One of the common neuraxial anesthesia complications is postdural puncture headache (PDPH) (1). PDPH usually starts in the occipital region and extends to the frontal area, shoulder, and neck. PDPH is worsened standing and is associated with various symptoms, such as retching, photophobia, diplopia, stiff neck, tinnitus, unsteadiness, and extreme agonizing headache (2).

The presence of PDPH does not only make the patients suffer, but also the hospital stay is prolonged with an increase in the total care costs (3). PDPH is first managed by conservative measures...
with bed rest, sufficient hydration, laxatives, analgesics (such as acetaminophen, nonsteroidal anti-inflammatory agents, and weak opiate analgesics), and caffeine (4,5). Also, gabapentinoids are used in treating PDPH, but their exact mechanism is unclear. Their structure is similar to gamma-amino-butyric acid (GABA), the endogenous neurotransmitter. Their activity may result from regulating voltage-dependent calcium channels, increasing GABA release, which may reduce pain neurotransmission (6).

There are invasive measures that could be added to the previous conservative measures that may enhance the outcome of PDPH, like the epidural blood patch (EBP). In EBP, the epidural space is located, then 15-20 mL of autologous blood is injected. The mechanism of EBP success is increased pressure of the spine in the lumbar region, pressing the intrathecal area, and trans-locating cerebrospinal fluid (CSF) to the skull. Maintaining its effect is due to preventing further CSF leakage by clot formation (7). An EBP has a success rate of around 70% to 90% (8). Rare adverse effects associated with EBP include chronic adhesive arachnoiditis, subdural or spinal hematoma, seizure, cerebral venous sinus thrombosis, transient bradycardia, infection, and intracerebral hemorrhage. Chronic adhesive arachnoiditis is a rare condition that occurs mostly with repeated EBP (9).

Recent approaches for treating PDPH include the blocks of the sphenopalatine ganglion and the greater occipital nerve (GON). These blocks are beneficial in reducing pain severity and can be used as an alternative safe technique to EBP (10,11).

A trial published by Kastler et al (12) showed that block of the GON at the intermediate site (i.e., the point where the GON initially curves around the inferior obliquus capitis inferior muscle) is safe and effective for managing occipital neuralgia.

Infiltration of the GON is commonly used in different types of headache syndrome, including cervicogenic headache (13), trigeminal neuralgia, migraine (14), cluster headache (15), and PDPH following neuraxial anesthesia (16) with variations in outcome.

Our present study compares the pain-relieving effect between distal and proximal ultrasound (US)-guided bilateral GON blocks (GONBs) for PDPH.

**Methods**

A comparative, randomized, double-blinded trial was conducted at Aswan University Hospital from April 2018 to April 2019. After approval of the institutional ethics committee (aswu/156/9/17) and registration (PACTR201804003292841), informed written consent from all cases was obtained.

The study included 50 patients of either gender, aged 20-60 years old, with body mass index < 35 kg/m², American Society of Anesthesiologists (ASA) physical status I-II, who received neuraxial anesthesia for any surgical intervention, and developed PDPH with sitting Numeric Rating Scale (NRS-11) ≥ 4 (Table 1). Patients with any anatomical anomalies of the head, other types of headaches, previous skull or head surgery, local infection, coagulation disorders, patients on anticoagulants, and allergy to amide local anesthetics or corticosteroids were excluded.

A preprocedure check was done before the intervention by history taking concerning symptoms of PDPH, history of other headache types, previous head trauma or surgery, hypertension, diabetes mellitus, and bleeding tendency. A thorough physical examination was done to exclude the presence of skull defect or infection in the occipital region. Routine preoperative investigations were checked.

The PDPH assessment was done by the NRS-11 of 0 to 10 (0 indicated no pain; 10 indicated the worst unbearable pain). All patients were instructed about the NRS-11.

An anesthesiologist who did not participate in the study hid the computer-generated random numbers inside closed opaque envelopes to randomize the patients. Both patients and the outcome assessor were blind to the grouping of patients.

Patients were allocated into 2 equal groups. Group D: Patients received a distal bilateral US-guided GONB injection at the superior nuchal line level. Group P: Patients received a proximal bilateral US-guided GONB at the second cervical vertebra level. Both blocks were performed by injecting 3 mL of isobaric bupivacaine 0.5% and 4 mg dexamethasone.

**Procedure**

Midazolam 2 mg was given as a premedication upon arrival at the operating theatre. As standard monitoring, a pulse oximeter, electrocardiogram, and noninvasive blood pressure were attached to every case.

The position of the patient was sitting with the head and neck flexed. The area of the posterior occiput was sterilized. The US probe used high linear frequency (8-12 MHz) (Sonoscape©; Sonoscape Medical Corp, Shenzhen, China).
**Distal GONB Technique**

The probe was first put in a transverse plane at the superior nuchal line level, and its center was at 2-3 cm lateral to external occipital protuberance. On a short-axis plane, the GON was shown. Then a 21-G 1.5-inch needle was placed from the lateral side to the medial side using the in-plane method of US scanning, and the needle’s tip was positioned near the nerve. On the other side, this technique was repeated.

**Proximal GONB Technique**

The US probe was positioned over the external occipital protuberance using a transverse midline alignment, then transferred inferiorly over the atlas (C1) to see the axis (C2) spinous process that is bifid, with 2 tubercles on the contrary to the smooth contour of the posterior arch of the C1. The GON is consistently and reliably associated with the obliquus capitis inferior muscle. After identifying the spinous process of the C2, the probe was transferred, and the obliquus capitis inferior muscle was laterally defined. This muscle attaches the back of the transverse process of the C1 and the bifid spine of the C2; it extends obliquely upward and outward. To bring the probe parallel to the muscle’s long axis, it was rotated slightly (with the lateral end positioned slightly more cranially than the medial end). The GON lies external to the obliquus capitis inferior muscle, traversing it from caudal to rostral and lateral to medial, and can be easily identified in this area with the US. A 1.5-inch 21-G needle was placed using the in-plane method and progressed medially till the needle tip was placed near the nerve. Finally, the technique was carried out again on the opposite side.

After the procedure, pressure was applied to the injected area for 2 minutes to promote hemostasis, and it was covered with a simple adhesive bandage.

NRS-11 was recorded in the sitting and lying down positions preblock and at 10 minutes, 6, 12, 24, 36, and 48 hours after injection. The success rate was considered a percent of patients with sitting NRS-11 < 4 without additional maneuvers. If lying down NRS-11 was ≥ 4, rescue analgesia was given in the form of tramadol hydrochloride 100 mg oral tablet without exceeding 3 daily tablets. If lying down NRS-11 was 2 or 3, oral paracetamol 500 mg with a maximum of 6 tablets per day was given.

The primary outcome was the assessment of improvement of PDPH by sitting position NRS-11. The secondary outcomes were success rate, lying down NRS-11, consumption of analgesics, and complications, such as injection site pain, hematoma, and systemic toxicity.

**Sample Size Calculation**

The sample size assessment was performed by G*Power Version 3.1.9.2 (Universitat Kiel, Germany). We conducted a pilot study (5 cases in each group), and we found that the mean (± standard deviation [SD]) of sitting NRS-11 at 24 hours (the primary outcome) was 2.2 ± 0.45 in group D and 1.2 ± 1.30 in group P. The sample size was based on the following considerations: 1.03 effect size, 95% confidence limit, 90% power of the study, group ratio 1:1, and 4 cases were added to each group to compensate for dropout. As a consequence, we allocated 25 patients to every group.

**Statistical Analysis**

Statistical analysis was performed by SPSS Version 25 (IBM Corporation, Armonk, NY). Quantitative variables were presented using the range, mean ± SD, median, range, and interquartile range and were compared by unpaired Student’s t test or Mann-Whitney U test. Qualitative variables were presented as frequency and percent and were compared by the chi-square or Fisher’s exact test. $P$ value $< 0.05$ was assumed statistically significant.

**RESULTS**

Sixty-three patients were enrolled, and 50 patients of them were randomly allocated into 2 groups, followed-up, and analyzed (Fig. 1).

The study groups were comparable regarding...
demographic data, including age, gender, weight, and ASA physical status ($P > 0.05$) (Table 1).

As regards PDPH, there was a significant decrease in lying down NRS-11 after intervention at all times of measurement when compared with before intervention in both studied groups ($P < 0.001$), with insignificant difference between both groups neither before nor after intervention at all times of measurement (Table 2).

NRS-11 during the sitting position was significantly lower after injection at all times of measurement than before injection in both groups ($P < 0.001$). Before the intervention, no statistically significant difference in NRS-11 was observed between both groups, while after intervention at 10 minutes, 6, 12, 24, 36, and 48 hours, NRS-11 was remarkably lower in group P in comparison with group D ($P < 0.001, 0.005, 0.010, 0.003, < 0.001, \text{ and } < 0.001$, respectively) (Table 3).

After the intervention, patients with sitting NRS-11 < 4 were insignificantly different between both groups at all measurement times. The success rate at 24 hours was 60% in group D and 84% in group P with an insignificant difference ($P = 0.059$), and at 48 hours was 84% in group D and 96% in group P with an insignificant difference ($P = 0.157$) (Fig. 2).

Regarding analgesic consumption, 20 patients (80%) in group D and 13 patients (52%) in group P requested additional analgesia in the form of tramadol 100 mg or paracetamol 500 mg all over the 48 hours after intervention, which was significantly lower in group P ($P = 0.037$). Also, the total 48 hours, tramadol and paracetamol consumption in group P were significantly lower than in group D ($P = 0.038$ and 0.036, respectively) (Table 4).

Regarding complications, transient cervicalgia occurred in 2 patients (8%) in each group ($P = 1$) without other major complications (Table 4).

**DISCUSSION**

PDPH happens in 10% to 40% of lumbar punctures after intrathecal injection, diagnosis, spinal anesthesia, or inadvertent dural puncture during epidural anesthesia (17).
US guidance is increasingly becoming the gold standard for regional anesthesia (18). In our trial, we have chosen the US guidance compared to the blind technique as it increases safety and effectiveness, especially with proximal GONB, as the nerve is near the spinal cord and vertebral artery and is relatively deeper in proximal GONB than distal GONB (19).

### Table 2. Comparison between the study groups regarding lying down NRS-11 score.

<table>
<thead>
<tr>
<th>NRS-11</th>
<th>Group D (n = 25)</th>
<th>P₀</th>
<th>Group P (n = 25)</th>
<th>P₀</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preblock</td>
<td>2-3 (2-3)</td>
<td></td>
<td>2-3 (2-2)</td>
<td></td>
<td>0.162</td>
</tr>
<tr>
<td>10 min</td>
<td>&lt; 0.001*</td>
<td></td>
<td>0-2 (0-1)</td>
<td>&lt; 0.001*</td>
<td>0.111</td>
</tr>
<tr>
<td>6 h</td>
<td>0-3 (1-0)</td>
<td>&lt; 0.001*</td>
<td>0-3 (0-1)</td>
<td>&lt; 0.001*</td>
<td>0.147</td>
</tr>
<tr>
<td>12 h</td>
<td>0-2 (0-2)</td>
<td>&lt; 0.001*</td>
<td>0-2 (0-2)</td>
<td>0.001*</td>
<td>0.096</td>
</tr>
<tr>
<td>24 h</td>
<td>0-2 (0-0)</td>
<td>&lt; 0.001*</td>
<td>0-1 (0-0)</td>
<td>&lt; 0.001*</td>
<td>0.293</td>
</tr>
<tr>
<td>36 h</td>
<td>0-1 (0-0)</td>
<td>&lt; 0.001*</td>
<td>0-0 (0-0)</td>
<td>&lt; 0.001*</td>
<td>0.317</td>
</tr>
<tr>
<td>48 h</td>
<td>0-1 (0-0)</td>
<td>&lt; 0.001*</td>
<td>0-0 (0-0)</td>
<td>&lt; 0.001*</td>
<td>0.317</td>
</tr>
</tbody>
</table>

Abbreviations: NRS-11: Numeric Rating Scale; n: number; min: minutes; h: hours; IQR: interquartile range; P₀: P value for comparing between the 2 studied groups; P: P value for post hoc test (Dunn’s) for Friedman test for comparing between before and each other periods; Group D: Distal, Group P: Proximal. *Statistically significant at P ≤ 0.05.

### Table 3. Comparison between the study groups regarding sitting NRS-11 score.

<table>
<thead>
<tr>
<th>NRS-11</th>
<th>Group D (n = 25)</th>
<th>P₀</th>
<th>Group P (n = 25)</th>
<th>P₀</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preblock</td>
<td>6-7 (6-6)</td>
<td></td>
<td>5-7 (5-6)</td>
<td></td>
<td>0.261</td>
</tr>
<tr>
<td>10 min</td>
<td>2-6 (3-5)</td>
<td>&lt; 0.001*</td>
<td>0-4 (1-2)</td>
<td>&lt; 0.001*</td>
<td>0.001*</td>
</tr>
<tr>
<td>6 h</td>
<td>1-5 (3-2)</td>
<td>&lt; 0.001*</td>
<td>0-4 (1-3)</td>
<td>&lt; 0.001*</td>
<td>0.005*</td>
</tr>
<tr>
<td>12 h</td>
<td>0-5 (3-1)</td>
<td>&lt; 0.001*</td>
<td>0-5 (1-2)</td>
<td>&lt; 0.001*</td>
<td>0.010*</td>
</tr>
<tr>
<td>24 h</td>
<td>0-5 (2-1)</td>
<td>&lt; 0.001*</td>
<td>0-4 (1-1)</td>
<td>&lt; 0.001*</td>
<td>0.003*</td>
</tr>
<tr>
<td>36 h</td>
<td>0-4 (2-1)</td>
<td>&lt; 0.001*</td>
<td>0-4 (0-1)</td>
<td>&lt; 0.001*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>48 h</td>
<td>0-4 (1-2)</td>
<td>&lt; 0.001*</td>
<td>0-4 (0-1)</td>
<td>&lt; 0.001*</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Abbreviations: n: number; min: minutes; h: hours; IQR: interquartile range; P₀: P value for comparing between the 2 studied groups; P: P value for post hoc test (Dunn’s) for Friedman test for comparing between before and each other periods; Group D: Distal, Group P: Proximal. *Statistically significant at P ≤ 0.05.

### Table 4. Comparison between the study groups regarding total 48-hour postoperative analgesic consumption and complications.

<table>
<thead>
<tr>
<th>Analgesic Consumption</th>
<th>Group D n = 25</th>
<th>Group P n = 25</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Request for Analgesia</td>
<td>20 (80%)</td>
<td>13 (52%)</td>
<td>0.037*</td>
</tr>
<tr>
<td>Total Paracetamol Consumption</td>
<td>Min-Max Medial (IQR)</td>
<td>0-2500 (0-1500)</td>
<td>0-1000 (0-500)</td>
</tr>
<tr>
<td>Total Tramadol Consumption</td>
<td>Min-Max Medial (IQR)</td>
<td>0-400 (0-300)</td>
<td>0-300 (0-100)</td>
</tr>
<tr>
<td>Complications</td>
<td>Transient Cervicalgia</td>
<td>2 (8%)</td>
<td>2 (8%)</td>
</tr>
</tbody>
</table>

Abbreviations: n: number; IQR: interquartile range; P value: P value for comparing between the 2 studied groups. *Statistically significant at P ≤ 0.05.

In our study, dexamethasone was used as an adjuvant to bupivacaine in both groups. It was used to extend the duration of the block, which may decrease the need for EBP (20).
Our current study compared the pain-relieving effect between distal and proximal US-guided bilateral GONB for PDPH. There was a significant decrease in the NRS-11 on lying down and sitting.

Greher et al (21) conducted 20 US-guided bilateral GONBs in 10 embalmed cadavers. They found that they can be performed at the superior nuchal line level or the second cervical vertebra level.

In the present study, we used bupivacaine 0.5% and dexamethasone 4 mg mixed in a 4 mL volume. The block was done as described in the previous study of Baek et al (22), who examined the GONB at the C2 level on 5 cadavers using 4-5 mL of solutions. They revealed that the dorsal rami of the upper cervical spinal nerve in the suboccipital area were also stained in conjunction with the GON with a given volume, so the GON together with the dorsal rami of upper cervical spinal nerves have been stained, and additional appropriate block could be achieved.

Also, Zipfel et al (23) reported that in several craniofacial pain syndromes, significant pain relief was found by using C2 level GON infiltration (5 mL) under the guidance of US between oblique capitis inferior and semispinalis capitis muscles.

In the current study, NRS-11 was statistically significantly lower than before the intervention at 10 minutes, 6, 12, 24, 36, and 48 hours in both approaches.

Similar results were found in Naja et al (24). They randomized 50 PDPH patients who underwent cesarean and lower limb operations under spinal anesthesia into 2 groups with 25 cases each. In one group (block group), bilateral greater and lesser occipital nerve blocks guided by the nerve stimulator were administered. After 1-2 blocks, complete relief of pain was in 68.4% of the block group. Therefore, the block group’s pain score was significantly lower after intervention.

Also, another study conducted by Niraj et al (10) audited 24 patients, and 19 of them failed conservative treatment. EBP was received by one patient and succeeded. The GONB was received in 18 patients, with a complete response in 12 (66.7%) patients and a partial response in the remaining patients. Patients with a partial response received EBP after that.

Similar to our results, Türkyılmaz et al (11) used landmark-guided bilateral GONBs with levobupivacaine and dexamethasone to treat PDPH after cesarean section under spinal anesthesia. They found that the pain score decreased significantly after the block.

Also, Matute et al (25) documented the impact of bilateral GONB on 2 cases of PDPH. Both patients had not improved with conservative management, and then a block was done by giving 4 mL 0.25% bupivacaine and 20 mg triamcinolone. The patients were released 48 hours after the pain subsided in 1 to 2 minutes.

Moreover, in a case report done by Takmaz et al (26), a patient with refractory to conservative treatment PDPH received the GONB (2 mL bupivacaine 0.5%) and should complete response within 2 minutes. The patient had mild pain without the restriction of the daily activity after 12 hours, which ultimately resolved after the repetition of the GONB.

In our study, when we compared NRS-11 scores between the 2 techniques of GONBs, we found an insignificant difference when lying down between both groups, except at 2 hours after the intervention when NRS-11 was significantly lower in the proximal GONB group. At the same time, NRS-11 scores of proximal GONB patients were significantly lower than distal GONB patients in the sitting position.

This agreed with Flamer et al (19), who randomized 40 patients with migraine to undergo a distal or proximal GONB with US guidance using bupivacaine and methylprednisolone acetate. Results demonstrated that both proximal and distal approaches could reduce headache intensity temporarily. The proximal GON approach conferred better long-lasting analgesic relief than the distal technique.

Similarly, in a study (27) in which patients with cervicogenic headache or occipital neuralgia were randomly assigned to undergo either a US-guided GONB at the C2 vertebral level or a landmark-based GONB with sham US at the superior nuchal line level, patients in the US-guided GONB group showed a remarkable decline in NRS-11 from baseline compared with the landmark-based GONB group. In neither group did any severe adverse events happen.

In contrast to the present study, Yoo et al (28) compared classical (distal) and proximal GONB techniques in treating primary headaches. Both the intensity and frequency of headaches decreased in both groups. Between the 2 groups, there was no obvious difference in the outcome. The study revealed that the classic and proximal approaches are comparable in reducing headache frequency and severity; this might be explained by short-term follow-up in our study.

Also, Pingree et al (29) found that in cervicogenic headache and occipital neuralgia, significant pain relief over 4 weeks was shown by using C2 level GONB under the guidance of US (4 mL steroid).

In our study, the success rate (NRS-11 < 4) at 24 hours
in distal US-guided GONB was 60% (Fig. 2). This result is in accordance with Akyol et al (1), who compared the therapeutic value of bilateral GONB with US guidance administered medial to the occipital artery between 2 groups of various grades of PDPH. They found that the percentage of recovered patients in both groups was 62%, while in proximal US-guided GONB was 84%, in contrast to the same previous study. This might be due to the different GONB technique, also in the current study, the success rate was considered to be NRS-11 of < 4, while in the previous study, the percentage of recovered patients was considered to be the Visual Analog Scale of 1.

The success rate at 48 hours was 84% with distal GONB and 96% with proximal GONB, which might be explained by the more precise and accurate spread of injectate with US-guided GONB where the plane is more obvious (Fig. 2).

This is near the results of Greher et al (21), who found that the block's success rate at the superior nuchal line level is 80% vs 100% at the C2 level, which is statistically significant (P = 0.002).

In the current study, 20 patients (80%) in the distal GONB group and 13 (52%) in the proximal GONB group requested additional analgesia in the form of paracetamol 500 mg or tramadol hydrochloride 100 mg all over the 48 hours after intervention with a statistically difference of significance among both study groups, also, for the total paracetamol and tramadol doses requested throughout the 48 hours; statistical difference of significance existed among studied groups where it was statistically significantly lower in group P in comparison to group D (P = 0.038 and 0.036, respectively) (Table 4).

There were no published researches that compared the paracetamol or tramadol consumption between distal and proximal GONBs for the management of PDPH or any headache, but studies that compared paracetamol or tramadol consumption between the GONB and conservative management showed a statistically significant reduction in the GONB groups, Mostafa et al (30) and Kamal et al (31).

In a study (32) that compared analgesic consumption in the form of dipyprone and diclofenac between classical (distal) and suboccipital (proximal) GONBs, they found no difference between the 2 approaches immediately after the intervention, but at 24 weeks postintervention, there was a significant reduction of analgesic consumption in the suboccipital approach (P < 0.05).

The superiority of the proximal GONB may be attributed to several justifications. Entrapment of the GON in the proximal part, i.e., the proximal location of the GON between tissue planes at the level of the second cervical vertebra, provides it with distinct sonographic features. This can allow for ease of US visualization and potentially more accurate nerve targeting, with less volume of injectate. Also, GON branches distally and targeting the GON distally is expected to be less effective (33-35).

Classically described adverse events included transient dizziness and vaso-vagal syncope following the injection, more severe headache, alopecia around the site of injection, Afridi et al (36), and Cushing’s syndrome (37) were not observed in our study, but minor side effect in the form of transient cervicalgia was found in 2 patients (8%) in each study group (Table 4).

Similarly, Zipfel et al (23) found no major adverse events with proximal GONB; transient cervicalgia occurred in one case and lasted for 6 days, and transient neck torticollis occurred in 2 cases and lasted for 5 and 10 days, respectively. Also, Niraj et al (10) and Türkyilmaz et al (11) showed no reported side effects with distal GONB.

Limitations

The small number of cases to prove the secondary outcomes and the absence of a control group. The efficacy of the GONB should be contrasted with the conservative treatment, but the results from patients treated with the conservative treatment in our hospital were not as strict as the GONB patients.

Conclusions

US-guided GONB is a minimally invasive, simple, and effective way to treat PDPH following neuraxial anesthesia with fewer complications, but proximal GONB is more efficient than distal GONB by decreasing pain score, paracetamol consumption, and tramadol consumption. Therefore, we recommend the use of proximal GONB for PDPH before the use of EBP.
References


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