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Effect of Gabapentin Premedication on Post Dural Puncture Headache in Patients Undergoing Elective Cesarean Section.

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Abstract

Background: Background: Gabapentin has widely been used to treat different types of headaches and as prophylaxsis against migraine. We aimed to access utility of pre-operative Gabapentin on characteristics of Post dural puncture headache (PDPH) in parturient patients undergoing elective cesarean section under spinal anesthesia.

Methods: A double blind study was conducted on100 parturients between the age group of 18 – 35 yrs with ASA II undergoing elective cesarean section under spinal anesthesia randomized to receive preoperative (group G) gabapentin 600 mg (2 capsules of 300mg each) or (group P) placebo (similar looking multivitamin), with a small sip of water 2 hours before admission to the operating room. Mothers were observed for hemodynamic variabilties, side effects, sedation score, VAS score intraoperatively as well as postoperatively till discharge. Babies were followed up by Apgar scores at 1min and5min, breastfeeding difficulties, and need for NICU admission. Any possible adverse events of gabapentin as sedation, ataxia, tremors, dizziness, nausea, and vomiting were recorded for 24 hours post-operatively.

Results: The incidence of headache and co-existing symptoms were similar in both groups. The onset of headache was significantly delayed in gabapentin group ($P < 0.05$). Also, severity and duration of headache were significantly less in gabapentin group ($P < 0.05$). The consumption of breakthrough analgesics in the form of caffeine and diclofenac was significantly less in gabapentine group. The incidence of sedation was more in gabapentin versus placebo group. Neonatal outcomes were statistically insignificant between both groups.

Conclusion: Gabapentin given pre operatively has no effect on incidence of (PDPH) but does delays its onset and reduces its severity as well as duration in parturients undergoing cesarean section with spinal anesthesia without any significant adverse effects either on the mother or the baby.

Key words: Gabapentin, Post dural puncture headache, spinal anesthesia.

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Introduction

Post-dural puncture headache (PDPH), was first description by August Bier in 1898, remains one of the most common complication for surgical patients undergoing lumbar puncture.[1-3]

According to International Headache Society (IHS), PDPH is a headache that develops following a lumbar puncture, occurs or worsens <15 min after assuming the upright position and improves in the recumbent position in <30 min with at least one of the following symptoms: Neck stiffness, tinnitus, hyperacusia, photophobia.[4] Mostly, it starts within 2 days and usually resolves spontaneously in a few days, but it can be severe and disabling and may last for up to 6 weeks.[5]

Risk factors for it are younger age, female gender, pregnancy and labour, large needle size, direction of the cutting needle bevel when puncturing the dura, multiple dural punctures and previous history of PDPH. Pregnant females in particular risk due to sex, age, and the widespread use spinal anesthesia. Headache can be so severe that it can affect the ability of the mother to care for her baby. Several methods such hydration, bed rest, caffeine, non-steroidal anti-inflammatory drugs, ACTH and invasive procedures like epidural blood patch has been suggested for its treatment. In order to decrease the incidence of the PDPH as well as reduce the cost of treatment various drugs such as acetaminophen, gabapentine, pregabaline, dexamethasone etc. are under study. Gabapentin is an anti-epileptic drug, an analogue of GABA which acts on alpha 2-deltatype voltage-dependant calcium channels. In 2002 it got approved by Food and drug association for use in neuropathic pain. In our study we will compare gabapentine group with a placebogroup inorder to study its efficacy in preventing PDPH as well as its side effects.

Materials and Methods

After taking due approval of the ethical committee of our institute a double blind study was conducted on100 parturients between the age group of 18 – 35 yrs with ASA II undergoing elective cesarean section under spinal anesthesia randomized to receive preoperative (group G) gabapentin 600 mg (2

capsules of 300mg each) or (group P) placebo (similar looking multivitamin). Patients with History of chronic headache, hepatic disease, known allergy to gabapentin, pregabalin or acetaminophen, physical status of ASA III or above, multiple lumbar punctures, severe bleeding (> 20% of blood volume), treatment with vasopressors, signs of meningismus, history of pancreatitis, galactosemia, history of intake of antiepileptic drug and analgesics, fetal compromise, prior exposure to spinal anesthesia, migraine, or asthma were excluded from the study. The participants were randomly assigned to one of both groups using chit method having number on it.
Every participant was assigned a number for, and the 2 capsules of gabapentin or placebo were placed in a numbered similar looking medication boxes. An assistant, not involved in the study, prepared the boxes, and another assistant blinded to the content of the boxes administered the capsules to the woman with the corresponding study number with a small sip of water 2 hours before admission to the operating room. In the operating room, an 18G venous cannula was inserted, and 10ml/kg of Ringer's lactate solution was given to every patient as a preload. Standard monitors were applied. After cleaning and draping in the left lateral position, spinal anesthesia was given using a 25-G quincke spinal needle, and a dose of 12.5 mg hyperbaric bupivacaine 0.5% was injected after free flow of CSF. Any drop in the blood pressure of more than 20% below the baseline was treated with colloids followed by intravenous 5 – 10 mg ephedrine. and the patient was excluded as headache is one of the possible side-effects of ephedrine, which may interfere with our study. Mothers were observed for hemodynamic variabilties, side effects, sedationscore, VAS score intraoperatively as well as postoperatively till discharge.
Babies were followed up by Apgar scores at 1min and5min, breastfeeding difficulties, and need for NICU admission. In the post-operative period, all women received the same fluid regimen and the same course of analgesics which included inj.paracetamol 1gramTDS. Any possible adverse events of gabapentin as sedation, ataxia, tremors, dizziness, nausea, and vomiting were recorded for 24 hours post-operatively. In case of sedation, the level was assessed using Ramsay sedation score. If patient complaint of headache then the onset and duration and any other symptoms as nausea and vomiting, neck stiffness, and diplopia or photophobia were determined by asking the patient and were recorded. Everyone who had a confirmed PDPH received the same protocol of bed rest, fluids, laxatives, antacids, and analgesics. Patients were discharged on 4th post-operative day .All the participants were instructed about the possibility of headache and were encouraged to notify about its occurrence.

Statistics

Results are expressed as means ± standard deviation (SD). Comparison between parametric data was performed using student t-test and non -parametric data was performed using the chi squared test. Data were considered significant if P values were <0.05. Statistical analysis was performed with the aid of SPSS 7computer program.

Results

Ninety four patients were randomized, and six were excluded. Demographic and hemodynamic variables were comparable in both the groups. The incidence of headache and co-existing symptoms were similar in both groups. The onset of headache was significantly delayed in gabapentin group ($P < 0.05$). Also, severity and duration of headache were significantly less in gabapentin group ($P < 0.05$). The consumption of breakthrough analgesics in the form of caffeine and diclofenac was significantly less in gabapentine group. The incidence of sedation was more in gabapentin versus placebo group. Neonatal outcomes were statistically insignificant between both groups.

Table 1: Demographic variables and duration of CS.

Variable	Gabapentine	Placebo	P value
Age(yrs)	28.1±4.5	29.7±4	P=0.166
Weight(kg)	75.8±4.4	78±4.7	P=0.187
Caesarean time (mins)	58.7±6.8	60.8±7.3	P=0.195

Table 2: Headache characteristics (incidence, onset, duration, and Mean VAS scores while sitting).

Characterstics of headache	GABAPENTINE (n=47)	PLACEBO (n=47)	P value
No.of cases	3	4	P value>0.795
Onset (days)	2.02±0.5	1.6±0.45*	P value=0.03
Duration (days)	3.00±0.5*	4.0±0.84	P=0.011
Mean VAS Score			
1st day	6.02±1.12	7.10±1.21	P=0.003 *
2nd day	4.89±1.14	5.98±0.56	P=0.002*
3rd day	1.52±0.55	3.06±1.13	P < 0.0001**
Co- existing symptoms	2	3	

Discussion

Post dural puncture headache is a common and distressing complication of spinal anesthesia. As mentioned before, female gender as well aspregnancy are among the risk factors for increase in incidence of PDPH. It not only leads to increase in maternal morbidity but incease in neonatal problems also.
The incidence of PDPH in spinal anesthesia ranges from 0.3% to 20% in different studies.[6] The exact pathophysiology of PDPH is not fully understood

yet.[7,8] It is assumed that CSF depletion due to leakage leads to traction of some pain-sensitive intracranial structures and so, causes PDPH. Different pharmacological and nonpharmacological methods are being devised for its treatment taking into special consideration treatment effect on neonate too.

Table 3: Number of paracetamol and diclofenac tablets given.

Medication given	Gabapentine	Placebo	P value
Caffeine tablets	12.85±0.76	19.8±0.68	P=0.005 *
Diclofenac tablets	7±1.6	11.6±1.67	P=0.001*

Table 4: Incidence of maternal adverse reactions in the first 24 h post-operatively.

Side effects	Gabapentine	Placebo	P value
Nausea and vomiting	7 (16.67%)	9 (20.45%)	P=0.863
Tremors	0	0	NA
Dizziness	0	0	NA
Sedation	11(26.19%)	3 (6.81%)	P=0.032*

Table 5: Neonatal outcomes

Variable	Gabapentine	Placebo	P value
Weight(kg)	3.051±522	2.947±581	P=0.423
Apgar at 1min	9 (8-9)	9 (8-9)	0.94
Apgar at 5 min	9 (9-9)	9 (9-9)	NA
Apgar at 10 min	9(9-9)	9(9-9)	NA
NICU admissions	2 (4.76%)	1 (2.27%)	P=0.967
Lactation difficulties(no.of babies)	2 (4.76%)	1 (2.27%)	P=0.967

Current treatment for PDPH involves complete bed rest, hydration, analgesics, oral or intravenous caffeine, sumatriptan, ACTH, corticosteroids, gabapentin, and epidural patch.[9] The present study was conducted on 100 patients divided into two groups one receiving gabapentin and other placebo group. Mechanism for gabapentin-mediated analgesia is the modulation of glutamate receptors (NMDA and AMPA/kainite). Gabapentin seems to decrease both NMDA and non-NMDA-mediated glutamate currents in the superfi cial lamina of the spinal cord of the rats and also inhibits nociceptive responses to intrathecal NMDA and AMPA in vivo.[10,11]

Suarez et al.[12] suggested that sodium entry through presynaptic NMDA-K channels facilitates axon excitability and the interaction of gabapentin with this mechanism might contribute to its analgesic benefits.

Our study showed that pre-operative administration of 600 mg of gabapentin signifi cantly delays the onset and reduces the intensity and duration of the PDPH. The decreased severity and duration of the headache in the gabapentin group could be refl ected on the analgesic doses needed for treatment, which was significantly lower in the same group. However, there was no difference in the incidence of the headache in gabapentine or placebo groups.

Our study is supported by similar study of Erol conducted on 20 patients which showed that gabapentine could significantly reduce the pain score, nausea and vomiting in patients with PDPH,[13] Turan et al.[14] showed that gabapentin decreased postoperative analgesic consumption and pain scores in patients undergoing rhinoplasty and endoscopic sinus surgery. Dirks et al.[15] determined that a single dose of gabapentin reduced post-operative morphine use and pain during movementin the first 4 hours after surgery.

Gabapentin was used before by Moore et al.[16] in a similar group of pregnant females undergoing caesarean section in a study conducted to assess the efficacy of different doses of gabapentin on post-cesarean section pain. They concluded that a single dose of gabapentin 600 mg given 1 h before cesarean section significantly improves pain scores in the first 48 h post-partum and increases patient satisfaction.

However, Short et al.[17] conducted a study on women undergoing elective cesarean section and were randomized to 3 groups to receive 300 or 600 mg gabapentin or placebo, 1 h before surgery. The study showed that the pre-operative dose didn't improve post-operative pain management or maternal satisfaction. Thus we selected 600mg dose as it was considered to be safe.

In a study conducted by Mahoori et al it showed pregabalin better than gabapentine but ultimately concluded that further studies should be carried on both these drugs.

Some studies show that gabapentin crosses the placenta and gets secreted in the breast milk.[18] That is why we examined the neonates for Apgar scores, NICU admission and difficulties in breast feeding initiation. The results were similar in both groups with no neonatal morbidity.

Sedation is a common side-effect of gabapentin. However, according to the Ramsey sedation score that we used, all the parturients had a score below 3, which didn't interfere with their caring for the babies and didn't delay their hospital discharge. Also, other side-effects of gabapentin were not reported in any of the two groups.

The gabapentin pregnancy registry reviewed 39 women who had received gabapentin during pregnancy, of which 36 had received gabapentin throughout pregnancy and concluded that the exposure didn't tend to any increased risk for adverse fetal or maternal events.[19]

On the effects of gabapentin on breastfeeding, many studies have been conducted on infants who were breastfed during maternal use of gabapentin for epilepsy with doses up to 2.1 gm and no adverse events on the newborn were noted.[18] However, the dose of Gabapentin chosen for our study was based on the studies that mentioned that a single oral dose of either 300 mg or 600 mg given to the mother before cesarean section appeared to have no effect on Breast feeding initiation or the baby well-being.

Conclusion

Gabapentin given pre operatively has no effect on incidence of (PDPH) but does delays its onset and reduces its severity as well as duration in parturients undergoing cesarean section with spinal anesthesia without any significant adverse effects either on the mother or the baby.

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