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**Epidural analgesia followed by epidural hydroxyethyl starch prevented post-dural puncture headache: Twenty case reports and a review of the literature**

Song LL *et al*. Epidural analgesia and HES prevented PDPH

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**Abstract**

BACKGROUND

Accidental dural puncture (ADP) and subsequent post-dural puncture headache (PDPH) remain common complications of epidural procedures for obstetric anesthesia and analgesia. No clear consensus exists on the best way to prevent PDPH after ADP.

CASE SUMMARY

We report our findings in twenty parturients who underwent an incorporated strategy of epidural analgesia followed by epidural hydroxyethyl starch (HES) to prevent PDPH after ADP with a 16-gauge Tuohy needle during epidural procedures. ADP with a 16-gauge Tuohy needle occurred in nine parturients undergoing a cesarean section (CS) and in eleven parturients receiving labor analgesia. An epidural catheter was re-sited at the same or adjacent intervertebral space in all patients. After CS, the epidural catheter was used for postoperative pain relief over a 48-h period. After delivery in eleven cases, epidural infusion was maintained for 24 h. Thereafter, 15 mL of 6% HES 130/0.4 was administered *via* the epidural catheter immediately prior to catheter removal. None of the parturients developed PDPH or neurologic deficits over a follow-up period of at least two months to up to one year postpartum.

CONCLUSION

An incorporated strategy of epidural analgesia followed by epidural hydroxyethyl starch may have great efficacy in preventing PDPH after ADP.

**Key Words:** Epidural analgesia; Hydroxyethyl starch; Accidental dural puncture; Post-dural puncture headache; Prophylaxis; Case report

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**Core Tip:** Accidental dural puncture (ADP) with a 16-gauge Tuohy needle occurred in nine parturients undergoing cesarean section (CS) and eleven parturients receiving labor analgesia. Through a re-sited epidural catheter, epidural analgesia was maintained at a rate of 4-5 mL/h over 48 h after CS or 24 h after labor. 15 mL of hydroxyethyl starch was administered *via* the epidural catheter prior to catheter removal. None of these parturients reported headache or any neurologic deficits postpartum. The incorporated strategy demonstrated great efficacy in preventing post-dural puncture headache after ADP in our case series.

**INTRODUCTION**

Accidental dural puncture (ADP) and subsequent post-dural puncture headache (PDPH) remain common complications of epidural procedures for obstetric anesthesia and analgesia. After ADP with a 16-gauge epidural needle, approximately 76%-85% of women may develop PDPH[1]. The headache can be extremely severe and can inhibit ambulation and the ability of a mother to care for herself or the newborn during the postpartum period. In addition, PDPH may substantially increase postpartum risks of severe morbidities including chronic headache, subdural hematoma, and cerebral thrombosis[2-5]. Expectant management of PDPH inevitably extends hospital length of stay. There is no universally established consensus on the most feasible way to prevent PDPH after ADP. We report our findings in twenty parturients who underwent an incorporated strategy of continuous epidural analgesia followed by epidural hydroxyethyl starch (HES) to prevent PDPH after ADP with a 16-gauge Tuohy needle during epidural procedures. The purpose of this study was to present our experience on the use of this incorporated prophylactic strategy for PDPH after ADP.

This retrospective study was conducted in the tertiary obstetric unit at Peking University First Hospital. From October 2019 to September 2020, a total of 5439 patients received epidural procedures during labor and delivery, of which 40 (0.74%) ADPs were reported. Among them, only 20 ADP parturients agreed to receive this incorporated prophylactic strategy. All parturients who had recognized ADPs during epidural procedures and received the incorporated prophylactic strategy were followed up by research personnel. We obtained written informed consent from the patients for the procedure and publication. Ethical approval for information retrieval was provided by the Ethical Committee of Peking University First Hospital, Beijing, China. Demographic data and clinical information of the patients in this case series are summarized in Table 1.

**CASE PRESENTATION**

***Chief complaints***

Nine parturients received elective or emergency cesarean sections (CS) under combined spinal-epidural anesthesia (CSEA). Eleven parturients were admitted for the induction of labor under epidural analgesia.

***History of present illness***

During CSEA for CS, a 16-gauge Tuohy needle (Tuoren, Henan, China) was advanced using the loss of resistance to saline technique at the L2-3 or L3-4 intervertebral space in the right decubitus position. ADP occurred during epidural needle placement. The epidural needle was withdrawn into the epidural space or re-sited at the adjacent intervertebral space. Four mL of plain bupivacaine 0.25% was administered *via* a 27-gauge Whitacre spinal needle to administer surgical anesthesia. Then, a 20-gauge epidural catheter was inserted 4 cm into the epidural space.

For labor epidural analgesia, epidural puncture was performed at the L2-3 or L3-4 intervertebral space with a 16-gauge Tuohy needle and ADP occurred. The epidural needle was withdrawn into the epidural space or re-sited at the adjacent intervertebral space. Pain relief during labor was achieved using a patient-controlled epidural analgesia (PCEA) device set to deliver a basal infusion of 0.07% ropivacaine and sufentanil 0.4 μg/mL at a basal rate of 4 mL/h (6 mL of bolus on demand and a lock-out interval of 30 min).

***History of past illness***

Prior to delivery, no patients reported existing headaches except for two patients with a history of migraine.

***Personal and family history***

No significant personal and family histories were noted.

***Physical examination***

Prior to delivery, the patients were alert and quickly responsive to commands. Clinical neurological examination revealed no significant results.

***Laboratory examinations***

Prior to the epidural procedure, coagulopathy was excluded with acceptable routine blood tests, biochemical tests, and coagulation parameter results in these patients.

***Imaging examinations***

No imaging examinations were available.

**FINAL DIAGNOSIS**

The final diagnosis of the presented case series was ADP with a large-bore epidural needle.

**TREATMENT**

After CS, a detailed explanation of the possibility of PDPH and its possible consequences were provided to the patients. These nine patients refused analgesics and prophylactic epidural blood patch (EBP) but agreed to the administration of epidural HES. No conservative strategies including bed rest, hydration, oral analgesics and caffeine were used. The epidural catheter was connected to a PCEA device postoperatively, which was set to deliver a continuous infusion of ropivacaine 0.1% and sufentanil 0.4 μg/mL at a rate of 5 mL/h. The patient was freely ambulated. The epidural catheter was left *in situ* for 48 h postoperatively according to the department’s routine. Immediately before removal of the catheter, 15 mL of 6% HES 130/0.4 (Voluven®, Fresenius Kabi, China) was slowly administered *via* the epidural catheter.

After vaginal delivery, epidural infusion was maintained using the same PCEA device at a basal rate of 4 mL/h for 24 h. Thereafter, 15 mL of voluven was slowly administered into the epidural space immediately prior to catheter withdrawal.

**OUTCOME AND FOLLOW-UP**

These patients were assessed daily by research personnel while in the hospital. Headache was assessed on a numeric rating scale ranging from 0 to 10, where 0 represents no pain and 10 represents the worst pain imaginable. After discharge, telephone follow-up was carried out one week later to ensure the absence of headache symptoms. Patients were instructed to contact the obstetric unit if headache or any neurologic deficits developed postpartum. PDPH and neurologic deficits (nuchal rigidity, mental status change, motor deficit, paresthesia) were not reported during the patients’ stay in the hospital. They were discharged as per the obstetric routine. They remained free of headache and neurologic symptoms for at least two months to up to one year.

**DISCUSSION**

We report that an incorporated strategy of continuous epidural analgesia at a rate of 4-5 mL/h (over 24 h after labor or 48 h after CS) followed by 15 mL of epidural HES successfully prevented PDPH after ADP with a 16-gauge Tuohy needle in twenty parturients. In October 2019, it was first observed that an ADP parturient remained free of PDPH following this incorporated prophylactic strategy. In this case series, this strategy had a 100% success rate in preventing PDPH after ADP, compared with a success rate of approximately 50%-75% reported in the existing literature for various other prophylactic strategies[6-8]. The excellent efficacy of our incorporated strategy might be attributed to the presence of the epidural catheter in the epidural space for the duration of 24-48 h, which may have promoted spontaneous healing in some way. The healing process was further facilitated by epidural HES following epidural infusion. Further prospective studies will be conducted at our hospital to establish the validity and reliability of the results obtained.

Various prophylactic interventions after ADP have been evaluated during obstetric procedures. The existing literature yielded no evidence to support the benefit of conservative management strategies including bed rest, oral/intravenous hydration, and analgesics for preventing PDPH after ADP[9,10]. Medications, including caffeine, gabapentin, cosyntropin, and theophylline showed some prophylactic benefit; however, there is still a lack of reliable evidence to support these benefits[11-13]. Epidural/intrathecal infusion of saline or morphine after ADP may decrease the risk of developing PDPH with various success rates, or at least alleviate the severity[14-18].Prophylactic EBP has been attempted with conflicting results. Two systemic reviews failed to show a significant reduction in PDPH after ADP with regard to prophylactic EBP[6,7]. Furthermore, EBP is an invasive intervention with minor symptoms (transient back and radicular pain) and potentially severe complications (chemical/infectious meningitis, arachnoiditis, and paralysis)[19,20]. Conflicting outcomes were also obtained in retrospective and observational studies involving the efficacy of intrathecal catheterization in preventing PDPH[6,8,21-23]. Recent meta-analyses demonstrated that there was no difference in the incidence of PDPH between spinal catheters and re-sited epidural catheters following ADP in parturients[8,24].

Re-siting an epidural catheter with continuous infusion of local anesthetic/saline after ADP has been proposed to provide effective PDPH prophylaxis with comparable benefits to intrathecal catheter placement, although some studies failed to demonstrate this[6,14,16,25,26]. The most likely mechanism seems that continuous epidural infusion reduces the pressure gradient between the epidural and subarachnoid spaces and the subsequent persistent CSF leakage. In our case series, twenty patients showed no symptoms of PDPH over the 24-48 h period of epidural analgesia before the administration of HES. However, its prophylactic benefit for PDPH *via* epidural infusion for the duration of 24-48 h only lasts for a short time after catheter removal, and some ADP parturients developed a PDPH several hours after catheter removal (noted in our clinical practice).

Several case reports have suggested that epidural injection of HES relieved PDPH resistant to conservative management[27,28]. Epidural HES could be used as an alternative to EBP for treating PDPH when EBP is contraindicated, such as systemic infection and metastatic diseases. It is thought that colloids result in increased epidural pressure and decreased CSF leakage. A colloid could be more efficient than epidural saline in preventing PDPH due to its high molecular weight and increased viscosity, which might delay its removal from the epidural space and prolong the duration to seal the defect. The superiority of colloids to EBP might be because they are non-invasive and easy to administer, and presumably have no severe risks of epidural/intrathecal hematoma, meningitis, and arachnoiditis. Earlier HES (within the first 24 h after ADP) might be less effective as HES may degrade or migrate and lose the “tamponade” effect prior to spontaneous repair of the body to close the defect. No neurologic deficits associated with epidural HES injection were observed during the follow-up period of at least two months to up to one year in this case series. In a study evaluating epidural volume extension using colloid in combined spinal-epidural anesthesia for CS, 33 pregnant patients received epidural 6% HES 200/0.5 and did not report any neurologic deficits postoperatively[29]. Two recent rat studies indicated that single or repeated intrathecal injection of HES did not induce any clinical or histopathological evidence of long-term neuronal toxicity[30,31].The CHEST trial, which included 7000 intensive care unit patients demonstrated that HES for intravenous fluid resuscitation is associated with increased renal replacement therapy and blood product use when compared with 0.9% saline[32]. It is suggested that HES, especially high molecular weight HES, has the potential to cause nephrotoxicity, impaired coagulation, and prolonged retention in the reticuloendothelial system[33]. The safety of the off-label use of HES administered epidurally should be investigated further.

The case series examined in this report was from a single center, which limits the generalizability of the obtained results to a broader circumstance. Furthermore, there is a high chance of selection bias inherent in observational retrospective studies of this nature, given that the decision to employ this incorporated prophylactic strategy is made by parturients themselves. Prospective studies are necessary to establish the causality between our incorporated prophylactic strategy and PDPH outcomes.

**CONCLUSION**

This case series of twenty parturients described an incorporated strategy that might have great efficacy in preventing PDPH after ADP with a 16-gauge Tuohy needle. The strategy involved continuous epidural analgesia over 24 h after labor or 48 h after CS followed by epidural HES prior to catheter removal. However, the safety and efficacy of this strategy should be further investigated in subsequent clinical studies.

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**Footnotes**

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**Table 1 Demographic data and clinical information**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient No.** | **Age (yr)** | **Pre-eclampsia** | **History of migraine** | **Nulliparous** | **BMI (kg/m2)** | **Mode of delivery** | **Anesthesia for delivery** |
| 1 | 38 | N | N | Y | 24.2 | CS | CSEA |
| 2 | 33 | N | N | N | 29.3 | NVD | EA |
| 3 | 31 | N | N | Y | 28.4 | CS | CSEA |
| 4 | 30 | N | N | Y | 27.7 | NVD | EA |
| 5 | 28 | N | N | N | 24.7 | NVD | EA |
| 6 | 30 | N | N | Y | 24.0 | NVD | EA |
| 7 | 38 | N | N | N | 28.8 | NVD | EA |
| 8 | 27 | N | Y | Y | 27.2 | CS | CSEA |
| 9 | 31 | N | N | Y | 25.7 | CS | CSEA |
| 10 | 31 | Y | N | Y | 33.3 | IVD | EA |
| 11 | 30 | N | N | Y | 31.6 | CS | CSEA |
| 12 | 31 | N | N | N | 26.7 | IVD | EA |
| 13 | 34 | N | N | Y | 31.3 | CS | CSEA |
| 14 | 35 | N | N | N | 24.7 | IVD | EA |
| 15 | 30 | N | N | Y | 21.3 | NVD | EA |
| 16 | 41 | N | Y | N | 23.4 | CS | CSEA |
| 17 | 35 | N | N | Y | 26.1 | CS | CSEA |
| 18 | 27 | N | N | Y | 26.2 | NVD | EA |
| 19 | 32 | N | N | N | 25.5 | NVD | EA |
| 20 | 39 | Y | N | Y | 30.5 | CS | CSEA |

N: No; Y: Yes; NVD: Normal vaginal delivery; IVD: Instrumental vaginal delivery; CS: Cesarean section; CSEA: Combined spinal-epidural anesthesia; EA: Epidural analgesia.