine. Lumbar puncture was performed through a midline approach using a 25G spinal needle and 8 mg bupivacaine with 25 μg fentanyl was administered intrathecally; then, the patient was positioned supine with 15° left lateral tilt.
- When satisfactory spinal anesthesia (adequate sensory and motor blockade) achieved surgeon was allowed to start.
- At the end of surgery all patients were transferred to post anesthesia care unit (PACU) where they were observed for the following:
  (1) The time to first postoperative rescue analgesic request, the number of doses was recorded as well as total duration of analgesia (defined as time elapsed from the onset of spinal anesthesia to time of first call for analgesics), which was assessed by a numerical rating scale (NRS) a scoring system used by the patient, the patient put a mark on a horizontal line which reads "no pain at all" at one end at 0, and "worst pain imaginable" at the other end at 10 and recorded initially every 2 h for the first 10 h and then after every 4 h till 24 h. If NRS $\geqslant$ 4, intravenous meperidine (pethidine) 1 mg/kg intramuscular was given as rescue analgesia (repeated if needed during the first 24 h postoperatively), the number of doses and total analgesic requirement was recorded.
  (2) The incidence of postoperative nausea and vomiting (PONV) and nausea severity: for each patient was assessed by the simplified PONV impact scale which uses the nausea ordinal response to quantify nausea intensity, where (i) 0, (ii) 1, (iii) 2, (iv) 3 and the vomiting count to quantify vomiting intensity, scored as the number of vomits (0–2, or 3 if three or more vomits). When PONV impact scale $\geqslant$ 5→ Ondansteron (Zofran), 4 mg and Ranitidine (zantac), 50 mg was administered to the patient.
  (3) The level of sedation was assessed at 3 h intervals for the first 12 h and then every 6 h for the next 12 h postoperatively by using the modified Ramsay Sedation Score.

2.1. Ramsay sedation score

Score responsiveness

1 Patient is anxious and agitated or restless, or both.

Please cite this article in press as: Hafez MHES et al. Randomized controlled trial of two oral regimens of gabapentin versus placebo in patients for Cesarean section under spinal anesthesia regarding postoperative pain, sedation, nausea and vomiting. Egypt J Anaesth (2016), http://dx.doi.org/10.1016/j.egja.2016.10.010