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Original article

Pregabalin as Alternative to Epidural Blood Patch in Treatment of Postdural Puncture Headache: A Randomized Controlled Clinical Trial

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Abstract:

Background: Postdural puncture headache (PDPH) commonly arises following a lumbar puncture. It is typically managed through conservative measures or an epidural blood patch (EBP), but each has limitations. This trial aimed to compare the efficacy and safety of pregabalin versus EBP in the management of PDPH. **Methods:** This randomized controlled trial was conducted on 75 cases with confirmed diagnosis of PDPH. Patients were equally randomized into three groups: Group A (pregabalin group) received oral pregabalin treatment administered at 150 mg daily, with 75 mg given every 12 hours. Group B (EBP group) received EBP and Group C (control group) received conservative treatment. **Results:** Complete relief of headache was experienced by 13 (52%) patients in group A, 18 (72%) patients in group B, and 5 (20%) patients in group C, with significant distinctions observed among the examined groups (P<0.001). The VAS scores, severity of headache, and frequency of attacks demonstrated a significant improvement at 12h, 24h,36h, and 48h post-treatment within all groups A, B, and C (P<0.001) compared to baseline. Group A was comparable at most time points during follow-up with EBP and better than conservative treatment in terms of VAS scores, severity of headache and frequency of attacks. **Conclusions:** Pregabalin was comparable at most time points during follow-up with EBP and better than conservative treatment in terms of pain, impact on daily activities and frequency of attacks. Being a non-invasive route, oral pregabalin showed lower back pain than EBP, making it a promising drug for the management of PDPH.

Keywords: Pregabalin; Epidural Blood Patch; Postdural Puncture Headache; Diagnostic Spinal Tap; Conservative.

Introduction

Lumbar puncture (LP), often known as a "spinal tap," is a standard medical technique pioneered in the late 1900s by Heinrich Quincke. It involves the retrieval and analysis of cerebrospinal fluid (CSF) from the spinal cord, serving as the benchmark for diagnosing conditions like subarachnoid haemorrhage, meningitis, and specific neurological conditions[1]. Furthermore, it is utilized to measure cerebral pressure and administer drugs or diagnostic substances [2].

Serious complications are rare, and the use of appropriate techniques and precautions can help minimize risks. Possible complications encompass postdural puncture headache (PDPH) including spinal hematoma, haemorrhaging, herniation of the brain, and infection. It's noteworthy that PDPH stands out as the most frequently encountered complication [3].

PDPH is primarily caused by CSF leakage into the epidural space via the dural rent. This leakage results in CSF volume and pressure reduction, which places strain on pain-sensitive areas when the patient is in an upright position. In addition to a headache, patients may experience symptoms such as vertigo, tinnitus, myalgia, and diplopia [4, 5].

Despite this consequence incidence and importance, most treatments are supportive and aimed at managing symptoms. Overhydration, oral treatment of theophylline and caffeine, sumatriptan, corticotropin, injection of saline epidural, or an epidural blood patch (EBP) are popular care interventions. These therapies are frequently adopted and employed [6].

Two key hypotheses seek to explain the efficacy of EBP in the treatment of PDPH. According to the first hypothesis, the injected blood forms a clot that clings securely to the dura mater, successfully closing the dural defect and limiting CSF leaking. The second explanation is that the improvement in symptoms is due to a rise in CSF pressure caused by the injection of blood into the epidural space. Both explanations are likely to have some merit, although the first theory is more likely to explain the persistent efficacy of EBP [7, 8].

Although EBP presents potential benefits, it carries inherent risks due to its invasive nature, leading to complications like infection and increased back pain [9]. Consequently, the exploration of alternative non-invasive approaches becomes imperative.

Pregabalin, an anticonvulsant medicine that blocks calcium entry, is used to treat a variety of diseases. It has been used to relieve pain in a variety of patient groups, including those with chronic pain, epilepsy, and anxiety disorders [10].

Pregabalin, akin to gabapentin, functions as antiepileptic medication and shares a structural resemblance to gamma-aminobutyric acid (GABA). Unlike gabapentin, Pregabalin is not linked to plasma proteins and is not metabolised by the liver. Renal excretion is the primary elimination route, with 98% of absorbed doses excreted unchanged in urine. Pregabalin exhibits linear pharmacokinetics due to non-saturable absorption, ensuring a predictable patient response.

Rapid absorption leads to peak blood concentrations within an hour, with a remarkable bioavailability exceeding 90%, surpassing that of gabapentin.t ½ for elimination, ranging from 5.5 to 6.7 hours, remains consistent across doses and repeated administrations [11]. Pregabalin's mechanism involves binding to the N-type calcium channel's α2δ subunit, modulating influx of calcium at the nerve endings. Consequently, this lowers the secretion of various neurotransmitters, such as substance P, glutamate, serotonin, noradrenaline, and dopamine [12].

The treatment with oral pregabalin resulted in a significant decline in PDPH severity, as reported in some case reports [12, 13]. However, the effects of pregabalin on PDPH in reference to EBP are still to be investigated. Therefore, this study aimed to compare the efficacy and safety of pregabalin versus EBP in the management of PDPH.

Methods:

This prospective randomized controlled trial was conducted on 75 individuals aged from 21 to 65 years old, both genders, with confirmed diagnosis of PDPH. Patients were consulted for lumbar puncture for diagnostic purposes, and subsequent patients complaining of headaches were attended and evaluated by a senior anesthesiologist to make a differential diagnosis of headache. Patients with a confirmed diagnosis of PDPH within 24 hours and less than 7 days from the spinal tap time were included in this study. The PDPH criteria used in the selection of study patients typically manifest as headaches that occur bilaterally across the frontal or occipital regions and are exacerbated by standing or sitting up but tend to improve when lying down. These headaches often come with additional symptoms such as nausea, dizziness, pain in the neck, changes in vision, and sometimes ringing in the ears, hearing impairment, or arm-related radicular symptoms. Furthermore, activities like coughing and performing the Valsalva manoeuvre can intensify the headache, even when the individual is lying down [14].

The study was conducted from May- 2023 to -October 2023. Benha University Hospitals served as the study's site.

Informed consent was given in writing by every patient. The research was conducted after the approval of the Ethical Committee Benha university Hospitals (approval code: RC. 40.5.2023), registration of clinicaltrials.gov (ID: NCT06271486).

The medical and surgical history of the patients were obtained, and laboratory investigations involving complete blood count (CBC), renal function, liver function, and coagulation studies were reviewed in the patient file. Additionally, a clinical examination of the patients was performed.

Exclusion criteria encompassed patient refusal, known allergy to the drug used in the study, patients with a history of convulsions, chronic headaches, as well as contraindications to regional anesthesia (such as local infection and coagulation abnormalities). Clinical indications of elevated intracranial pressure or associated risk factors and deteriorated patients were also excluded from the study.

Lumbar puncture

Prior to the LP, patients were placed in a lateral recumbent position to ensure precise opening pressure determination and minimize the likelihood of PDPH.

Patients were guided to adopt the fetal position, promoting spinal flexion. This positioning enhances the gap between spinous processes, facilitating smoother needle insertion.

A set of items was acquired, including a stylet attached to a spinal needle (22-gauge needle), four vials for CSF collection, a sterile drape, a manometer equipped with a tripple valve, local anesthetic, needles in syringes(for drawing up anesthetic and using a 25-gauge needle for skin injection), sanitizing solution (70 % alcohol and 0.5 % chlorhexidine),sterilized gloves, and a mask with a surgical tip and face shield. Both the assistant and the person doing the LP were dressed in sterile gowns and used sterile precautions the entire time.

The CSF fluid should not be aspirated. Each collecting vial was filled to a capacity of 1 mL.. Following sample collection, the spinal needle was used in place of the stylet, and the needle was then taken out. The place where the needle was inserted was gently compressed with sterile gauze, and the area was covered with a small bandage.

Randomization and blindness

A computer system produced random numbers, which were then used to divide 75 patients equally into three groups at a 1:1:1 ratio. Group A (pregabalin group) received oral pregabalin treatment at a dose of 150 mg per day (75 mg at 12-hour intervals). Group B (EBP group) received active therapy in the form of an EBP. Group C (the control group) received conservative treatment. An impartial nurse utilised sealed, opaque, and sequentially numbered envelopes to guarantee a random distribution.

The experimental drug was concealed from the result assessors as a junior resident who was unaware of group allocation assessed the outcome. One more pharmacist prepared the drugs; this pharmacist did not participate in the trial's next stages. Due to different appearance and administration methods, the patient and investigator couldn’t be blinded to the patient’s allocation. Non-responders with persistent severe PDPH were managed according to hospital policy and excluded. Figure 1

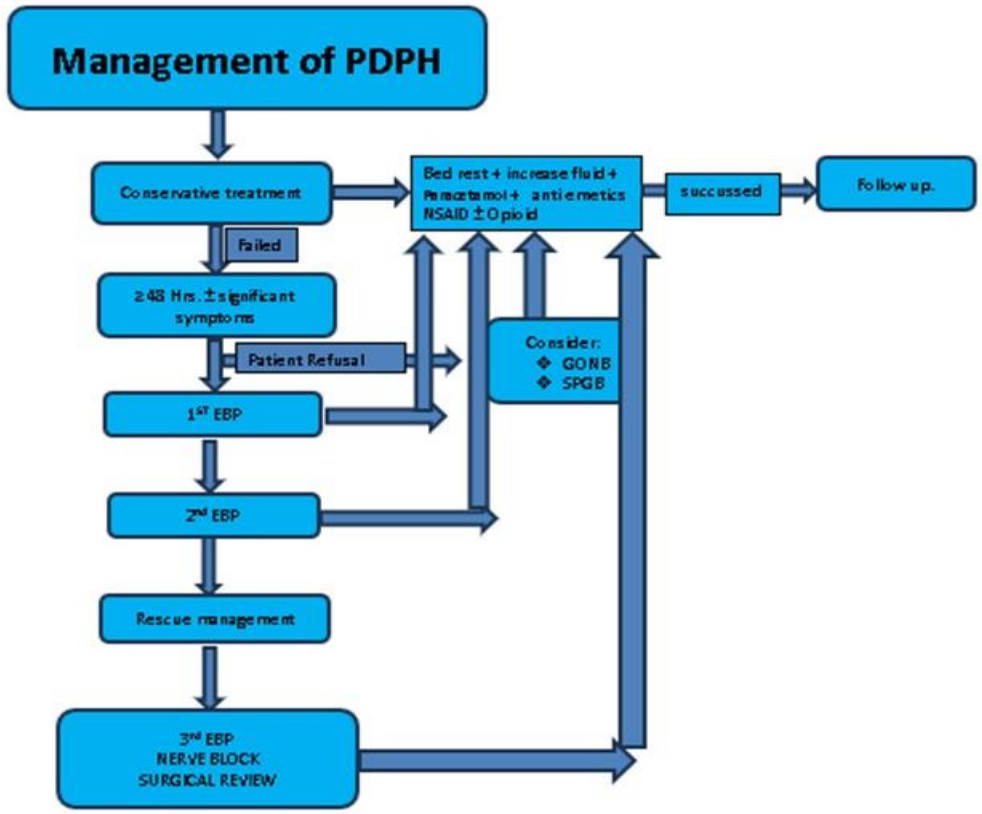

Figure 1: Hospital policy for PDPH (GONB: Greater occipital nerve block, SPGB: Sphenopalatine ganglion block)

EBP Technique

The patient was positioned in a lateral posture after being informed about the treatment and given consent. Both the extremity that must have blood drawn from and the back injection site, a spinal interspace one above the prior dural puncture, were sterilely prepared and draped. The epidural space was detected using the conventional loss-of-saline resistance test. Once the needle tip of the 18-gauge epidural needle was properly positioned, 20 mL of autologous blood was extracted from the patient in a sterile manner. To construct a blood patch, the blood was slowly injected (30-60 seconds). To construct a blood patch, the blood was slowly injected (30-60 seconds). Any adverse effects were recorded.

Conservative treatment:

Conservative treatment in this study involved providing recommendations to the patients, including 24 hours of bed rest, stool softener, and consuming a minimum of 2.0 litters of fluid daily. Analgesics were permitted for pain relief depending on the patient's disease status. The used analgesics were paracetamol orally 10mg/8 hr and diclofenac sodium 0.5 mg/ kg/ 12 hr.

The intensity of the headache was measured using VAS. The scale uses a scoring system in which values of 0, 1-3, 4-6, and 7-10 correspond, respectively, to the absence of pain, mild, moderate, and severe pain. This benefited the patients in visually evaluating and conveying their degree of discomfort properly [15].

The severity of the headache was assessed based on a headache questionnaire. The

headaches in question were determined to be postural, exerting minimal impact on daily activities. Patients did not experience any associated symptoms and were not confined to bed, indicating mild headache. A moderate headache signified a postural discomfort that necessitated some bed rest during the day without necessarily being accompanied by related symptoms. A severe headache was defined as a postural discomfort that kept the patient bedridden for the entire day, along with persistent symptoms such as dizziness, nausea, vomiting, hearing loss, neck stiffness, tinnitus, photophobia, hyperacusis, diplopia, and scapular discomfort [16].

Complications were the assessment of back pain measured with VAS score.

Outcomes

The primary outcome was the incidence of complete relief, as reflected in the success rate of the intervention at 48 hours. The intensity of headache as measured by VAS score at different time intervals post-treatment, impact of headache on daily activities, frequency of attack at different time intervals post-treatment, and complication of each intervention were the secondary outcomes.

Sample size estimation:

The sample size calculation was done utilizing G. power 3.1.9.2 (University of Kiel, Germany). The incidence of complete relief at 48 hours, which was the primary outcome, was obtained from a pilot study including 10 cases in each group. The frequency of complete relief was 35 % in group A and 72 % in group B. The sample size determination considered factors such as a 0.99 effect size, 95% confidence level, 80% statistical power, a 1:1:1 group ratio, and an additional 3 cases in each group to account for potential dropouts. Therefore, a total of 25 patients were recruited for each group.

Statistical analysis

Statistical analysis was done by SPSS v28 (IBM©, Armonk, NY, USA). The Shapiro-Wilks test and histograms were used to ascertain whether the data distribution was normal. Parametric quantitative data were given as mean and standard deviation (SD) and tested using the ANOVA (F) test with post hoc comparisons (Tukey), and the means between two related populations were compared with the paired sample t-test. Quantitative non-parametric data were expressed as median and interquartile range (IQR) and compared across groups using the Kruskal-Wallis test and the Mann-Whitney test. The Chi-square test was utilized to examine qualitative variables expressed as frequency and percentage (%). A two-tailed P value of 0.05 or less was judged statistically significant.

Results:

In this study, a comprehensive evaluation was conducted on 97 patients to determine their eligibility. Among them, 7 patients were found to be ineligible based on the inclusion criteria, 10 did not respond to the intervention, and an additional 5 patients chose not to participate. Consequently, the study proceeded with the remaining 75 patients, randomly divided into three groups, each consisting of 25 patients. Importantly, these patients were successfully followed up and included in the subsequent statistical analysis. Figure 2 Age, sex, weight, height, BMI, and referred department insignificantly differed among the three groups. Table 1.

Table 1: Demographic data and referred department of the studied groups.

		Group A (n=25)	Group B (n=25)	Group C (n=25)	P value
Age (years)		38.6 ± 8.99	36.2 ± 8.83	40.4 ± 8.83	0.253
Sex	**Male**	10 (40%)	7 (28%)	12 (48%)	0.344
	Female	15 (60%)	18 (72%)	13 (52%)	
Weight (kg)		68.1 ± 9.44	67.7 ± 11.32	69.2 ± 10.13	0.863
Height (m)		1.5 ± 0.08	1.6 ± 0.08	1.5 ± 0.09	0.114
BMI (Kg/m^2)		30.6 ± 6.16	27.9 ± 4.94	29.9 ± 5.32	0.205
Referred department	**Internal medicine**	13 (52%)	14 (56%)	14 (56%)	0.974
	Neurosurgery	9 (36%)	7 (28%)	8 (32%)	
	Neurology	3 (12%)	4 (16%)	3 (12%)	

Data presented as mean ± SD or frequency (%), BMI: body mass index.

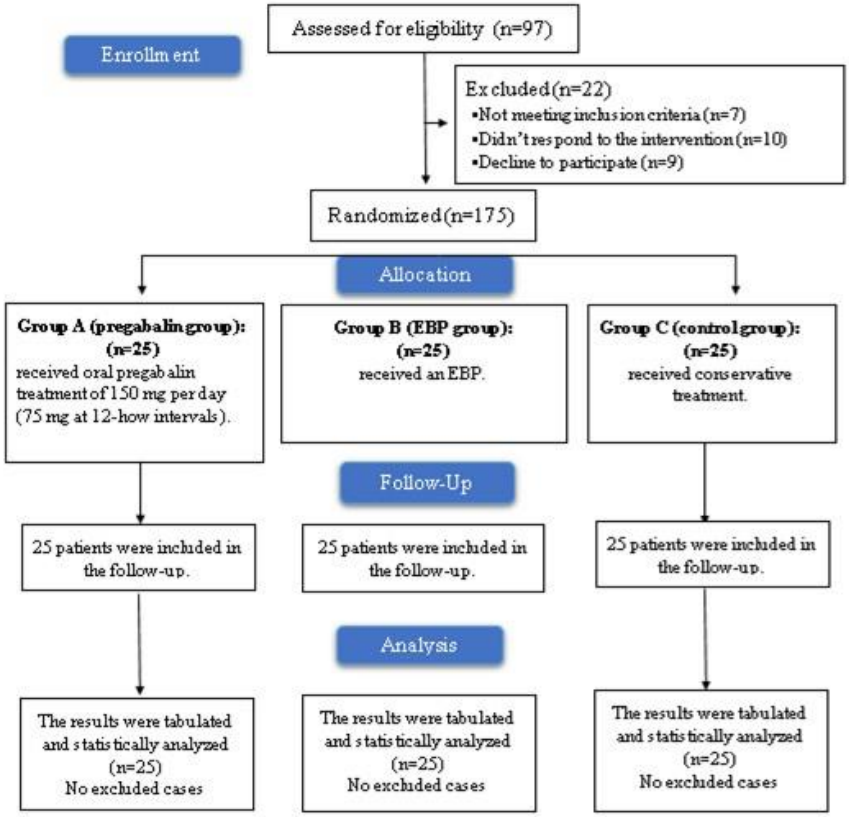

Figure 2: CONSORT flowchart of the enrolled patients

Regarding success rate, complete relief was experienced by 13 (52%) patients in group A, 18 (72%) patients in group B, and 5 (20%) patients in group C at 48h. The success rate significantly differed among the studied groups(P<0.001). Figure 3

The VAS scores demonstrated a significant improvement at 12h, 24h, 36h, and 48h post-treatment within all groups A, B, and C (P<0.001) compared to baseline.

Regarding the comparison between groups, the VAS score was insignificantly different among the three groups at

baseline (P>0.05). At 12h post-treatment, the VAS score was significantly lower in group B compared to group A and group C (P<0.05) but without a significant difference between group A and C (P=.0807).

At 24h post-treatment, the VAS score was significantly lower in group B compared to group C (P<0.001) but without significant difference between group A and group B and between group A and group C and C (P= .651 and .070 respectively).

Furthermore, at 36h and 48h after treatment, there was significant differences in VAS score among the studied groups (P<0.001). Specifically, the VAS score was significantly lower in A and B than in C (P<0.001) without significant differences between groups A and B (P>0.05). Table 2

Regarding the severity of attacks, it was insignificantly different among the three groups at baseline and 12h post-treatment (P>0.05), while there was a significant difference among the three groups at 24h, 36h, and 48h post-treatment (P<0.05) revealing insignificant difference between group A and B and significantly better results in both group A and B compared to the control group. Table 3

Regarding the frequency of attack, intragroup comparison revealed a significant improvement in groups A and B at 12h, 24h, 36h, and 48h post-treatment compared to baseline (P<0.05). Group C showed significant improvement at 24h, 36h, and 48h post-treatment (P<0.05), while at 12h, there was an insignificant difference compared to baseline (P=0.103).

Regarding comparison between groups, the frequency of attack was insignificantly different among the three groups at baseline (P=.882). The frequency of attack was significantly lower in groups A and B compared to group C at 12h, 24h, 36h, and 48h post-treatment (P<0.001). The frequency of attack was insignificantly different between groups A and B at 12h, 24h, and 36h post-treatment (P>0.05), while at 48h, it was significantly lower in group B compared to group A (P=.048). Table 4

Regarding complications, back pain measured with VAS score before intervention and after diagnostic Tap was comparable among the three groups (P=.988). VAS score after 48h of the intervention was significantly higher in group B than group A and C (P<0.001without significant differences between A and C groups (P =.172). Intra group comparison revealed that in group A, there was a significant decrease in VAS score after 48h of the intervention compared to before intervention (P =.003). In group B, there was a significant increase in VAS score after 48h of the intervention compared to before intervention (P =.003). In group C, there was a significant decrease in VAS score after 48h of the intervention compared to before intervention **(**P =.049). Figure 4

Table 2: Visual analogue scale (VAS) of the studied groups.

	Group A (n=25)	Within group	Group B (n=25)	Within group	Group C (n=25)	Within group	P value	Post hoc
Base line	6 (6 - 8)		7 (6 - 8)		6 (5 - 8)		.457	…
12h	5 (5 - 6)	<0.001	4 (3 - 5)	<0.001	5 (4 - 6)	<0.001	. 0.004	P1= 006 P2= .807 P3 =.003*
24h	4 (4 - 5)	<0.001	4 (3 - 5)	<0.001	5 (4 - 6)	<0.001	.002*	P1= .651 P2= .070 P3 =.001*
36h	4 (3 - 4)	<0.001	3 (3 - 4)	<0.001	5 (5 - 5)	<0.001	<0.001*	P1= .377 P2= .002** P3< .000*
48h	4 (2 - 5)	<0.001	3 (2 - 4)	<0.001	5 (4 - 5)	<0.001	<0.001*	P1= .072 P2= .002* P3< .000*

Data presented as median (IQR) ,*: statistically significant as P value < 0.05, P1: p value between group A & B, P2: p value between group A&C, P3: p value between group B&C. Within group comparison: compared to baseline.

Table 3: Severity of attack of the studied groups.

		Group A (n=25)	Group B (n=25)	Group C (n=25)	P value	Post hoc
	Mild	1 (4%)	1 (4%)	0 (0%)		
Baseline	**Moderate**	13 (52%)	13 (52%)	13 (52%)	0.901	….
	Severe	11 (44%)	11 (44%)	12 (48%)		
	Mild	2 (8%)	3 (12%)	0 (0%)	0.308	
At 12h	**Moderate**	21 (84%)	21 (84%)	21 (84%)		….
	Severe	2 (8%)	1 (4%)	4 (16%)		
	Mild	5 (20%)	9 (36%)	0 (0%)	0.015*	P1=.446
At 24h	**Moderate**	19 (76%)	15 (60%)	25 (100%)		P2=.033
	Severe	1 (4%)	1 (4%)	0 (0%)		P3=.002
	Mild	10 (40%)	15 (60%)	2 (8%)	0.004*	P1=.264
At 36h	**Moderate**	14 (56%)	10 (40%)	22 (88%)		P2=.028
	Severe	1 (4%)	0 (0%)	1 (4%)		P3=.0004
	Mild	12 (48%)	18 (72%)	0 (0%)	<0.001*	P1=.083
At 48h	**Moderate**	13 (52%)	7 (28%)	24 (96%)		P2=.0003
	Severe	0 (0%)	0 (0%)	1 (4%)		P3 < .0001

Data presented as frequency (%), *: statistically significant, P1: p value between group A & B, P2: p value between group A&C, P3: p value between group B&C.

Table 4: Frequency of attacks of the studied groups.

	Group A (n=25)	Within group	Group B (n=25)	Within group	Group C (n=25)	Within group	P value	Post hoc
Baseline	4 ± 0.89		4 ± 0.87		4.1 ± 0.83		.882	…
12h	3.1 ± 0.4	<0.001	2.9 ± 0.57	<0.001	4 ± 0.68	0.103	P<0.001*	P1=.574 P2<0.001* P3<0.001*
24h	2.7 ± 0.61	<0.001	2.5 ± 0.77	<0.001	3.7 ± 0.84	0.009*	P<0.001*	P1= .497 P2<0.001* P3<0.001*
36h	2.4 ± 0.51	<0.001	2 ± 0.71	<0.001	3.6 ± 0.87	0.006*	P<0.001*	P1=.079 P2<0.001* P3<0.001*
48h	2.4 ± 1.44	<0.001	1.7 ± 0.8	<0.001	3.5 ± 0.51	0.003*	P<0.001*	P1=.048* P2<0.001* P3<0.001*

Data presented as mean ± SD *: statistically significant as P value < 0.05, P1: p value between group A & B, P2: p value between group A&C, P3: p value between group B&C. Within group comparison: compared to baseline.

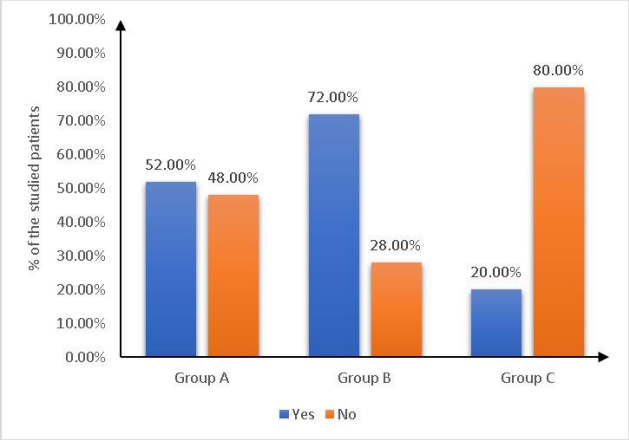

Figure 3: Success rate of the studied groups.

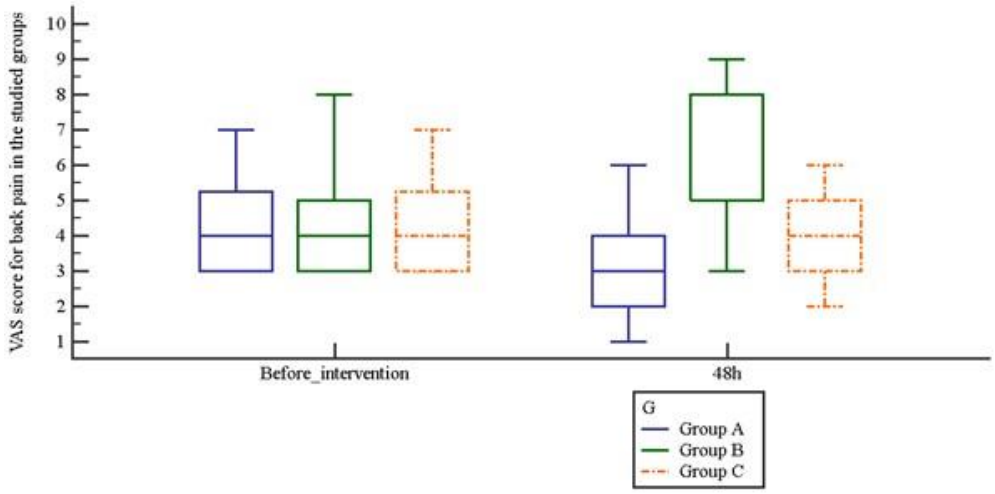

Figure 4: Back pain in the studied groups.

Discussion

PDPH commonly arises following a lumbar puncture and is typically managed through either conservative measures or EBP. Nevertheless, the efficacy of conservative approaches is limited by a lower success rate. Additionally, the invasive nature of EBP underscores the necessity for exploring innovative strategies for managing PDPH [17].

The oral route of drug administration is the most preferred and commonly utilized method due to several advantages, including safety and patient compliance, as the oral route is considered safe, and patients typically find it easy to comply with, contributing to better adherence to medication regimens [18]. Also, oral medications are easy to ingest, enhancing patient convenience and acceptance of the treatment. Unlike other administration routes, such as injections, the oral route avoids the pain associated with invasive methods, making it more tolerable for patients. The oral route accommodates

various types of drugs, providing versatility in drug administration. Being the most convenient, safest, and usually the least expensive route, oral administration is frequently chosen in clinical practice [19].

Pregabalin, an oral medication, exhibits high bioavailability, with oral bioavailability greater than or equal to 90% and independence from dose. Compared to gabapentin, pregabalin demonstrates distinct pharmacokinetic advantages. These advantages may translate into an improved pharmacodynamic effect. In clinical settings, pregabalin has shown efficacy in treating neuropathic pain syndromes, partial seizures, and anxiety disorders [20]. Additionally, a pharmacokinetic equivalence study demonstrated consistency between different formulations of pregabalin [21].

In the present study, oral pregabalin at a dosage of 150 mg per day, taken in two equal doses of 75 mg at 12-hour intervals, was adopted. This dose was chosen based on pervious case reports [12, 13] and based on our clinical experience of the most safe and effective dose. Previous trials have investigated the effects of different dosages of pregabalin. In one trial [22], patients of the intervention group received pregabalin at a dose of 150 mg the night before spinal anesthesia.

In our study, following therapy, a substantial decrease in the frequency of attacks was observed in the A, B, and C groups at different time intervals during patient monitoring.

In his case reports, Zencirci [12] identified that administering oral pregabalin resulted in a notable reduction in the intensity of challenging and severe PDPH for both cases that showed no improvement with conventional treatments. Also, another study[13] indicated that administering a 75 mg single dose of pregabalin seems effective in alleviating moderate to severe PDPH. Moreover, in the study done in 2021 [22], concentrating on the pregabalin group, it was discovered that the intervention group (pregabalin) showed a significant decrease in the intensity and frequency of PDPH, as measured by VAS.

EBP is widely acknowledged as the definitive solution for PDPH. According to a 2010 systematic review, EBP demonstrated significant reductions in both the duration and severity of PDPH when compared to conservative approaches and sham procedures [23]. This conclusion was drawn from the findings of randomized controlled trials involving a total of 86 participants [24, 25].

PDPH is frequently accompanied by impaired vision, nausea, and vomiting. Cases of nausea and vomiting were also seen in another investigation [22]. According to reports of of a study done by researchers[26], seventy percent of individuals who have spinal anesthesia develop PDPH during the first week following surgery. Patients with PDPH have responded well to non-invasive therapy, including fluids, rest, analgesics, theophylline, sumatriptan, caffeine, and adrenocorticotropic hormones [27]. However, if the disease persists, these non-invasive treatments may be unsuccessful and may cause further side effects. Therefore, the development of pharmacological therapy to lessen reliance on invasive procedures for the management of PDPH is required [5].

In our study, complete relief of headache was experienced by 13 (52%) patients in group A, 18 (72%) patients in group B, and 5 (20%) patients in group C.

EBP typically yields immediate relief, with success rates ranging from 65 to 98 percent after the initial procedure. However, it is worth noting that the effectiveness of EBP may diminish in cases where dural puncture occurs with a larger diameter needle (≥20 gauge) [28].

It is worth noting that the reported efficacy of EBP in the literature varies significantly due to differences in defining success, patient demographics, and EBP methods employed in the studies which involved 504 patients and confirmed the effectiveness of EBP in treating symptoms associated with CSF leak following dura mater puncture[29]. In their study, 75% of patients experienced complete relief of symptoms, indicating the success of EBP in alleviating CSF leak-related symptoms. The failure rate of EBP was only 7%. The authors also identified two predictors of EBP failure, namely, increasing the diameter of the needle used for dural puncture and a shorter duration between dural puncture and EBP administration. These factors were associated with a higher likelihood of EBP not being successful. Consistent with previous reports, the initial EBP showed high efficacy in treating PDPH, with 93% of cases demonstrating either complete or partial alleviation of symptoms considered as successful outcomes [30, 31].

In another study [32], 72% of their patients received an EBP containing 7 to 25 mL of autologous blood. Following the first blood patch, 67% of patients experienced complete headache relief, while 95% reported either complete or partial relief. However, severe headache recurred in 31% of patients, and 28% required multiple blood patches. On the other hand, 12 patients (6 in the EBP group and 6 in the same treatment group) were enrolled. It was reported that EBP resulted in 83% relief, whereas the sham treatment showed 0% relief [33].

According to our knowledge, no previous studies have compared EBP and pregabalin effectiveness and safety in PDPH treatment. Our results revealed that patients administered pregabalin were comparable at most time points during follow-up with EBP and better than conservative treatment in terms of pain, impact on daily activities, and frequency of attacks. These interesting results open the door for further research to confirm these findings and evaluate different doses of pregabalin to determine the optimum effective and safe dose.

Regarding safety measurements, back pain measured with VAS score after 48h of the intervention was significantly higher in group B than in groups A and C (P<0.001without significant differences between A and C groups (P =.172).

The mechanism of associated back pain with EBP in managing PDPH may be attributed to the local inflammatory response to the blood injected into the epidural space during the procedure. The injection of blood into the epidural space is intended to seal the dural puncture site and restore CSF pressure, relieving the symptoms of PDPH. However, introducing blood into this space can lead to inflammation, potentially causing back pain as a side effect [34].

Finally, this study had some limitations as it was a single-center study with a relatively small sample size. Therefore, further multicenter studies with larger sample sizes are needed to generalize our findings. Also, trials are necessary to explore the effect of different dosages of pregabalin and validate our results.

Conclusion

Pregabalin was comparable at most time points during follow-up with EBP and better than conservative treatment in terms of pain, impact on daily activities, and frequency of attacks. Being a non-invasive route, oral pregabalin showed lower back pain than EBP, making it a promising drug for the management of PDPH.

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