Retrospective Study

# Prophylactic Epidural Blood Patch or Prophylactic Epidural Infusion of Hydroxyethyl Starch in Preventing Post–Dural Puncture Headache – A Retrospective Study

Yan-Ting Fan, MD[1], Tian-Yun Zhao, PhD[1], Jing-Hui Chen, MD[1], Yan-Li Tang, BS[2], and Xing-Rong Song, MD[1]

From: [1]Department of Anesthesiology, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, People's Republic of China; [2]Department of Surgery, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, People's Republic of China

Address Correspondence:
Xing-Rong Song, MD
Department of Anesthesiology, Guangzhou Women and Children's Medical Center, Guangzhou Medical University
No. 9 Jinsui Road
Zhujiang New Town
Tianhe District, Guangzhou, People's Republic of China
E-mail: sxjess@126.com

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**Background:** Post–dural puncture headache (PDPH) is particularly likely to happen in patients under obstetric care due to an unintentional dural puncture (UDP). There is as yet no ideal strategy for preventing UDP-induced PDPH.

**Objectives:** The primary objective of this study was to assess whether a prophylactic epidural blood patch (EBP) or prophylactic epidural infusion of hydroxyethyl starch (HES) is effective in preventing PDPH for parturients with UDP compared with conservative treatments.

**Study Design:** Retrospective analysis from a single center's inpatient data.

**Setting:** Department of Anesthesiology at a single center.

**Methods:** A retrospective study was conducted of a single center's inpatient data from January 2017 through March 2020. The study included parturients with UDP during neuraxial anesthesia. The interventions of UDP included conservative treatment, prophylactic EBP, and prophylactic epidural infusion of HES. The incidence of PDPH, the use of intravenous aminophylline, therapeutic EBP, symptom onset, duration of headache, and duration of hospital stay were compared.

**Results:** A total of 85 patients were analyzed. The incidences of PDPH were 84%, 52.6% and 54.5% with conservative, prophylactic EBP, and prophylactic epidural HES treatments, respectively. Compared with the conservative treatment, prophylactic EBP and prophylactic epidural HES treatment significantly reduced the incidence of PDPH ($P < 0.05$). No significant difference was found between the prophylactic EBP and prophylactic epidural HES groups. Compared with the conservative treatment group, therapeutic EBP was significantly less used in the prophylactic EBP and prophylactic epidural HES groups ($P < 0.05$). Prophylactic EBP shortened the length of hospital stay of parturients with UDP ($P < 0.05$) while prophylactic epidural HES showed no statistical difference compared with conservative treatment. No severe complications, such as central nervous system and puncture site infection or nerve injury, were found in those patients.

**Limitations:** Retrospective nature and single center data with a relatively small sample size.

**Conclusions:** Prophylactic management with EBP and epidural infusion of HES has an effect in preventing the occurrence of PDPH; prophylactic EBP significantly shortened hospital stay length in parturients with UDP.

**Key words:** Unintentional dural puncture, epidural blood patch, hydroxyethyl starch, post–dural puncture headache, parturient

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Post–dural puncture headache (PDPH) is a major obstetric anesthesia issue. Neuraxial anesthesia is the preferred method of anesthesia for cesarean delivery or labor analgesia (1). Unintentional dural puncture (UDP) during a neuraxial anesthesia procedure occurs in approximately 0.7–1.5% of all epidural anesthesia (2,3). Approximately 60%–80% of these patients develop PDPH, which is particularly likely to happen and is more obvious in patients under obstetric care than in the general patient population (4-6). PDPH is generally considered to be reversible without long-term consequences. However, there is increasing literature that reports PDPH causes long-term headache (7), even severe complications such as subdural hematoma, cranial nerve palsies and venous sinus thrombosis (8). In addition, PDPH exacerbates pre-existing disability, negates the mother's ability to care for her newborn, and increases health care costs due to the increased length of hospitalization stay (5,6).

To date, several strategies exist to manage PDPH, such as conservative treatments like bed rest, hydration, and oral caffeine. Epidural blood patch (EBP) is identified as the definitive treatment for PDPH (4,9). However, prophylactic EBP to prevent the occurrence of PDPH is controversial, since EBP may lead to complications such as infection, meningitis, permanent spastic paraparesis and back pain (10).

Most PDPH are self-resolving and not all patients with a dural puncture develop PDPH (4,11). However, in practice, the urge for rapid PDPH symptom relief often necessitates aggressive management and earlier EBP (11). Besides, fear remains that the application of therapeutic EBP may cause a new UDP or injury from a second puncture. Some clinicians have found a prophylactic blood patch may eliminate the need for a second EBP (12,13). The practice of administering a prophylactic EBP has been reported to be employed in patients under obstetric care after UDP in approximately half of the academic centers in North America (14).

As an alternative to blood for injection into the epidural space for the treatment of PDPH, saline is also usually selected (15). However, the shorter long-term efficacy of an epidural saline patch has been demonstrated compared with EBP (16,17). Thus, hydroxyethyl starch (HES) is considered to be an ideal candidate with less antigenicity, plus a higher molecular weight and viscosity, which allows it to remain in the epidural space longer thereby providing sustained effects. Previous reports have described epidural HES injection as a viable treatment option for PDPH if a blood patch is contraindicated (18-20). However, one study suggested the duration of increased pressure was less than 10 minutes with a single injection of epidural HES (21).

In our medical center, prophylactic EBP and prophylactic epidural infusion of HES through an epidural catheter are commonly used to manage UDP in patients under obstetric care. Prophylactic epidural infusion through an epidural catheter eliminates the need for another needle insertion and is more accepted by patients as well as physicians. We undertook this retrospective study to assess whether prophylactic EBP or prophylactic epidural infusion of HES is beneficial for parturients with UDP compared with conservative treatments.

## Methods

The data from all patients with UDP in the Department of Obstetrics of our institution from January 2017 through March 2020 were retrospectively analyzed. Ethical approval for this retrospective study (Ethical Committee No. 202020601) was provided by the Ethical Committee of our institution on April 28, 2020.

Our obstetric anesthesia service follows a strict protocol for collecting adverse events such as UDP and PDPH. The use of electronic forms to record obstetric complications was introduced in 2017. Throughout the duration of this investigation, our obstetric anesthesia team employed standardized, consistent anesthetic procedures.

Patients scheduled for cesarean delivery were mostly given combined spinal-epidural anesthesia, with some receiving epidural anesthesia. For patients scheduled for labor, epidural analgesia was performed. Our center employed 16G Tuohy epidural needles and 25G pencil-point spinal needles.

Throughout the course of the study, procedures for reporting and recording problems such as UDPs and PDPH were standardized and consistent. The diagnosis of a UDP was made when there was a free flow of cerebrospinal fluid through an epidural needle (wet tap) when attempting epidural puncture. A PDPH diagnosis was based on International Headache Society criteria: the headache develops within 5 days of the neuraxial procedure; is usually accompanied by neck stiffness, photophobia, or hearing changes; may have a postural element; and is not accounted for by any other reason (22). The exclusion criteria include preeclampsia, eclampsia, migraine, meningitis, cerebral thrombosis, intracranial hemorrhage, and tension headaches.

### Hospital Protocol for UDP Management

When UDP occurs in our hospital, the anesthesiologist performs another attempt with one interspace cephalad to the first attempt.

Management for UDP is initiated with conservative treatment as the protocol in our medical center. Conservative treatment includes intravenous infusion of 2,000-3,000 mL of fluid per day and bed rest for 72 hours. Until 2016, local protocols were altered to include prophylactic EBP and prophylactic epidural infusion of HES through the epidural catheter as first-line management. Exclusion criteria of EBP included a temperature greater than 37.8°C, coagulopathy and leukocytosis > 10.0 X $10^3$ /μL (reference range 3.5 – 9.5. X $10^3$ /μL).

The prophylactic EBP includes injection 20 mL of autologous blood via an epidural catheter at 6 hours after UDP or the end of delivery (if the delivery time was more than 6 hours after UDP) and then bed rest for at least 2 hours.

The epidural catheter is then removed after the injection. In patients with prophylactic epidural infusion of HES, 6% hydroxyethyl starch 130/0.4 (150 mL) was infused at a rate of 6 mL/h via epidural catheter from the end of vaginal delivery or cesarean delivery and bed rest for 24 hours. Patients were asked to get adequate hydration and bed rest for another 48 hours if PDPH still occurred.

If the pain Numeric Rating Scale (NRS-11) was ≥ 4, 250 mg of aminophylline dissolved in 100 mL saline was given through intravenous injection. Injection were administered twice daily for 2 consecutive days. Therapeutic EBP was recommended in patients when the above treatment was not effective. All patients who experienced a UDP were followed daily until all symptoms were resolved and further assessed before discharge.

### Outcomes

The incidence of PDPH, use of intravenous aminophylline, use of therapeutic EBP, symptom onset, duration of headache, duration of hospital stay, and delay after expected discharge among the 3 treatments were analyzed. Expected discharge is 2 days after vaginal delivery and 3 days after cesarean delivery in our center. Postoperative complications, low back or combined low back and leg pain (NRS-11 > 3), recurrence of headache (NRS-11 > 3) within one week after discharge, and need for readmission after discharge (reported difficulties performing childcare) were also collected. Demographic data, American Society of Anesthesiologists physical status, anesthetic technique, delivery type, and intervention were also collected.

### Statistical Analysis

Continuous data (symptom onset, duration of headache, length of hospital stay after neuraxial anesthesia) was compared by one-way analysis of variance (ANOVA) followed by Newman-Keuls for normal distribution data and the Bonferroni test or by the Kruskal-Wallis H test for non-normal distribution data. Categorical variables (incidence of PDPH, aminophylline treatment, postoperative complications, recurrence of headache within one week after discharge, readmission after discharge, low back or combined low back and leg pain) were compared by the $\chi^2$ test or Fisher's exact test. Statistical analyses were performed using IBM SPSS Statistics 25.0 (IBM Corporation). Statistical significance was set at a *P* value < 0.05 (2-tailed for all tests).

## Results

A total of 88 patients were recorded; 2 patients with preeclampsia or eclampsia and one patient with a history of migraine were excluded. The data from 85 patients were analyzed. Of them, 25 patients were treated with the conservative treatment; 38 patients received prophylactic EBP, and 22 patients received a prophylactic epidural infusion of HES (Fig. 1). Data re-

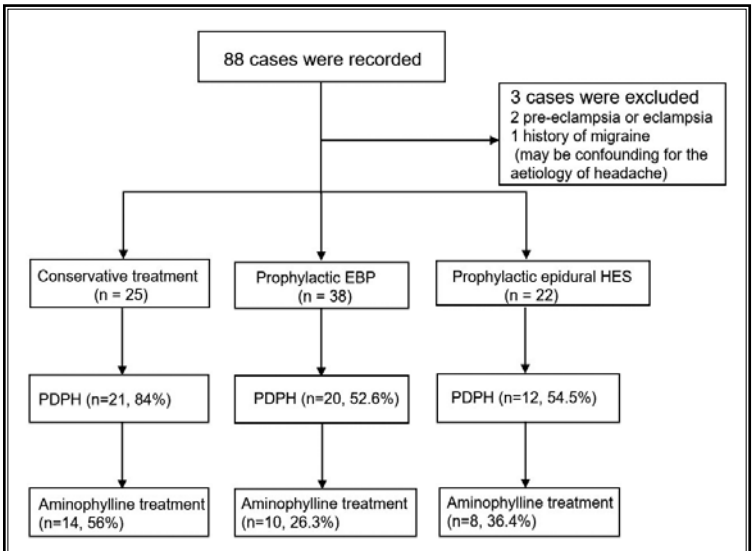


Fig. 1. *Patient recruitment flow chart.*

garding patient characteristics and analgesic/anesthetic technique used are shown in Table 1.

## Main Outcomes

In the conservative treatment group, 21 of 25 patients had PDPH (84%). In the prophylactic EBP group, 20 of 38 patients had PDPH (52.6%) and 12 of 22 patients had PDPH (54.5%) (Table 2) in the prophylactic use of epidural HES group. Compared with the conservative treatment group, prophylactic EBP and HES both significantly decreased the incidence of PDPH ($P < 0.05$, Table 2) while there was no significant difference in the incidence of PDPH between the prophylactic EBP and HES groups.

The percentage of parturients requiring aminophylline was 56%, 26.3% and 36.4% in the conservative treatment, prophylactic EBP, and prophylactic epidural HES groups, respectively ($P = 0.058$) (Table 2).

Compared with the conservative treatment group, therapeutic EBP was significantly less used in the prophylactic EBP and prophylactic epidural HES groups ($P < 0.05$) (Table 2). There was no significant difference in the percentage of therapeutic EBP between the prophylactic EBP and HES groups.

For parturients who developed PDPH, the onset of headache and the duration of headache were not statistically different among the 3 groups ($P = 0.450$ and $P = 0.612$ respectively, Table 2).

There were statistical differences in length of hospital stay and delay after expected discharge among the 3 groups ($P = 0.005$ and $P = 0.020$ respectively, Table 3). Compared with the conservative treatment group (5.9 ± 2.1 day), length of hospital stay was significantly shorter in the prophylactic EBP group (4.3 ± 1.6 days, $P < 0.05$, Table 3). Delay after expected discharge in the prophylactic EBP group was shorter than the conservative treatment group (1.8 ± 1.5 day vs 3.1 ± 2.0 day, $P < 0.05$, Table 3). The length of hospital stay and delay after expected discharge in the prophylactic epidural HES group were 5.2 ± 1.9 days and 2.5 ± 2.0 days respectively (Table 3). However, the length of hospital stay and delay after expected discharge in the prophylactic epidural HES group had no statistical difference when further compared with the conservative treatment and prophylactic EBP groups.

## Safety Outcomes

No epidural infection or central nervous system infection or other neurologic deficits were found in all studied patients. Patients with therapeutic EBP were excluded from the analysis of postoperative complications (Table 4). Patients reporting low back pain or combined low back and leg pain during their hospital stay were 5 (31.3%), 10 (28.6%) and 7 (36.8%) in the

Table 1. *Characteristics of patients with unintentional dural puncture (UDP).*

| Characteristics | Conservative treatment (n = 25) | EBP (n = 38) | HES (n = 22) | *P* Value |
|---|---|---|---|---|
| Age, years | 32.7 ± 4.16 | 32.6 ± 4.74 | 31.8 ± 3.89 | 0.740 |
| Height, cm | 160.9 ± 3.97 | 159.6 ± 5.89 | 158.7 ± 6.46 | 0.355 |
| Weight, kg | 66.8 ± 9.62 | 64.0 ± 7.80 | 67.1 ± 6.81 | 0.228 |
| BMI, kg/m$^2$ | 25.8 ± 3.55 | 25.1 ± 2.47 | 26.7 ± 2.91 | 0.153 |
| Technique, n (%) | | | | 0.113 |
| Epidural | 6 (24%) | 19 (50%) | 8 (36.4%) | |
| CSE | 19 (76%) | 19 (50%) | 14 (63.6%) | |
| Delivery type, n (%) | | | | 0.224 |
| Labor analgesia | 6 (24%) | 17 (44.7%) | 7 (31.8%) | |
| Cesarean delivery | 19 (76%) | 21 (55.3%) | 15 (68.2%) | |

Data was presented as mean ± SD, or number (percentage).
CSE: combined spinal-epidural; EBP: prophylactic epidural blood patch; HES: prophylactic epidural infusion of hydroxyethyl starch.

Table 2. *Incidence, onset, duration and treatment of post–dural puncture headache (PDPH).*

| | Conservative treatment (n = 25) | EBP (n = 38) | HES (n = 22) | *P* Value |
|---|---|---|---|---|
| PDPH, n (%) | 21 (84%) | 20 (52.6%) | 12 (54.5%) | 0.036 |
| Aminophylline treatment, n (%) | 14(56%) | 10 (26.3%) | 8 (36.4%) | 0.058 |
| Therapeutic EBP, n (%)* | 9 (36%) | 3 (7.9%) | 3 (13.6%) | 0.023 |
| Onset of PDPH, hour (median, IQR) | 48 (30 to 55) | 36 (18 to 55.5) | 48 (36 to 55) | 0.450 |
| Duration of PDPH, day (mean ± SD) | 4.4± 2.06 | 4.2 ± 2.09 | 5.0± 2.12 | 0.612 |

Data are presented as mean ± SD, median (IQR) or number (percentage). *Fisher's exact test.
EBP: Prophylactic epidural blood patch; HES: Prophylactic epidural infusion of hydroxyethyl starch.

conservative, prophylactic EBP, and the prophylactic epidural HES group, respectively ($P$ = 0.822, Table 4). No statistical difference was found in the incidence of low back or combined low back and leg pain during telephone interviews after discharge from the hospital among the 3 groups ($P$ = 0.851, Table 4). The follow-up interview since neuraxial anesthesia at the time of the phone interview was 1.7 ± 0.7 years, 1.5 ± 0.7 years and 1.9 ± 0.8 years in the conservative, prophylactic EBP group, and prophylactic epidural HES groups, respectively ($P$ = 0.08, Table 4). In addition, there was no statistical significance in the incidence of recurrence of headache within one week after discharge and re-admission after discharge among the 3 groups ($P$ = 0.863 and $P$ = 0.836 respectively, Table 4).

## Discussion

In this retrospective study, we found that prophylactic EBP and prophylactic epidural infusion of HES significantly reduced the incidence of PDPH compared with conservative treatment while there was no significant difference between the 2 aggressive intervention groups. Compared with conservative treatment, prophylactic EBP shortened the hospital stay length of parturients with UDP while prophylactic epidural HES showed no statistical difference. In addition, prophylactic EBP and epidural infusion of HES significantly reduced the requirements of therapeutic EBP in the parturients who developed PDPH. No significant differences in safety parameters were found in the patients in the 3 groups. These results suggest that prophylactic intervention with EBP or epidural infusion of HES after UDP might be an effective and safe strategy in preventing PDPH in parturients.

Obstetric patients are at an increased risk for developing PDPH after UDP because of the relatively large needle size use, their gender, high levels of circulating estrogen, and their young age (23,24). Dural puncture by an epidural needle causes PDPH in approximately 81% of patients (25). Our study showed 84% of parturients with UDP in the conservative group would develop PDPH, which is similar to what previous studies have reported (6,25). In addition, conservative treatment with long-term bed rest is not good for gastrointestinal function recovery. Parturients are considered to be in a hyper-coagulable state (26) and are prone to developing deep vein thrombosis when they are in a condition of long-term inactivity. On the whole, the increased risk for developing PDPH and demand for rapid symptom relief necessitate aggressive management in the obstetric population with UDP.

Table 3. *Length of hospital stay in patients with unintentional dural puncture (UDP) with different treatments.*

| | Conservative treatment (n = 25) | EBP (n = 38) | HES (n = 22) | *P* Value |
|---|---|---|---|---|
| LOS, days | 5.9 ± 2.1 | 4.3 ± 1.6[a] | 5.2 ± 1.9 | 0.005 |
| DD, days | 3.1 ± 2.0 | 1.8 ± 1.5[a] | 2.5 ± 2.0 | 0.020 |

Data are presented as mean ± SD.
a Bonferroni test, compared with conservative treatment, $P < 0.05$.
DD: delay after expected discharge; EBP: prophylactic epidural blood patch; HES: prophylactic epidural infusion of hydroxyethyl starch; LOS: length of hospital stay after neuraxial anesthesia; PDPH: post–dural puncture headache.

Table 4. *Postoperative complications.*

| | Conservative treatment (n = 16) | EBP (n = 35) | HES (n = 19) | *P* Value |
|---|---|---|---|---|
| Epidural infection | 0 | 0 | 0 | N/A |
| CNS infection | 0 | 0 | 0 | N/A |
| Nerve injury | 0 | 0 | 0 | N/A |
| LBLP (during hospital stay) | 5 (31.3%) | 10 (28.6%) | 7 (36.8%) | 0.822 |
| Recurrence of headache within one week* | 3 (18.8%) | 7 (20%) | 5 (26.3%) | 0.863 |
| Readmission* | 1 (6.3%) | 2 (5.7%) | 2 (10.5%) | 0.836 |
| LBLP (phone interview) | 6 (37.5%) | 12 (34.3%) | 8 (42.1%) | 0.851 |
| Mean years since phone interview | 1.7 ± 0.7 | 1.5 ± 0.7 | 1.9 ± 0.8 | 0.08 |

Data are presented as number (percentage) or as mean ± SD. *Fisher's exact test.
CNS: central nervous system; EBP: prophylactic epidural blood patch; HES: prophylactic epidural infusion of hydroxyethyl starch; LBLP: low back or combined low back and leg pain.

There is as yet no ideal strategy for preventing UDP-induced PDPH. Administration of fluids and pharmacologic agents (morphine, cosyntropin, ondansetron, and caffeine) as prophylactic treatment for PDPH is insufficient (11,27,28). Exposure to opioids after UDP may not lessen the risk of PDPH or the requirement for therapeutic EBP (29). The effectiveness of prophylactic EBP in preventing PDPH has been demonstrated to have either a positive or no effect on the incidence and severity of PDPH (13,30). A randomized controlled trial found that 11 of 60 (18.3%) patients in a prophylactic EBP group developed PDPH compared with 39 of 49 (79.6%) in a conservative treatment group ($P < 0.0001$)

(13). One meta-analysis showed that for every 2.1 patients treated with a prophylactic EBP, one PDPH will be avoided (31). Our data indicate the incidence of PDPH in prophylactic EBP was 52.6%, which is consistent with the result of the previous study (31). It has been proposed that the mechanism by which an EBP relieves PDPH is the injection of blood clots; these blood clots may plug the cerebrospinal fluid leak from the dural hole and speed up the healing of the puncture (11).

Prophylactic EBP shortened the length of hospital stay of parturients with UDP by decreasing the incidence of PDPH. In addition, in our medical center, patients with prophylactic EBP treatment were allowed to return to off-bed activity for about 8 hours after accidental dural puncture, while patients receiving conservative treatment needed 72 hours and patients receiving prophylactic epidural HES needed 24 hours. Early mobilization is beneficial for enhanced recovery after surgery (32). Prophylactic EBP accelerated the mobilization of parturients with UDP, which may be one of the reasons that it shortened their hospital stay length.

The use of epidural HES as a substitute for a blood patch was a single injection in most studies; a continuous infusion of epidural HES was seldom reported. Several case reports described the success of epidural HES in the relief of PDPH with no immediate adverse effects (18,33,34). Three parturients with UDP had no PDPH after 2 prophylactic epidural injections of HES 20 mL combined with sufentanil 5 μg (18). Another study showed that continuous epidural analgesia at a rate of 4-5 mL/h for more than 24 hours or 48 hours followed by an epidural injection of HES 15 mL successfully prevented PDPH in 20 parturients with UDP (34).

It has been reported that when 6 mL/h of epidural saline was administered to 68 patients with UDP, 49 (72.1%) developed PDPH, whereas all patients in the conservative therapy group developed PDPH ($P = 0.009$) (15). Prophylactic epidural HES or saline may minimize the risk of PDPH by raising cerebrospinal fluid pressure, which may then exert a tamponade effect that relieves PDPH (21). HES is a synthetic colloidal solution with a high molecular weight and is widely used for increasing blood volume. Compared with epidural saline (single or continuous injection), which is used as one of the strategies for the treatment of PDPH and is demonstrated to be less effective(17), HES may be more effective in preventing PDPH due to its relatively longer stay in the epidural space and the prolonged effect of sealing the damaged dura mater.

Nevertheless, epidural infusion of HES still raises safety concerns. Lumbar discomfort has been reported after epidural injections of HES (33). Our study found a prophylactic epidural HES group had a higher incidence of low back pain or combined low back and leg pain. However, the difference was not statistically significant. There have been both preclinical and clinical studies demonstrating that intrathecal HES injection produces no histopathological changes in rats (35,36) and that an epidural HES injection can be used to prevent PDPH in patients with UDP (18,33,34). Further clarification is still needed on the safety of epidural infusion of HES. In addition, the issue of epidural catheter detachment or displacement should be a focus during epidural infusion of HES.

The long-term safety of an EBP or continuous infusion of epidural HES in preventing PDPH is limited. Our study followed long-term recovery after discharge. The long-term telephone follow-up found no significant difference in the incidence of back pain or leg pain and found no other neurologic deficits in this case series. However, neurological deficits are rare and reports are anecdotal; more patients would need to be studied to determine safety.

It has been previously reported that EBP is independently associated with an increased prevalence of subsequent symptoms of low back pain (37,38). However, the effect of EBP on back pain remains unclear. Hasoon et al (39) suggested that patients with a dural puncture who undergo EBP do not experience low back pain with increased frequency compared to those who do not undergo EBP (39). Our result shows EBP has no significant effect on the incidence of back pain in parturients with UDP. A recent case-controlled prospective observational study found no statistically significant difference in chronic back pain development 18-24 months postpartum between conservatively treated and EBP-treated patients (40), which is similar to our observation.

According to the routine UDP management in our medical center, intravenous aminophylline was given to patients with severe PDPH (NRS-11 $\geq$ 4) after any 3 types of treatment. When an aminophylline treatment was used, the onset of headache and the duration of headache were not statistically different among the 3 groups, which may reflect that headache severity after the 3 different treatments was similar once PDPH occured.

If intravenous aminophylline did not relieve the PDPH, therapeutic EBP was recommended. The use of therapeutic EBP was significantly lower in the prophylactic treatment groups than in the conservative treatment group. However, the therapeutic EBP alternative offered to patients remained poorly standardized. A

repeated EBP always needs another epidural puncture, which may cause a new UDP. In addition, repeated EBPs within a short time correlate with subdural and intrathecal hematomas and arachnoiditis (41,42). Patients and clinicians in our study were aware of the benefits and risks of the different treatments; this may have resulted in significant bias.

EBP has been related to rare complications, such as epidural or subdural abscess, meningitis, intrathecal hematoma, and arachnoiditis (11,42,43). Intrathecal hematoma and arachnoiditis following large-volume EBP has been reported (42). High epidural pressure caused by large-volume EBP may facilitate the reflux of blood into the subarachnoid space through the initial dural puncture (43). Clinicians should be aware of rare but serious complications. To reduce the risk of infection, patients in our study were strictly screened and EBP was performed with aseptic practices. We used 20 mL of autologous blood which has been recommended (44).

Prophylactic EBP was given through the detained epidural catheter, which avoided the recurrence of UDP and thus avoided injecting the blood directly into the subarachnoid space. PDPH is also occasionally accompanied by severe morbidity: cranial nerve palsy, venous sinus thrombosis, and subdural hematoma (7,8,45). The very rare but severe possible consequences of arachnoiditis or infection must be weighed against the possibility of an increased risk of PDPH without a prophylactic EBP and severe morbidity related to PDPH in parturients.

### Limitations

Our study's limitations include its retrospective nature and its setting in a single center, providing limited data due to its relatively small sample size, which potentially limits external validity. Also, no more detailed pain scores for PDPH after aminophylline treatment were recorded, so data about the more detailed severity of PDPH cannot be obtained. Finally, we were unable to provide results about the risk factors of PDPH and further treatment with aminophylline and therapeutic EBP because of the small sample size and lack of information on some risk factors.

A recent study found development of PDPH was significantly correlated with prelumbar puncture headache, a history of previous PDPH, and the number of lumbar puncture attempts (46). Parturients with PDPH that had a vaginal delivery or lower body mass index were more likely to need more than one EBP (6). Further studies are needed to identify the population at high risk of PDPH and refractory PDPH after UDP for precise application of prophylactic measures.The effect of prophylactic epidural HES infusion on the prevention of PDPH in our study was similar to that of prophylactic EBP. However, it should be pointed out that epidural HES infusion requires patients staying in bed during infusion which may be considered as an advantage of this strategy as prolonged bed rest may be beneficial in relieving PDPH. Nevertheless, our study showed 2 effective managements in preventing PDPH without a second puncture for injection and the safe profile of epidural HES use although further multi-centre study is needed.

## Conclusions

Prophylactic management with EBP and epidural infusion of HES through an epidural catheter has an effect in preventing PDPH in parturients with a UDP. Prophylactic EBP significantly shortened hospital stay length, which is beneficial for the rapid recovery of parturients. When autologous blood is contraindicated, such as when there is suspected infection or metastatic diseases, a continuous infusion of epidural HES may serve as a substitute for EBP. However, more evidence-based study is needed for further verification of the effectiveness and safety of prophylactic management with EBP and epidural HES.

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## References

1. Anim-Somuah M, Smyth RM, Cyna AM, Cuthbert A. Epidural versus non-epidural or no analgesia for pain management in labour. *Cochrane Database Syst Rev* 2018; 5:CD000331.
2. Peralta F, Higgins N, Lange E, Wong CA, McCarthy RJ. The relationship of body mass index with the incidence of postdural puncture headache in parturients. *Anesth Analg* 2015;121:451-456.
3. Peralta FM, Wong CA, Higgins N, et al. Prophylactic intrathecal morphine and prevention of post-dural puncture headache: A randomized double-blind trial. *Anesthesiology* 2020; 132:1045-1052.
4. Buddeberg BS, Bandschapp O, Girard T. Post-dural puncture headache. *Minerva Anestesiol* 2019; 85:543-553.
5. Angle P, Tang SL, Thompson D, Szalai JP. Expectant management of postdural puncture headache increases hospital length of stay and emergency room visits. *Can J Anaesth* 2005; 52:397-402.

6. Costa AC, Satalich JR, Al-Bizri E, et al. A ten-year retrospective study of post-dural puncture headache in 32,655 obstetric patients. *Can J Anaesth* 2019; 66:1464-1471.
7. Barad M, Carroll I, Reina MA, Ansari J, Flood P. Did she have an epidural? The long-term consequences of postdural puncture headache and the role of unintended dural puncture. *Headache* 2021; 61:1314-1323.
8. Guglielminotti J, Landau R, Li G. Major neurologic complications associated with postdural puncture headache in obstetrics: A retrospective cohort study. *Anesth Analg* 2019; 129:1328-1336.
9. Siegler BH, Oehler B, Kranke P, Weigand MA. Postdural puncture headache in obstetrics : Pathogenesis, diagnostics and treatment. [Article in German] *Anaesthesiologie* 2022; 71:646-660.
10. Peralta F, Devroe S. Any news on the postdural puncture headache front? *Best Pract Res Clin Anaesthesiol* 2017; 31:35-47.
11. Patel R, Urits I, Orhurhu V, et al. A Comprehensive update on the treatment and management of postdural puncture headache. *Curr Pain Headache Rep* 2020; 24:24.
12. Ackerman WE, Colclough GW. Prophylactic epidural blood patch: The controversy continues. *Anesth Analg* 1987; :66:913.
13. Stein MH, Cohen S, Mohiuddin MA, Dombrovskiy V, Lowenwirt I. Prophylactic vs therapeutic blood patch for obstetric patients with accidental dural puncture--A randomised controlled trial. *Anaesthesia* 2014; 69:320-326.
14. Berger CW, Crosby ET, Grodecki W. North American survey of the management of dural puncture occurring during labour epidural analgesia. *Can J Anaesth* 1998; 45:110-114.
15. Che X, Zhang W, Xu M. Continuous epidural pumping of saline contributes to prevent and treat postdural puncture headache. *J Clin Anesth* 2016; 34:154-158.
16. Apfel CC, Saxena A, Cakmakkaya OS, et al. Prevention of postdural puncture headache after accidental dural puncture: A quantitative systematic review. *Br J Anaesth* 2010; 105:255-263.
17. Kakinohana M, Odo Y, Matsuda S, Taira Y, Sugahara K. Epidural injection with saline for treatment of postspinal headache: Comparison with epidural blood patch. *J Anesth* 2001; 15:185-187.
18. Sun S, Huang SQ. Epidural injection of hydroxyethyl starch in the management of post-dural puncture headache: A case series. *Int J Clin Exp Med* 2015; 8:8254-8258.
19. Hardy M, Dangoisse M, Van der Linden P. Severe cerebrospinal fluid-cutaneous fistula treated by an epidural tetrastarch patch: A case report. *Eur J Anaesthesiol* 2020; 37:334-337.
20. Haldar R, Kannaujia AK. Treating postdural puncture headache with hydroxyethyl starch patch: A novel method. *Am J Ther* 2020; 27:e619-e620.
21. Kroin JS, Nagalla SK, Buvanendran A, et al. The mechanisms of intracranial pressure modulation by epidural blood and other injectates in a postdural puncture rat model. *Anesth Analg* 2002; 95:423-429.
22. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia* 2018; 38:1-211.
23. Shaparin N, Gritsenko K, Shapiro D, et al. Timing of neuraxial pain interventions following blood patch for post dural puncture headache. *Pain Physician* 2014; 17:119-125.
24. Lucas S. Migraine and other headache disorders: ACOG Clinical Updates In Women's Health Care Primary and Preventive Care Review Summary Volume XVIII, Number 4. *Obstet Gynecol* 2019; 134:211.
25. Banks S, Paech M, Gurrin L. An audit of epidural blood patch after accidental dural puncture with a Tuohy needle in obstetric patients. *Int J Obstet Anesth* 2001; 10:172-176.
26. Zhang GM, Zhang W, Zhang GM. Age-specific reference intervals for PT, aPTT, fibrinogen and thrombin time for parturient women. *Thromb Haemost* 2019; 119:894-898.
27. Arevalo-Rodriguez I, Ciapponi A, Munoz L, Roque I, Figuls M. Posture and fluids for preventing post-dural puncture headache. *Cochrane Database Syst Rev* 2013; CD009199.
28. Masoudifar M, Aghadavoudi O, Adib S. Effect of venous dexamethasone, oral caffeine and acetaminophen on relative frequency and intensity of postdural puncture headache after spinal anesthesia. *Adv Biomed Res* 2016; 5:66.
29. Wu L, Chen S, Jiang X, Cheng Y, Zhang W. Opioids for the prevention of post-dural puncture headache in obstetrics: A systematic review and meta-analysis of efficacy and safety. *Pain Physician* 2021; 24:E1155-E1162.
30. Scavone BM, Wong CA, Sullivan JT, et al. Efficacy of a prophylactic epidural blood patch in preventing post dural puncture headache in parturients after inadvertent dural puncture. *Anesthesiology* 2004; 101:1422-1427.
31. Bradbury CL, Singh SI, Badder SR, Wakely LJ. Prevention of post-dural puncture headache in parturients: A systematic review and meta-analysis. *Acta Anaesthesiol Scand* 2013; 57:417-430.
32. Macones GA, Caughey AB, Wood SL, et al. Guidelines for postoperative care in cesarean delivery: Enhanced Recovery After Surgery (ERAS) Society recommendations (part 3). *Am J Obstet Gynecol* 2019; 221:247.e1-247.e9.
33. Vassal O, Baud MC, Bolandard F, et al. Epidural injection of hydroxyethyl starch in the management of postdural puncture headache. *Int J Obstet Anesth* 2013; 22:153-155.
34. Song LL, Zhou Y, Geng ZY. Epidural analgesia followed by epidural hydroxyethyl starch prevented post-dural puncture headache: Twenty case reports and a review of the literature. *World J Clin Cases* 2021; 9:1946-1952.
35. Vassal O, Del Carmine P, Beuriat PA, et al. Neurotoxicity of intrathecal 6% hydroxyethyl starch 130/0.4 injection in a rat model. *Anaesthesia* 2015; 70:1045-1051.
36. Vassal O, Del Carmine P, Desgranges FP, et al. Assessment of neurological toxicity of hydroxyethyl starch 130/0.4 injected in the intrathecal space in rats. *Pain Med* 2018; 19:2016-2020.
37. Martinez B, Canser E, Alonso A, et al. Postdural puncture headache and epidural blood patch in a large obstetric anaesthesia population. *Asian J Anesthesiol* 2018; 56:23-32.
38. Ranganathan P, Golfeiz C, Phelps AL, et al. Chronic headache and backache are long-term sequelae of unintentional dural puncture in the obstetric population. *J Clin Anesth* 2015; 27:201-206.
39. Hasoon J, Urits I, Burroughs M, et al. Epidural blood patch does not contribute to the development of chronic low back pain in patients who undergo lumbar punctures: A pilot study. *Psychopharmacol Bull* 2020; 50:17-24.
40. Binyamin Y, Heesen P, Orbach-Zinger S, et al. Chronic pain in parturients with an accidental dural puncture: A case-controlled prospective observational

study. *Acta Anaesthesiol Scand* 2021; 65:959-966.

41. Verduzco LA, Atlas SW, Riley ET. Subdural hematoma after an epidural blood patch. *Int J Obstet Anesth* 2012; 21:189-192.
42. Riley CA, Spiegel JE. Complications following large-volume epidural blood patches for postdural puncture headache. Lumbar subdural hematoma and arachnoiditis: Initial cause or final effect? *J Clin Anesth* 2009; 21:355-359.
43. Roy-Gash F, Engrand N, Lecarpentier E, Bonnet MP. Intrathecal hematoma and arachnoiditis mimicking bacterial meningitis after an epidural blood patch. *Int J Obstet Anesth* 2017; 32:77-81.
44. Paech MJ, Doherty DA, Christmas T, Wong CA. The volume of blood for epidural blood patch in obstetrics: A randomized, blinded clinical trial. *Anesth Analg* 2011; 113:126-133.
45. Sprigge JS, Harper SJ. Accidental dural puncture and post dural puncture headache in obstetric anaesthesia: Presentation and management: A 23-year survey in a district general hospital. *Anaesthesia* 2008; 63:36-43.
46. Al-Hashel J, Rady A, Massoud F, Ismail II. Post-dural puncture headache: A prospective study on incidence, risk factors, and clinical characterization of 285 consecutive procedures. *BMC Neurol* 2022; 22:261.