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Research Article

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Epidural Blood Patch as a Treatment Intervention in Post-Dural Puncture Headache: A Systematic Review of Randomised-Controlled Trials

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Abstract

Background: *Post-dural puncture headache (PDPH) is a significant complication of interventions that deliberately or inadvertently involve perforation of the dura mater, which results in persistent cerebrospinal fluid (CSF) leak. If not promptly recognised or treated, it may be complicated by cranial nerve palsies, seizures and subdural haemorrhage. Epidural blood patch (EDBP) injection has been a widely used treatment in PDPH that remains refractory to conservative treatment (fluid replacement, analgesia and caffeine). The aim of this article is to systematically review the evidence underpinning EDBP in the treatment of established PDPH.*

Methods: *We searched PubMed, EMBASE and Medline databases for original Randomised-Controlled Trials (RCTs) that compared EDBP with conventional, sham or no treatment, in adult patients with established PDPH independent of aetiology.*

Results: *Three RCTs (n=84) met the inclusion criteria in this systematic review. These encompassed a total of 41 patients managed with EDBP versus 43 patients treated with conventional or sham treatments. All three RCTs individually showed superior therapeutic effects of EDBP over conventional or sham treatment in alleviating headache in PDPH.*

Conclusions: *Although this review supports the therapeutic efficacy of EDBP, which is consistent with observational studies, long-held expert opinion and trials that have outlined the prophylactic benefits of this procedure in preventing PDPH, the data identified is surprisingly limited. Further well-powered multi-centre RCTs, recruiting greater patient numbers, are required in order to enable definitive conclusions to be drawn on the therapeutic benefits of EDBP in the treatment of established PDPH.*

Keywords: Post-Dural Puncture Headache, Epidural Blood Patch, Dura Mater, Cerebrospinal Fluid.

Introduction

Post-dural puncture headache (PDPH) is defined as headache occurring within 5 days of a lumbar puncture and is caused by cerebrospinal fluid (CSF) leakage through a dural perforation, resulting in a low intracranial CSF pressure state [1]. The location, character and intensity of the headache can be highly variable and it may be associated with nausea, photophobia, hypoacusia, tinnitus and/or neck pain [1]. Aside from the temporal relationship with the index diagnostic or therapeutic spinal intervention, a key discerning clinical feature that helps differentiate PDPH from other headache syndromes is the postural nature of the pain - headache that is significantly exacerbated shortly after sitting or standing upright and relieved on lying flat is suggestive of PDPH [1,2].

Although the precise mechanisms underpinning the generation of pain in PDPH is unclear, two explanations have traditionally been proposed. The first is that the lowering of CSF pressures, as a consequence of leakage through the dural puncture, causes basal intracranial structures to sag caudally, which leads to traction and activation of pain-sensitive dural structures when in the upright posture [3, 4]. The second is predicated on the Monro-Kellie doctrine, which states that the total volume of brain parenchyma, CSF and blood within the cranium remains constant [3]. Thus, a fall in CSF pressure and volume must be accompanied by a compensatory, concomitant rise in cerebral blood flow and volume. The subsequent cerebral vaso- and veno-dilatation would therefore be responsible for the headache in PDPH [5].

PDPH occurs in nearly one-third of patients after lumbar puncture with symptoms typically lasting several days, but can be more protracted [6]. In the latter cases, PDPH can carry significant patient morbidity, rendering patients immobile and unable to work [7]. Although the majority of PDPH cases would be expected to

spontaneously resolve within 7 days, up to 28% can persist for longer durations, which necessitates active intervention [3, 8-10]. If not promptly treated, cases can be complicated by cranial nerve palsies, seizures and subdural haematoma, which can be catastrophic [11-13].

Conservative treatment measures of PDPH commonly utilised in clinical practice include encouragement of oral hydration, which may be supplemented by intravenous fluids, analgesia (e.g. non-steroidal anti-inflammatories, NSAIDs) and caffeine. If these measures fail, epidural blood patch (EDBP), which involves injection of autologous blood into the epidural space, is employed. This is thought to create a fibrin-rich clot that helps seal the site of dural perforation in order to prevent further CSF leakage, although other theories have also been proposed [14]. The aim of this article is to systematically review the evidence underpinning the role of EDBP intervention in patients with PDPH.

Methods

We performed a literature search in PubMed, EMBASE and Medline databases for original Randomised-Controlled Trials (RCTs) that compared EDBP intervention with conservative treatment, placebo or no treatment in adult patients with PDPH regardless of aetiology. Articles were excluded if they were not RCTs, used EDBP as prophylactic therapy (at the same time as dural puncture), used EDBP as a control group for comparison with an alternative intervention under investigation or if they were not published in the English language. The following search terms were used: epidural blood patch and post-dural puncture headache.

The following trial data were extracted: total number of patients recruited (n), patient demographics (including age and sex), nature of intervention (EDBP compared with control interventions such as conservative or no treatment), primary and secondary outcome measures (changes in duration and severity of headache within specified time periods following intervention) and study conclusions.

Results

Three RCTs were identified that met the inclusion criteria (see figure 1) [15-17]. Table 1 illustrates the aetiologies of PDPH for the respective trials. This included diagnostic lumbar puncture, spinal anaesthesia or inadvertent dural puncture during epidural anaesthesia.

A total of 41 patients were treated with EDBP, compared with sham (n=6) or conservative treatment (n=37). Sham treatment involved venesection and local anaesthesia of lumbar skin but no epidural blood injection whereas conservative treatment involved fluid replacement, analgesia, bed rest and/or caffeine administration. EDBP typically involved injection of 10-20ml of autologous blood into the epidural space in patients with PDPH.

Each of the three RCTs demonstrated superiority of EDBP over sham or conservative intervention in the alleviation of headache in adult patients with PDPH (see Table 2).

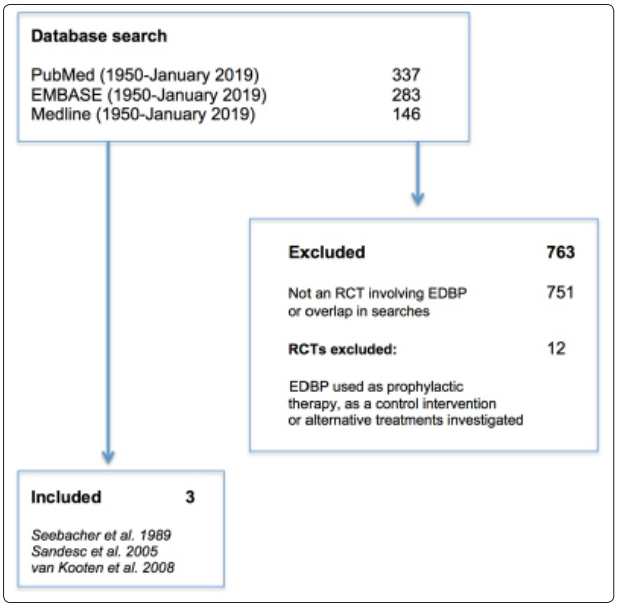

Figure 1: Literature search flow chart

Table 1: Aetiology of PDPH for each RCT

Study	Aetiology
Seebacher et al. 1989 [15].	Diagnostic lumbar puncture (n=2), spinal anaesthesia (n=3) or accidental puncture during epidural anaesthesia (n=7)
Sandesc et al. 2005 [16].	Diagnostic lumbar puncture (n=19), spinal anaesthesia (n=4) or accidental puncture during epidural (n=9)
van Kooten et al. 2008 [17].	Diagnostic lumbar puncture (n=40, after 2 excluded post-randomisation)

Table 2: Summary of results. Age is expressed as mean ± standard deviation in years and time in hours (h) unless otherwise specified. EDBP – epidural blood patch, PDPH – post-dural puncture headache, VAS- visual analogue scale (values expressed as mean ± standard deviation). All three RCTs demonstrated superiority of EDBP over conservative or sham intervention in the treatment of PDPH

Study	N	Headache	Intervention	Primary outcome measures	Secondary outcome measures	Results	Study conclusions
Seebacher et al. 1989 [15].	12 (2M, 10F)	PDPH lasting more than 4 days despite conservative treatment (lying flat, rehydration and analgesia)	**EDBP** (n=6, 1M, 5F, age range 21-68 in both groups) [10-20 ml autologous blood injected] **Sham** (n=6, 1M, 5F, age range 21-68 in both groups) [venesection, preparation and anaesthesia of lumbar skin but no epidural injection]	- Headache relief at 2h and 24h after intervention on the VAS (- headache relief at 15 days follow up in a subgroup analysis)	None specified	**Primary** -EDBP group: headache relief in 5 (83%) at 2h and 24h - Sham group: headache relief in 0 (0%) at 2h and 24h 1 patient in the EDBP group experienced headache relief after a second EDBP at 2h, 24hr and 15 days. All 6 patients in the sham group experienced relief (at 2h, 24h and 15 days follow up) following crossover to EDBP group.	EDBP was superior to sham treatment in treating PDPH
Sandesc et el. 2005 [16].	32 (9M, 23F)	PDPH lasting less than 24h	**EDBP** (n=16, 4M, 12F, mean age 35.1 ± 10) [15-20ml autologous blood injected] **Conservative** (n=16, 5M, 11F, mean age 34.5 ±14) [IV and PO fluids up to 3L daily, NSAIDs, IV caffeine 500mg every 6h]	-Headache severity 2h and 24h after intervention on the VAS	None specified	**Primary** -EDBP group:headache severity decreased from 8.0 ± 1.6 to 1.0 ± 0.18 at 2h, and to 0.7 ± 0.16 at 24h - Conservative group: headache severity was 8.2 ± 1.4 at baseline, 8.2 ± 1.4 at 2h and 7.8 ± 1.2 at 24h Comparison of both groups was statistically significant ($p<0.0001$ at 2h and 24h)	EDBP was superior to conservative treatment in reducing headache severity
van Kooten et al. 2008 [17].	42 (14M, 28F)	PDPH lasting 24h to 7 days	**EDBP** (n=19, 6M, 13F, mean age 36.9 ±10.5) [15-20ml autologous blood injected] **Conservative** (n=21, 8M, 13F, mean age 36.6 ±12.6, 2 refused) [bed rest for 24 h, fluid intake >2L +/- analgesia].	-Headache 24h after treatment	-Headache at 7 days (- Back pain and general well-being at 24h and 7 days)	**Primary** - Headache at 24h: 11(58%) in EDBP group versus 19 (90%) in conservative [RR 0.64, 95% CI 0.43-0.96] **Secondary** - Headache at day 7: 3 (16%) in EDBP group versus 18 (86%) in conservative [RR 0.18, 95% CI 0.06-0.53]	EDBP was superior to conservative treatment in reducing duration, severity and number of patients with headache.

Discussion

PDPH is an important and common complication of interventions that involve perforation of dura mater. This may occur following diagnostic procedures such as lumbar punctures and myelograms, or therapeutic procedures including spinal anaesthesia, administration of intrathecal chemotherapy or inadvertent perforation during epidural anaesthesia in obstetric patients. Risk factors for PDPH include needle size (risk increases from less than 1% with a 25-gauge needle, to 36% with a 20- or 22-gauge needle, to 75-80% with a 17-gauge epidural needle), young age (<60 years) and female gender [18]. Obstetric patients are thus particularly predisposed to PDPH. This is also due to the increased technical difficulty encountered when performing epidural anaesthesia due to the narrowed epidural space, which may require multiple attempts and also due to straining during delivery, which can lead to CSF leakage at the dural puncture orifice [16,19].

Failure of conservative treatment measures (fluid replacement, analgesia and intravenous or oral caffeine) of PDPH often calls for EDBP as a second-line intervention in clinical practice, with reported success rates as high as 90% [18]. Despite that EDBP is firmly established in clinical practice, rather surprisingly in this systematic review, only three RCTs were identified that compared EDBP with conservative or sham intervention in adult patients with PDPH. Although these RCTs recruited small sample sizes, all studies demonstrated superiority of EDBP over conventional or sham interventions, in reducing headache frequency, duration and/or severity. Multiple studies, which have also demonstrated the success of EDBP, but were not included in this review, have utilised EDBP as a prophylactic procedure before the clinical establishment of PDPH, which lends further evidence for its reported success [20,21]. This is also consistent with observational studies, which have highlighted the effectiveness of EDBP in PDPH [22-24].

A key drawback to the included trials, however, is the limited follow-up durations, which may potentially overestimate any benefits of EDBP, due to the well-known risk of recurrence of PDPH [25,26]. There are also no RCTs that have compared EDBP with epidural injection of alternative agents such as normal saline, so it's not clear from the reviewed evidence whether it is blood *per se* or any fluid

injected into the epidural space that exerts the therapeutic impact on PDPH. Although epidural injection of blood in patients with PDPH is conventionally believed to create a fibrin-rich plug that seals the dural puncture, this would not explain the often-immediate pain relief experienced by many patients [14]. An explanation for this phenomenon could be the mass-effect exerted by epidural injection, which boosts epidural and subarachnoid pressures, reduces epidural distensibility and shifts CSF in a cephalad direction, which helps reduce traction of pain-sensitive dura in PDPH [14,27].

Conclusion

In this systematic review, only three RCTs were identified that investigated the therapeutic effects of EDBP in patients with established PDPH, independent of aetiology. Although these RCTs recruited very small sample numbers, they all demonstrated superiority of EDBP over conventional or sham treatments. These results are consistent with long-held expert opinion, observational studies and in trials that have shown the prophylactic benefits of EDBP in preventing PDPH. However, the dearth of RCTs that met the inclusion criteria in this review is nonetheless an unexpected finding and precludes reliable conclusions to be drawn. Further well-powered multi-centre RCTs, recruiting greater patient numbers, are required to help justify the ongoing use of EDBP in the treatment of established PDPH, and to allow for further research into the therapeutic optimisation of this and related techniques.

Contributions

SE contributed to the literature search, drafted the initial manuscript and contributed to final revisions.
AS contributed to the literature search and to final revisions.
MME contributed to editing of the final manuscript.

References

1. Headache Classification Committee of the International Headache Society (2018) The International Classification of Headache Disorders. Cephalalgia 38: 1-21.
2. Kwak KH (2017) Postdural puncture headache. Korean J Anesthesiol 70: 136-143.
3. Turnbull DK, Shepherd DB (2003) Post-dural puncture headache: pathogenesis, prevention and treatment. Br J Anaesth 91: 718-729.
4. Morewood GH (1993) A rational approach to the cause, prevention and treatment of postdural puncture headache. CMAJ 149: 1087-1093.
5. Levine DN, Rapalino O (2001) The pathophysiology of lumbar puncture headache. J Neurol Sci 192: 1-8.
6. Evans RW, Armon C, Frohman EM, Goodin DS (2000) Assessment: prevention of post-lumbar puncture headaches: report of the therapeutics and technology assessment subcommittee of the american academy of neurology. Neurology 55: 909-914.
7. Ahmed SV, Jayawarna C, Jude E (2006) Post lumbar puncture headache: diagnosis and management. Postgrad Med J 82: 713-716.
8. Costigan SN, Sprigge JS (1996) Dural puncture: the patients' perspective. A patient survey of cases at a DGH maternity unit 1983-1993. ActaAnaesthesiol Scand 40: 710-714.
9. MacArthur C, Lewis M, Knox EG (1992) Accidental duralpuncture in obstetric patients and long term symptoms. BMJ 304: 1279-1282.
10. Vandam LD, Dripps RD (1956) Long-term follow up of patients who received 10 098 spinal anesthetics. JAMA 161: 586-591.
11. Hofer JE, Scavone BM (2015) Cranial nerve VI palsy after dural-arachnoid puncture. AnesthAnalg 120: 644-646.
12. Shearer VE, Jhaveri HS, Cunningham FG (1995) Puerperal seizures after post-dural puncture headache. Obstet Gynecol 85: 255-260.
13. Newrick P, Read D (1982) Subdural haematoma as a complication of spinal anaesthetic. Br Med J (Clin Res Ed) 285: 341-342.
14. Paech M (2005) Epidural blood patch – myths and legends. Can J Anesth 52: R1-R5.
15. Seebacher J, Ribeiro V, LeGuillou JL, Lacomblez L, Henry M, et al. (1989) Epidural blood patch in the treatment of post dural puncture headache: a double blind study. Headache 29: 630-632.
16. Sandesc D, Lupei MI, Sirbu C, Plavat C, Bedreag O, et al. (2005) Conventional treatment or epidural blood patch for the treatment of different etiologies of post dural puncture headache. ActaAnaesthesiol Belg 56: 265-269.
17. van Kooten F, Oedit R, Bakker SL, Dippel DW (2008) Epidural blood patch in post dural puncture headache: a randomised, observer-blind, controlled clinical trial. J NeurolNeurosurg Psychiatry 79: 553-558.
18. Tubben RE, Murphy PB (2018) Epidural Blood Patch – StatPearls. Treasure Island (FL): StatPearls Publishing; 2018 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482336/.
19. Lu IC, Huang SH, Hsu CD, Chiu CH, Wu SH (2011) Lumbar epidural space was narrower in parturients than that in nonpregnant women by ultrasound assessment. Kaohsiung J Med Sci 27: 20-24.
20. Stein MH, Cohen S, Mohiuddin MA, Dombrovskiy V, Lowernwirt I (2014) Prophylactic vs therapeutic blood patch for obstetric patients with accidental dural puncture – a randomised controlled trial. Anaesthesia 69: 320-326.
21. Trivedi NS, Eddi D, Shevde K (1993) Headache prevention following accidental dural puncture in obstetric patients. J ClinAnesth 5: 42-45.
22. Safa-Tisseront V, Thormann F, Malassiné P, Henry M, Riou B, Coriat P, Seebacher J (2001) Effectiveness of epidural blood patch in the management of post-dural puncture headache Anesthesiology 95: 334-339.
23. Vercauteren MP, Hoffmann V, Mertens E, Sermeus L, Adriaensen H (1999) Seven year review of requests for epidural blood patches for headache after dural puncture: referral patterns and effectiveness of blood patches. Eur J Anaesthesiol16: 298-303.
24. Williams E, Beaulieu P, Fawcett W, Jenkins J (1999) Efficacy of epidural blood patch in the obstetric population. International Journal of Obstetric Anaesthesia 8: 105-109.
25. Sidebotham D, Willoughby E, Schug SA (1997) Late recurrence of postdural puncture headache. RegAnesth. 22: 382-384.
26. Haller G, Loures V, Savoldelli GL (2011) Risk factors for recurrence of post-dural puncture headache following blood patch in obstetric patients: 11AP3-5. EJA 28: 162.
27. Harrington BE (2004) Postdural puncture headache and the development of the epidural blood patch. RegAnesth Pain Med 29: 136-163.