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Original Research Article

Evaluation of Efficacy of Oral Pregabalin versus Acetaminophen in the Management of Postdural Puncture Headache after Spinal Anesthesia in Lower Abdominal and Pelvic Surgeries

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ABSTRACT

Purpose: Various drugs have been tried for prevention of postdural puncture headache. This prospective, observational study was conducted to evaluate the efficacy of oral pregabalin in the management of postdural puncture headache after spinal anaesthesia in lower abdominal and pelvic surgeries and to compare its effectiveness with acetaminophen.
Method: Eighty patients, who developed postdural puncture headache (PDPH), were randomly assigned to two groups. Group A (n=42) received oral acetaminophen. Group P (n=38) received oral pregabalin. For each case, heart rate, mean arterial pressure and pain scores using Visual Analogue Scale (VAS) were recorded in the postoperative period; requirement for postoperative rescue analgesia was also noted.
Results: The groups were similar in terms of baseline characteristics, and distribution of study subjects. VAS scores at the onset of PDPH were comparable between the two groups, (p-value>0.05) and remained as such at next 24 hrs, however a comparison of VAS scores at 48 hrs and 72 hrs, showed significantly low VAS scores for pregabalin group with respect to acetaminophen group (p-value<0.05).
Conclusion: Oral pregabalin provides an effective alternative means for managing PDPH and may obviate the need for invasive modalities like epidural blood patch in such cases.
Keywords: Spinal anesthesia, postdural puncture headache, neuraxial anesthesia, pregabalin.

Introduction

Although spinal anesthesia has emerged as an effective means of providing neuraxial blockade for a myriad of surgical procedures and offers a variety of advantages, [(1)] it is however, not without demerits and complications. Postdural puncture headache is perhaps the most unpleasant complication of spinal anesthesia so far. [(2)]

Various methods for prevention and treatment of postdural puncture headache have been proposed by different workers from time to time, which range from simple conservative measures like bed rest, adopting a prone position and use of abdominal binders, to more invasive ones as an epidural blood patch. In addition, a number of therapeutic options have been suggested, including adequate intravenous hydration, and the use of drugs, such as, acetaminophen, non-steroidal anti-inflammatory drugs, opioids, antiemetics, and caffeine to name a few. [(3)]

In order to obviate the need for invasive methods, such as epidural blood patch, the search for newer and effective pharmacological agents to manage postdural

puncture headache continues. Pregabalin being one such pharmacological agent, its efficacy in the management of postdural puncture headache has been proven in many studies. [4,5]

The present study was designed to evaluate the analgesic efficacy of pregabalin to alleviate postdural puncture headache following spinal anaesthesia in lower abdominal and pelvic surgeries, and to draw a comparison with acetaminophen.

METHODS

After obtaining approval from the Institutional Ethics Committee and informed consent from patients undergoing lower abdominal and pelvic surgeries, a total of 6982, ASA I-II patients were observed over a span of two years. We ended up with a final sample size of 80 patients, who developed postdural puncture headache and were included in a prospective observational study. Patients were randomly divided into two groups after the onset of headache depending upon the medication they received.

GROUP A (n=42) – Acetaminophen group: These patients were given oral acetaminophen 500 mg TID for three days.

GROUP P (n=38) – Pregablin group: These patients were given oral pregabalin 75 mg TID for three days.

Patients were excluded, if there was a history of, chronic headache, allergy to pregabalin or acetaminophen. Pregnant ladies and lactating mothers were also excluded from the study.

All the patients were connected to standard monitoring and, the anaesthetic procedure was standardized for the study group. The patients received spinal anesthesia in sitting position with 27 G or 26 G Quinckes spinal needle, 2.5 to 3.5 ml of 0.5% hyperbaric bupivacaine along with 25 micrograms of fentanyl were injected into the subarachnoid space, the patients were then immediately placed in supine position. After ensuring the desired level of sensory block and confirming motor blockade using the modified Bromage motor scale (Grade 0: No motor block, Grade 1: Inability to raise extended leg; able to move knees and feet, Grade 2: Inability to raise extended leg and move knee; able to move feet, Grade 3: Complete motor block of limb), the surgical procedure was started.

After the completion of the surgical procedure, each patient was shifted to the concerned ward for postoperative monitoring and, were followed for headache during their postoperative stay in the hospital.

Headache was labeled as postdural puncture headache as per following criteria:

- Aggravated by erect or sitting position and coughing, sneezing or straining.
- Occurring after Mobilization.
- Relieved by lying flat.
- Generalized headache or mostly localized to occipital or frontal cranial areas.

The severity of headache was assessed on the CROCKER (1 to 4) scale (crocker1976):

1. Mild headache which permits long period of sitting/erect position and no other symptoms.
2. Moderate headache which makes it difficult for the patient to stay upright for more than half an hour. Occasionally accompanied by nausea, vomiting, auditory and ocular symptoms.
3. Intense headache occurring immediately upon getting up from bed, alleviated while lying horizontally on bed. Often accompanied by nausea, vomiting, auditory and ocular symptoms.
4. Headache that occurs even while lying horizontal in bed and greatly aggravated immediately upon standing up. Eating is impossible because of nausea and vomiting.

After the onset of postdural puncture headache the patients were strictly instructed regarding the intake of medication by the doctor of the concerned department. The patients suffering from postdural puncture headache were divided into two groups (Group A & Group P) on the basis of the medication received. Treatment was started immediately

following diagnosis of postdural puncture headache in all the patients with either of the two drugs. Oral fluid therapy and relative bed rest as per protocol was identical among the groups.

Headache severity was measured using a Visual Analog Scale (VAS), at the time when postdural puncture headache started and was then followed at 24 h, 48 h and 72 h after the onset.

Primary outcome in this study was to know the efficacy of pregabalin in the management of postdural puncture headache. The secondary outcome included a comparative analysis of the efficacy with acetaminophen and to know any undesirable side effects of the two drugs.

RESULTS

Eighty patients made it to the final study, with 33 males (41.3%) and 47 females (58.8%), indicating a slight female preponderance. Forty two received acetaminophen and thirty eight received pregabalin. The study groups were comparable in terms of demographic characteristics like, age, gender, weight, and ASA status and baseline hemodynamic parameters (table 1). Most of the study patients belonged to age group of 25-34 years (Mean±SD=35.9±8.47). The data indicated that the incidence of postdural puncture headache was 1.15% at our institute. The number of attempts for successful insertion of spinal needle into the subarachnoid space was similar in both the groups, with first attempt being successful in most of the cases [group-P 89.5% & group-A 88.1% first attempt success, p-Value>0.05]. Crocker scale was used to record the severity of headache at the onset, and most of the patients were categorized as Crocker-2, based on the severity of their symptomatology [group-P 71.1% & group-A 78.6% fell into Crocker-2 category, p-value<0.05]. The postdural headache was localized to frontal area of cranium in majority of patients [(group-P 44.7% & group-A 45.2%), p-value>0.05], followed by occipital [(group-P 34.2% & group-A 38.1%), p-value>0.05] and generalized [(group-P 21.1% & group-A 16.7%) p-value>0.05]cranial regions. The average onset time of headache, following dural puncture was 22-26 h in both the groups (fig 1), [Mean± SD (group-P 23.8±1.19 & group-A 24.3±1.45), p-value>0.05].

VAS scores at the onset of PDPH were comparable between the two groups, [(group-P =8.42±1.08 & group-A=8.10±1.26), p-value>0.05] and remained as such at next 24 hrs. [(group-P=5.63±1.89 & group-A=6.26±1.97), p-value>0.05], however a comparison of VAS scores at 48 hrs and 72 hrs, showed significantly low VAS scores for pregabalin group with respect to acetaminophen group {[(group-P 2.15±1.27 & group-A 4.55±1.48 at 48 hrs) p-value<0.05] and [(group-P 0.51±0.83 & group-A 3.05±1.29 at 72 hrs) p-value<0.05]}. (Table 2, fig 4)

Table 1 Comparison of demographic characters

Parameter	Group P	Group A	Remarks
Age (years)	35.2±7.87	36.6±9.01	P=0.452
Gender (M/F)	14/24	19/23	P=0.446
Weight (kg)	61.8±6.83	62.7±7.01	P=0.576
ASA (I/II)	35/3	38/4	P=0.797
Headache onset (Hours)	23.8±1.19	24.3±1.45	P=0.086

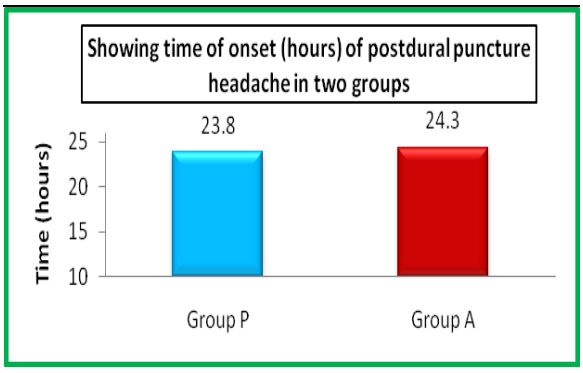

Figure 1. Onset time (hours) of postdural puncture headache

Statistical data suggested an upward trend in the patients' heart rate and mean arterial pressures with the onset of postdural puncture headache, however both these values tended towards baseline on subsequent days, the normalization of these values was more pronounced in pregabalin group compared to acetaminophen group (fig 2, fig 3).

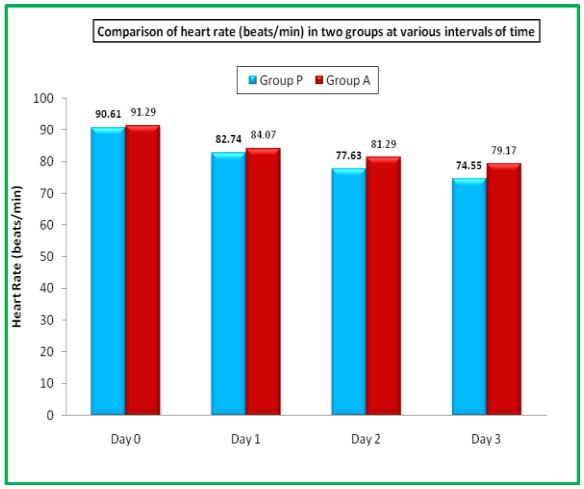

Figure 2. Comparison of heart rate between the groups at various time intervals

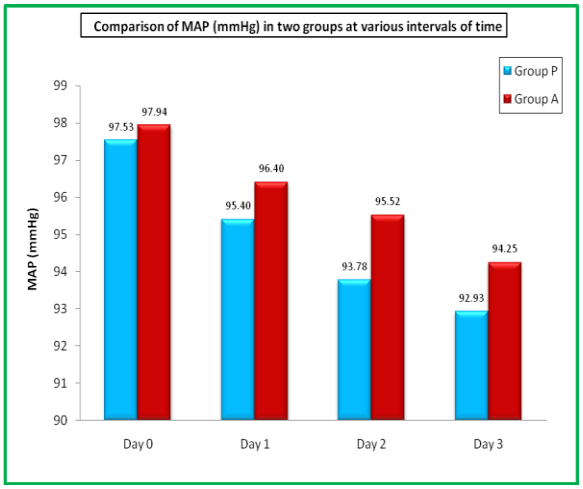

Figure 3. Comparison of mean arterial pressure between the two groups postoperatively

Table 2: Comparison based on VAS score in two groups at various intervals of time

Time Interval	Group P		Group A		P-value
	Mean	SD	Mean	SD	
Day 0 At zero hour	8.42	1.08	8.10	1.26	0.223
Day 1 At 24 hour	5.63	1.89	6.26	1.97	0.149
Day 2 At 48 hour	2.15	1.27	4.55	1.48	<0.001*
Day 3 At 72 hour	0.51	0.83	3.05	1.29	<0.001*

**Statistically significant Difference (P-value<0.05)*

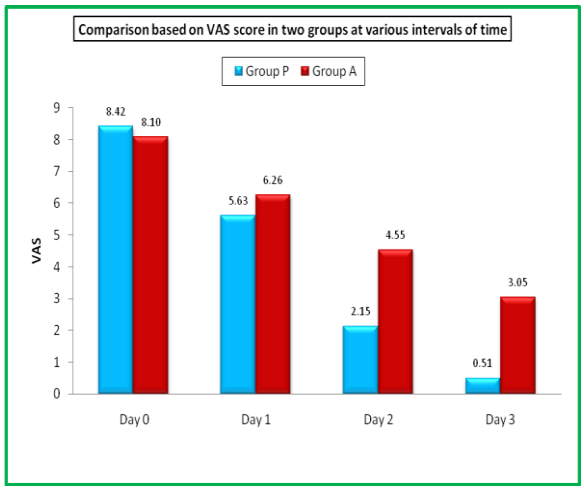

Figure 4. Comparison based on VAS score in two groups at various intervals of time

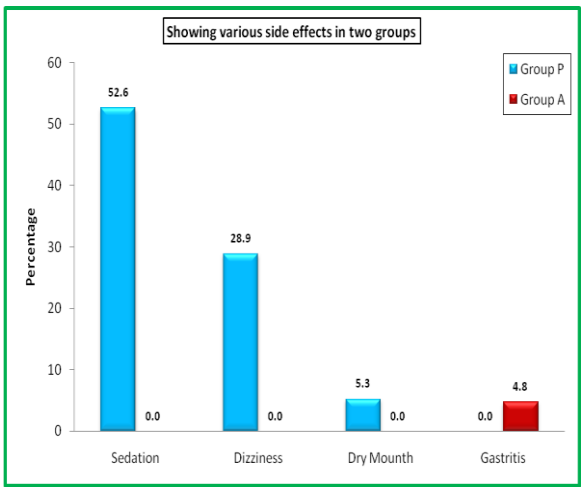

Figure 5. Comparison with respect to side effect profile in two groups.

Pregabalin use in the management of postdural puncture headache was associated with side effects, like dizziness and sedation in some individuals, which were not seen in acetaminophen group (fig 5). However, being only minor effects they did not result in withdrawal of patients from the study.

DISCUSSION

The primary goals of this study were to know the efficacy of pregabalin, as a non-invasive modality, in the management of postdural puncture headache after spinal anaesthesia in lower abdominal and pelvic surgeries.

The statistical analysis of the collected data indicated that most of the

study patients belonged to age group of 25-34 years (Mean±SD=35.9±8.47), indicating a predilection for younger age group, an observation well supported by a study of Kartman et al who recorded 33% incidence of postdural headache in patients aged 20-29 years and 6.2% in patients aged 60-69 years,Clarke and Power reported similar findings using 26 G spinal needle. [(6)]

Among the study subjects, the occurrence of postdural puncture headache was found to be more in females (58.8%) compared to males (41.3%), which is much in agreement with the conclusion drawn by WU CL, Rowlingson, Cohen SR et al, from their study. [(7)] Current study did not show any relationship between body weight and the incidence of postdural headache. Faure E, Moreno R and Thisted R along with some other workers on the subject, have implicated a lower body mass index with greater incidence of postdural puncture headache. [(8,9)] However, Miu M, Paech MJ and Nathan E, from their retrospective analysis of accidental dural punctures following 18,315 epidural anesthetics reported no such relation. [(10)]

The incidence of postdural puncture headache following dural puncture, as reported by many studies, ranges from 0.3% to 20% in spinal anesthesia and up to 70% after accidental dural puncture in epidural anesthesia. [(11)] The present study reported a 1.15 % incidence of postdural headache, the low incidence recorded in the study can be implicated to the smaller gauge needle used for the purpose, a fact supported by many prior studies. [(12-14)]

No significant relationship was noted between the number of attempts to successfully locate the subarachnoid space and the incidence of postdural headache in the present study, an observation that may be related to the lack of sufficient number of subjects who required a second or a subsequent attempt to locate the subarachnoid space, since the first such attempt was successful in most of the patients, however, the current observation is supported by the study conducted by Hans Lybeckerm, Jakob T. Moller, Ole May et al, who reported no such relationship, [(15)] yet there are others, who have linked an increased incidence of postdural puncture headache with repeated dural punctures. [(16)]

The headache severity at the onset was mostly recorded as crocker 1 & 2, which may be related to the smaller size needles (26G and 27G), used in our study, so that the severity of the reported headache was less. These results are in agreement with a number of other studies, including the observations of Dittmann and Rankl [(17)] and another independent study by M Cesarini et al, both of which reported only moderate headaches using smaller size needles. [(18)]

Frontal headache was reported by a majority of study subjects, followed by occipital and generalized headaches, in that order. Our study showed that both groups were comparable with respect to location of headache. Arjun et al, demonstrated a frontal predominance of postdural headache in their study subjects, followed by generalized headache using smaller needles, however, none of their patients complained of occipital headache. [(19)] Although, Jones R reported frontal, parietal, occipital and generalized forms of postdural headaches. [(20)]

The mean onset time of postdural puncture headache was 22-26 hrs, {[mean±SD, (24.3±1.45 in group A & 23.8±1.19 in group P)p-value>0.05]}. Huseyinoglu and co-workers found that time of onset of PDPH(after hours of surgery) was 11.00 ± 11.03 for Pregabalin group and10.05 ± 9.37 for Placebo group. [(21)] Rahmawy et al demonstrated an onset time of postdural puncture headache between 24 to 48 hours in most cases [(22)] further, Xiangming Che et al, concluded from their retrospective study, the occurrence of postdural headache within first 48 hours after surgery in majority of cases. [(23)]

An analysis of the VAS scores at the onset and then at 24 hrs, 48 hrs, and 72 hrs, followed by comparison of VAS between

the two groups, yielded interesting results. The higher VAS scores were reported in both the groups at the onset of postdural puncture headache, which remained so at 24 hours also, the VAS scores decreased by 48 hours and were even lower by 72 hours, in both the groups, indicating a significant relief in headache. Nevertheless, patients treated with pregabalin showed far more reduction in their pain score compared to the ones treated with acetaminophen. These observations were similar to those of, Alireza Mahoori, Heydar Noroozinia, Ebrahim Hasani et al, who compared the efficacy of gabapentin and pregabalin with acetaminophen and found that all the three agents were effective in lowering VAS scores at 24, 48 and 72 h after headache's onset but pregabalin alleviated the pain more effectively. [(24)] Huseyinoglu and coworkers found a significant lowering of VAS scores by oral pregabalin used in treatment of postdural puncture headache after the second day of treatment. [(21)] The superior role of pregabalin in the management of postdural puncture headache has been supported by many studies. [(22,25,26)]

Although, both the medications were well tolerated by most of the patients, however, minor side effects in the form of dizziness and sedation were reported by patients who received pregabalin, while no such side effects were reported by the acetaminophen group. Nevertheless, these side effects were not severe enough to result in patient withdrawal from the study. Alireza Mahoori, Heydar Noroozinia, Ebrahim Hasani et al reported no complications following administration of pregabalin in their study, hence the safety of short term administration of pregabalin is well established. [(24)] However, many other observers like Sarawat V et al. have reported dizziness and somnolence with both gabapentin as well as pregabalin. [(27)]

At the conclusion, it is imperative to mention a few shortcomings encountered over the course of conduct of this entire project.

1. Obstetric patients, which constitute a major fraction of potential candidates for the development of postdural puncture headache had to be excluded from the study, on account of safety concerns regarding the use of pregabalin with literature indicating its secretion in the breast milk. [(28)]
2. A substantial number of patients were discharged before full recovery from the postdural puncture headache, so they had to be contacted over telephone calls.
3. Spinal anesthesia was given by different operators with varying levels of expertise.
4. The study would have been more precise if both the patient and the examiner were blinded for the treatment received by individual patients.
5. Although patients were closely monitored in postoperative period for headache yet determination of actual incidence of postdural puncture headache is difficult and minor headaches may not urge patients into seeking medical attention.

CONCLUSION

The incidence of postdural puncture headache was found to be more in young female patients. Most of the study patients developed mild to moderate frontal or occipital headache, owing to the small size spinal needles used. Following treatment, the VAS score showed a downward trend with respect to the VAS at onset in both the groups, however the decrease was significantly more in patients receiving pregabalin, highlighting the enhanced effectiveness of pregabalin over acetaminophen in the management of postdural puncture headache. Fewer patients in pregabalin group however, developed minor side effects in the form of dizziness and sedation.

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