Epidural injection of hydroxyethyl starch in the management of postdural puncture headache

O. Vassal,¹ M.C. Baud,² F. Bolandard,³ M. Bonnin,³ E. Vielle,¹ J.E. Bazin,³ D. Chassard⁴
¹ Département Anesthésie Réanimation, Hôpital Mère enfant, Bron, ² Département Anesthésie Réanimation, Hôpital Gabriel Montpied, Clermont-Ferrand, ³ Département Anesthésie Réanimation, Hôpital D’Estaing, Clermont-Ferrand, France

ABSTRACT
Epidural blood patch is the standard treatment for postdural puncture headache when symptomatic therapy is ineffective. We report the cases of two patients who received an epidural injection of hydroxyethyl starch when an epidural blood patch was contraindicated; one due to Streptococcus agalactiae bacteraemia and one due to acute leukaemia. Relief of headache was achieved in both patients with no adverse effects. The use of an epidural hydroxyethyl starch injection may be a suitable alternative for treatment of postdural puncture headache if epidural blood patch is contraindicated.

Introduction
Epidural blood patch (EBP) is considered the gold standard treatment for postdural puncture headache (PDPH).¹ ² However, contraindications to the injection of autologous blood into the epidural space, which may include infective and metastatic sequelae, must be considered. We report the cases of two patients with PDPH resistant to conservative management who received epidural hydroxyethyl starch (HES) for treatment.

Case 1
A healthy 37-year-old G2P0 woman was admitted in spontaneous labour at 41 weeks of gestation. There was no contraindication to epidural analgesia. The epidural space was identified in the sitting position at L2–3 using a loss-of-resistance to saline technique with an 18-gauge Tuohy needle (Portex®, Smith Medical, Hythe, Kent, UK) at 3 cm from the skin. An epidural multihole catheter was advanced uneventfully 4 cm into the epidural space. Patient-controlled epidural analgesia (PCEA) was used to good effect throughout labour. Instrumental vaginal delivery occurred after a 9-h labour and the epidural catheter was removed 2 h after delivery. Maternal hyperthermia (39°C) was noted at the end of labour; C-reactive protein was 29 IU/L.

The following day, the patient complained of an occipital headache and neck ache that disappeared when lying supine. Neurological examination was normal, with no nuchal rigidity, mental status change or fever. Maternal blood cultures, placental bacteriology and genital culture as well as neonatal gastric liquid, umbilical, meconium and vernix cultures grew Streptococcus agalactiae B. Intravenous amoxicillin 1 g with clavulanic acid 200 mg was started 8-hourly. Conservative management of PDPH, with oral hydration, acetaminophen 1 g 6-hourly, ketoprofen 50 mg 6-hourly and caffeine 30 mg daily was started. Headache, without fever, nuchal rigidity or mental status change, persisted for three days. In view of meningal irritation, non-contrast cerebral magnetic resonance imaging (MRI) was performed, which was normal.

On the fourth postnatal day, in view of ineffective medical treatment for PDPH, the presence of treated bacteraemia and maternal difficulty in caring for her baby, an epidural injection of 30-mL 130000 Daltons hydroxyethyl starch (HES) (Voluven®, Fresenius Kabi Laboratories, France) was offered. Written, informed patient consent was obtained. Epidural injection was performed at L4–5, following which PDPH disappeared immediately. The patient remained supine for 2 h. The next day, PDPH of lower intensity returned, and maternal bonding with the baby was again compromised. Another HES patch was performed at the same lumbar interspace. After injection of 25 mL the patient reported lumbar discomfort. Again this was followed by complete resolution of headache. The patient was discharged home on day seven with oral antibiotics continued for two weeks. Telephone follow-up three weeks later confirmed that PDPH had not recurred and there were no neurologic sequelae. The patient presented two years later for a second pregnancy and was free of neurologic symptoms.
Case 2

A 28-year-old non-pregnant patient with a three-month history of acute leukaemia was scheduled for ovarian preservation surgery. She had undergone three lumbar punctures with a 22-gauge needle, the first two of which were associated with headache and were treated with intravenous acetaminophen. After the third lumbar puncture, a frontal, parietal and occipital headache occurred daily. PDPH management with oral hydration, acetaminophen, opioids, caffeine and intravenous corticosteroids was started, but painful symptoms persisted for three weeks. There was no fever, nuchal rigidity, mental status change or motor deficit. MRI of the brain excluded cerebral thrombophlebitis, toxic leucoencephalopathy or intrathecal methotrexate toxicity.

Ovarian surgery was performed laparoscopically under general anaesthesia. The headache disappeared immediately after surgery but recurred a few hours later and became disabling on the second postoperative day. An EBP was planned using HES, since injection of autologous blood was contraindicated in the context of acute leukaemia. Following informed, written consent, epidural cannulation was performed in the sitting position at L4–5 using a loss-of-resistance to saline technique with an 18-gauge Tuohy needle. An epidural multi-hole catheter (Perifix®, Braun, Melsungen, Germany) was advanced 3 cm into the epidural space without difficulty or pain. A 3-mL test dose of 2% lidocaine with adrenaline was injected. A slow injection of Voluven® was given until the patient complained of pressure in her lower back, when PDPH disappeared suddenly. This occurred after 15 mL total. A continuous infusion of Voluven® at 5 mL/h was given and the patient remained supine for 3 h. She continued to be pain-free and the epidural catheter was removed after 24 h due to a sensation of lumbar pressure. The patient was discharged to the oncology hospital 4 h later. The headache did not recur. At telephone follow-up 15 days later, she was free of neurologic symptoms. Three months later, while receiving continuing treatment for leukaemia, she developed pneumonia and died.

Discussion

To our knowledge, this is the first report of using epidural injection of HES for treatment of PDPH. Initial medical treatment for both patients consisted of analgesia, hydration and oral caffeine. HES epidural injection was considered only after failure of medical management. The mechanism of action is unclear. A liquid injected into the epidural space may exert a tamponade effect that relieves PDPH. We hypothesized that HES could be used to treat PDPH because its high molecular weight and viscosity might delay removal from the epidural space. However, the duration of pressure increase has been shown to be < 10 min with single injection of epidural saline or HES, while continuous infusions may cause sustained increases in epidural pressure.3

In clinical practice, a second blood patch may be required. In Case 1, a second patch was performed due to temporary relief from the first. The second epidural injection of 25-mL HES relieved the headache. In Case 2, a slow epidural HES infusion was used following the initial bolus.

Streptococcal sepsis and leukaemia are considered contraindications to an EBP. Alternatives to blood have been suggested. The use of percutaneous fibrin glue is anecdotal.4 The use of allogeneic blood is more convincing; one septic patient was successfully treated with allogeneic blood donated by his wife,5 and one woman in the postpartum period was treated with blood from an unrelated friend.6 Autologous blood for an EBP must be cross-matched immediately before use.

Primary intracranial hypotension with severe cognitive dysfunction has been successfully treated by continuous saline infusion rate of 20–30 mL/h,7 and several case reports describe the success of epidural saline to relieve PDPH.8–10 Kakinohana et al reported that a 15-mL saline bolus injection followed by a continuous infusion at a rate of 20 mL/h over 3 h relieved PDPH in 75% of patients, but the technique had a lower success rate than EBP.9 Epidural saline injection to prevent PDPH has also been evaluated in a group of 15 patients with acute lymphoblastic leukaemia.10 Headaches were significantly more common in the group without epidural saline than in the epidural saline group (48.8% vs. 16.4%, P < 0.001). An anaesthesiologist’s survey of the treatment of PDPH reported that epidural saline boluses or infusions were used infrequently, but considered an option by 32% of respondents.11 Comparative trials with EBP have not demonstrated the long-term efficacy of an epidural saline patch.12

Epidural injection of Dextran-40 has previously been reported. Spontaneous intracranial hypotension in a pregnant woman has been successfully treated with epidural Dextran-40,13 and has also been used in 56 adult patients who developed post-lumbar puncture headache. In another study, relief of headache was accomplished in all patients with epidural bolus injection of Dextran-40 using a mean volume of 20 mL.14 Aldrete used a bolus of Dextran-40 20 mL, followed by a continuous infusion of 3 mL/h over 12 h, in 13 patients suffering from PDPH after spinal or epidural anaesthesia. In all patients the headache disappeared within 20 h of initiating therapy.15 Reynvoet et al. reported the case of a patient with two consecutive EBP for PDPH which were ineffective, in whom epidural injection of Dextran-40 was successful.16 Previous studies using an epidural Dextran-40 patch have not reported neurologic damage.17–19 A study of 66 patients treated by epidural injection of Dextran-40 showed that 3.5% had a burning sensation during the
injection and 7.1% dysaesthesia at the injection point.14
These were not observed in our two patients.

Dextran-40 solutions are not available in all countries due to the risk of allergic reaction. The use of epidural HES to treat PDPH has not yet been reported, and the safety of the technique is under investigation. Our University Hospital Ethics Committee approved the use of HES for epidural patch only for the two patients in this case report.

A review on the SOAP website indicates that gelatins are an alternative to blood for epidural patching despite being unlicensed for this use.19 A single intrathecal HES injection in piglets produced no histopathological changes after 10 h.20 A recent study involving 99 pregnant patients showed that HES can be used for epidural volume extension in combined spinal–epidural technique anaesthesia for caesarean delivery.21 However, safety concerns still exist with epidural HES. Colloids have been viewed as a class of interchangeable fluids but differences in the physical properties, pharmacokinetics and safety profile exist amongst this class. Although no short-term side effects of epidural HES have been reported, long-term adverse effects cannot be excluded. The follow-up of the patient in this case report were two years and three months respectively; no side effects attributable to the use of epidural HES were reported.

In summary, epidural HES was used as an alternative to blood for treating PDPH resistant to medical treatment, and gave relief of headache with no immediate adverse effects. However, the technique should be reserved for situations when epidural blood injection is contraindicated. Further experimental and clinical studies demonstrating the lack of long-term neurologic toxicity of epidural HES are warranted.

References