British Journal of Anaesthesia **105** (3): 255–63 (2010)
Advance Access publication 3 August 2010 · doi:10.1093/bja/aeq191

BJA

Prevention of postdural puncture headache after accidental dural puncture: a quantitative systematic review

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Key points

- PDPH occurs in >50% of cases of accidental dural puncture.
- Various treatments including intrathecal catheter, epidural saline or morphine, and prophylactic blood patch have been studied.
- All have shown some efficacy; no clear recommendation can be made.
- Large, multicentre randomized controlled trials are needed to identify best treatment option.

Summary. No clear consensus exists on how to best prevent severe headache from occurring after accidental dural puncture. We conducted a quantitative systematic review to identify all available evidence for the prevention of postdural puncture headache (PDPH) and included 17 studies with 1264 patients investigating prophylactic epidural blood patch (PEBP), epidural morphine, intrathecal catheters, and epidural or intrathecal saline. The relative risk (RR) for headache after PEBP was 0.48 [95% confidence interval (CI): 0.23–0.99] in five non-randomized controlled trials (non-RCTs) and 0.32 (0.10–1.03) in four randomized controlled trials (RCTs). The RR for epidural morphine (based on a single RCT) was 0.25 (0.08–0.78). All other interventions were based on non-RCTs and failed statistical significance, including long-term intrathecal catheters with an RR of 0.21 (0.02–2.65). There are a number of promising options to prevent PDPH, yet heterogeneity between the studies and publication bias towards small non-RCTs with positive results limits the available evidence. Thus, a large multicentre RCT is needed to determine the best preventative practices.

Keywords: accidental dural puncture; epidural morphine; intrathecal catheters; postdural puncture headache; prophylactic epidural blood patch

Postdural puncture headache (PDPH) can occur as a result of diagnostic lumbar puncture, spinal anaesthesia, and accidental dural puncture during epidural anaesthesia.[1] PDPH has the potential to cause significant morbidity in the obstetric patient. Depending on the severity of the headache, the mother may be unable to adequately care for her newborn or herself for quite some time. This condition can also prolong hospital stay for both mother and child and consequently contribute to an increase in the cost of health care in the maternity ward.[2]

Several surveys have assessed the rate of accidental dural puncture after epidural catheter placement and recorded frequencies varying from 0.19% to 3.6%.[3–6] Should accidental dural puncture occur, PDPH develops in more than 50% of these patients.[7] In a national census in the UK, about 6300 obstetric epidural blocks were performed over the course of 2 weeks, translating to ~161 550 obstetric epidural blocks annually.[8 9] For a lower end estimate, a 0.9% accidental puncture rate with 50% of those patients experiencing PDPH thus leads to about 800 cases of severe PDPH occurring per year in the UK alone.

Conservative measures such as hydration and bed rest have a history of not being very effective.[10 11] Therefore, numerous invasive strategies have instead been suggested to prevent PDPH. A recent survey of clinical practice in the UK showed that the most common invasive prophylactic measures used to minimize the risk of PDPH after accidental dural puncture were long-term intrathecal catheter placement (15%) and epidural saline bolus (13%). The UK survey also demonstrated that the least frequently utilized approach is a prophylactic blood patch (1–2%).[12] A survey of anaesthetists in the USA showed that 19% placed an intrathecal catheter, 12–25% used epidural saline, and 10–31% applied an epidural blood patch as a prophylactic measure.[13]

However, because results for these interventions have been mixed, there is no clear consensus as to which

prophylactic measure is the most effective. The fact that few institutions have a written protocol for managing accidental dural puncture is indicative of this uncertainty.[14] To facilitate this process, we performed a systematic review and meta-analysis of all available evidence for the prevention of PDPH in patients after accidental dural puncture to compare the efficacy of existing strategies in the hope of making an evidence-based recommendation to clinicians.

Methods

We performed a systematic search for studies examining the efficacy of preventative measures for PDPH after accidental dural puncture. We searched PubMed, EMBASE, Science Citation Index, and Cochrane Library databases without any language restrictions using the following free text and associated MeSH terms: (postdural puncture headache AND prevention) OR [dural puncture AND (accidental or inadvertent or unintentional)]. Clinicaltrials.gov was screened for any ongoing unpublished studies that may be relevant, and abstracts and proceedings of major anaesthesia conferences were electronically and hand-searched. References within all identified studies were hand-searched until no new references were found. The last electronic search was performed in January 2010, and when possible, searches included activated weekly e-mail alerts for potentially relevant newly published studies.

Articles were reviewed in full by two authors (A.S. and O.R.) for inclusion in the trial and quality of study design. Inclusion criteria were guided by the Cochrane Handbook for Systematic Reviews and were as follows: the focus study population was defined as patients receiving an epidural who had accidental dural puncture, and an invasive preventative measure must have been administered and the incidence of PDPH must have been reported in a dichotomous form.

Studies were excluded if there was no control group. Studies with intentional spinal punctures for diagnostic purpose were also excluded. Since most interventions for PDPH are conspicuous and sham procedures are rarely performed, blinding was not mandatory for studies to be included.

The primary outcome for our analysis was the incidence of PDPH, which was generally defined as headache occurring after dural puncture that may or may not be positional in its nature. A secondary outcome was the need for a therapeutic epidural blood patch as a surrogate outcome for the severity of headache.

The study results and data about the study design were extracted from each trial with the use of manufactured forms. If data or methodological details were absent, the first author was contacted. If after two attempts at contact no reply was given, the trials were only included if sufficient information was available. Studies were grouped whenever possible. For studies with more than one study group, only groups of relevance for this review were included.

Statistical analysis was performed using Cochrane Collaborations Review Manager 5 software [Review Manager (RevMan), Version 5.0.14, Copenhagen: the Nordic Cochrane Centre, The Cochrane Collaboration, 2008]. A random effects model was used for the calculation of relative risks (RRs), the ratio of the risk of PDPH in the group who received a prophylactic intervention compared with the control group. An RR below 1 indicates a potentially beneficial effect for the intervention. All estimates are given as RRs with 95% confidence intervals (CIs). When the 95% CI around the risk ratio did not include the number 1, we assumed a statistically significant difference between the preventative measure and the control.

For sensitivity analyses, we further explored the data for the prophylactic epidural blood patch (PEBP) by separating the included trials into randomized controlled trial (RCT) or non-randomized controlled trial (non-RCT). With the exception of epidural morphine (where there was one RCT), all other interventions were based on non-RCTs, so that a sensitivity analysis was not applicable here. In addition, we performed a funnel plot to visualize a potential source for publication bias.

Results

Twenty-nine studies met the inclusion criteria, but 12 were excluded for lack of a control group. A total of 17 studies, in particular 15 full papers and two abstracts, were included in our review (Table 1, Fig. 1A and B). These 17 studies fit into the following five intervention groupings: one with epidural morphine,[15] nine with PEBP,[16–24] three with epidural saline,[18 24 25] one with intrathecal saline,[26] and six with intrathecal catheter placement.[20 27–31] Three studies were used to gather data on more than one intervention, with each intervention being compared with the same control group.[18 20 24] In total, 1264 patients enrolled in 17 studies are considered in this analysis.

Epidural morphine

The utility of epidural morphine was investigated in only one RCT.[15] Epidural morphine 3 mg was given after the end of anaesthesia and another 3 mg was given on the following day. This reduced the incidence of PDPH from 48% (12/25) to 12% (3/25), which translates to a statistically significant reduction in the RR of 0.25 (0.08–0.78). There was no respiratory depression, but nausea was numerically more frequent in the morphine group (44% *vs* 16%, $P=0.06$).

Prophylactic epidural blood patch

In five non-RCTs, the use of a PEBP was associated with a significant reduction in PDPH, giving an RR of 0.48 (0.23–0.99, Fig. 1A).[16 18 20 22 24] However, pooled results of the other four randomized trials failed to show statistical significance with an RR of 0.32 (0.10–1.03), but there was significant heterogeneity in the study results ($P<0.001$, Fig. 1B).[17 19 21 23]

Overall, 5–20 ml of blood was used for the blood patch during the studies (Table 1, 'comment'). The four RCTs used 15–20 ml of blood for the blood patch,[17 19 21 23] while the

Table 1 Overview of studies. PDPH, postdural puncture headache; TEBP, therapeutic epidural blood patch; RCT, randomized controlled trial; ADP, accidental dural puncture

Reference	Procedure	Study Type	Intervention(s)	Outcomes	Comment
Brownridge[18] (*n*=58)	Labour and c-sections	Cohort study	PEBP. Epidural saline infusion or bolus	PDPH, TEBP	10–20 ml blood patch performed within 24 h in two patients. Epidural saline infusion (1.5–2 litre over 24 h) in 25 patients. Epidural saline bolus (40–60 ml) injected every 6 h for 24 h in 12 patients
Craft and colleagues[25] (*n*=33)	Labour	Non-RCT	Epidural saline	PDPH	Two 60 ml saline injections. First one administered immediately after delivery and the second one was administered the following morning. 16 G Tuohy needle was used
Trivedi and colleagues[24] (*n*=74)	Labour	Non-RCT	PEBP. Epidural saline	PDPH, TEBP	15 ml blood administered upon completion of the planned obstetric procedure. Saline patch of 40–60 ml administered upon completion of the planned obstetric procedure. 18 G Tuohy needle was used
Charsley and Abram[26] (*n*=43)	Labour and orthopaedics and pain	Non-RCT	Intrathecal saline	PDPH, TEBP	10 ml of intrathecal saline administered immediately after ADP. 17 G needle was used
Ayad and colleagues[27] (*n*=103)	Labour	Retrospective chart review	Short-term intrathecal catheter placement. Long-term intrathecal catheter placement	PDPH, TEBP	Catheter placed immediately after ADP and removed after delivery. Catheter placed immediately after ADP and left in place for 24 h after delivery. 18 G needle was used
Cohen and colleagues[28] (*n*=45)	C-sections	Retrospective chart review	Short-term intrathecal catheter placement. Long-term intrathecal catheter placement	PDPH, TEBP	Catheter placed immediately after ADP and removed after delivery. Catheter placed immediately after ADP and left in place for at least 24 h after delivery. 17 G needle was used
Kaul and colleagues[20] (*n*=334)	Labour	Retrospective chart review	PEBP. Long-term intrathecal catheterization (>24 h)	PDPH, TEBP	8–20 ml blood patch administered after the complete resolution of the sensory block and before the removal of the epidural catheter. Intrathecal catheter left *in situ* for 24 h
Norris and colleagues[29] (*n*=56)	Labour	Non-RCT	Short-term intrathecal catheter placement	PDPH, TEBP	Catheter placed immediately after ADP and left *in situ* for at least 2 h. 18 G needle was used with bevel oriented parallel to dura
Paech and colleagues[30] (*n*=75)	Labour and c-sections	Prospective audit	Short-term intrathecal catheter placement	PDPH, TEBP	Catheter placed immediately after ADP and removed after delivery. 16 and 18 G Tuohy needles were used
Rutter and colleagues[31] (*n*=71)	Labour	Retrospective chart review	Short-term intrathecal catheter placement	PDPH, TEBP	Inadequate documentation of the duration of catheterization. Needle gauge varied
Al-Metwalli[15] (*n*=50)	Labour	RCT	Epidural morphine	PDPH, TEBP	Two 3 mg morphine in 10 ml saline injections. First one administered after delivery and after resolution of analgesia and the second one administered 24 h later before removal of epidural catheter. 17 G needle was used
Ackerman and colleagues[16] (*n*=11)	Labour	Non-RCT	PEBP	PDPH, TEBP	15 ml of blood injected 15–20 min after delivery. 18 G Tuohy needle was used

Continued

Table 1 *Continued*

Reference	Procedure	Study Type	Intervention(s)	Outcomes	Comment
Ackerman and colleagues[17] (n=21)	Labour	RCT	PEBP	PDPH, TEBP	18–20 ml of blood administered immediately upon admission to recovery room after delivery. 18 G Tuohy needle was used.
Colonna-Romano and Shapiro[19] (n=39)	Labour and c-sections	RCT	PEBP	PDPH, TEBP	15 ml blood administered 2–14 h after ADP and always after delivery. 17 G Tuohy needle was used
Lowenwirt and colleagues[21] (n=49)	Labour and c-sections	RCT	PEBP	PDPH, TEBP	15–20 ml blood administered at least 5 h after the last dose of local anaesthetic. 16 or 17 G needle was used
Palahniuk and Cumming[22] (n=86)	Labour and c-sections	Cohort study	PEBP	PDPH, TEBP	5–10 ml blood administered after delivery. 16 G Tuohy needle was used
Scavone and colleagues[23] (n=64)	Labour and c-sections	RCT	PEBP	PDPH, TEBP	20 ml blood administered after resolution of analgesia/anaesthesia. 17 G needle was used. The trial was double-blinded since the patients in the control group were given a sham patch

volume of blood patch involved in the five non-RCTs varied from 5 to 20 ml.[16 18 20 22 24]

Intrathecal catheters

On the basis of a number of studies, threading the catheter through the dural hole and using it as an intrathecal catheter do not reduce the incidence of PDPH when removed on the same day (RR=0.88, 0.68–1.14).[27–29–31] Interestingly, two comparisons suggested a significant reduction in PDPH when the catheter was left in place for at least 24 h,[27 28] yet a much larger analysis[20] found no protective effect. This leads to a pooled RR for the development of PDPH that is no longer statistically significant (RR=0.21, 0.02–2.65). As in the epidural blood patch studies, the results are highly heterogeneous ($P<0.001$, Fig. 1A).

Saline

The RR from three studies investigating the use of epidural saline as a preventative measure against PDPH failed to reach statistical significance, with a value of 0.65 (0.40–1.05).[18 24 25] The one study exploring the intrathecal injection of 10 ml saline for the prevention of PDPH similarly failed to reach statistical significance (RR=0.51, 0.26–1.03).[26]

Pooled results for both non-RCTs and RCTs showed evidence for heterogeneity at $P<0.05$. In addition, skew of the funnel plot to the left of the line of unity (i.e. 1.0) suggests a publication bias towards small non-RCTs with positive results (Fig. 2). The RRs for our secondary outcome, the need for a therapeutic epidural blood patch, are shown in Table 2.

Discussion

The majority of interventions investigated showed at least some efficacy for the prevention of PDPH, but the immediate placement of an intrathecal catheter or the use of a PEBP before catheter removal demonstrated the best risk/benefit ratio. However, study results are heterogeneous, and there is strong evidence for a publication bias. Thus, no clinical recommendations for how to best avoid PDPH after accidental dural puncture can be made until the superiority of one preventative intervention over another has been unequivocally proven in a definitive multicentre RCT.

PDPH is described as a bilateral, non-throbbing pain, usually fronto-occipital, which is aggravated in the standing position and alleviated in the supine position.[32] It usually develops within 24 h, but emergence up to 7 days has also been described.[7] Accompanying symptoms may include nausea, vomiting, visual disturbances, and altered hearing.[1] The most likely cause of PDPH is cerebral venous dilation. It is assumed that dilation occurs due to a loss of cerebral spinal fluid (CSF) pressure as the CSF seeps through the dural tear caused by the large diameter epidural needle used to enter the epidural space. Although studies have examined interventions that could reduce the size of this tear in the event of dural puncture,[33–35] the focus of our

analysis was on tactics for preventing PDPH that are applied after accidental dural puncture occurs.

The use of *epidural morphine* has only been investigated in one RCT.[15] Although this result has the highest risk reduction of all interventions studied, the only other evidence supporting morphine as a prophylaxis for PDPH after accidental dural puncture comes from two case reports.[36 37] As a caveat, epidural morphine administration was associated with an increased incidence of nausea and itching; however, no respiratory depression was observed. Unfortunately, the study is too small to fully assess the risk/benefit ratio of this intervention. Epidural morphine may thus be a beneficial treatment option, but further studies are needed.

Of all the interventions, PEBP has been studied the most extensively, with nine studies included in our analysis.

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Study or subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk ratio M-H, Random, 95% CI
1.1.1 Epidural saline *vs* no saline						
Craft and colleagues[25]	2	16	13	17	2.6%	0.16 (0.04, 0.61)
Brownridge[18]	24	37	16	19	9.1%	0.77 (0.57, 1.05)
Trivedl and colleagues[24]	20	30	21	24	9.2%	0.76 (0.57, 1.02)
Subtotal (95% CI)		**83**		**60**	**21.0%**	**0.65 (0.40, 1.05)**
Total events	46		50			
Heterogeneity: τ^2=0.11; χ^2=7.12, df=2 (*P*=0.03); I^2=72%						
Test for overall effect: *Z*=1.75 (*P*=0.08)						
1.1.2 Intrathecal saline *vs* no intrathecal saline						
Charsley[26]	7	22	13	21	5.8%	0.51 (0.26, 1.03)
Subtotal (95% CI)		**22**		**21**	**5.8%**	**0.51 (0.26, 1.03)**
Total events	7		13			
Heterogeneity: Not applicable						
Test for overall effect: *Z*=1.87 (*P*=0.06)						
1.1.3 Short-term intrathecal catheter *vs* no catheter						
Cohen and colleagues[28]	8	17	5	15	4.6%	0.41 (0.59, 3.39)
Norris and Leighton[29]	19	35	11	21	7.3%	1.04 (0.62, 1.72)
Ayad and colleagues[27]	18	35	34	37	8.9%	0.56 (0.40, 0.78)
Rutter and colleagues[31]	24	34	30	37	9.4%	0.87 (0.67, 1.14)
Paech and colleagues[30]	21	24	44	51	10.0%	1.01 (0.84, 1.22)
Subtotal (95% CI)		**145**		**161**	**40.2%**	**0.88 (0.68, 1.14)**
Total events	90		124			
Heterogeneity: τ^2=0.05; χ^2=11.02, df=4 (*P*=0.03); I^2=64%						
Test for overall effect: *Z*=0.99 (*P*=0.32)						
1.1.4 Long-term intrathecal catheter *vs* no intrathecal catheter						
Cohen and colleagues[28]	0	13	5	15	0.7%	0.10 (0.01, 1.72)
Ayad and colleagues[27]	2	31	34	37	2.6%	0.07 (0.02, 0.27)
Kaul and colleagues[20]	30	60	84	162	9.2%	0.96 (0.72, 1.29)
Subtotal (95% CI)		**104**		**214**	**12.5%**	**0.21 (0.02, 2.65)**
Total events	32		123			
Heterogeneity: τ^2=4.23; χ^2=23.07, df=2 (*P*=0.00001); I^2=91%						
Test for overall effect: *Z*=1.20 (*P*=0.23)						
1.1.6 Prophyiactic epidural blood patch *vs* no blood patch						
Ackerman and Colclough[16]	0	6	5	5	0.8%	0.08 (0.01, 1.14)
Trivedi and colleagues[24]	1	20	21	24	1.4%	0.06 (0.01, 0.39)
Brownridge[18]	1	2	16	19	2.4%	0.59 (0.15, 2.41)
Palahniuk and Cumming[22]	6	11	44	75	6.8%	0.93 (0.52, 1.65)
Kaul and colleagues[20]	36	112	84	162	9.1%	0.62 (0.46, 0.84)
Subtotal (95% CI)		**151**		**285**	**20.5%**	**0.48 (0.23, 0.99)**
Total events	44		170			
Heterogeneity: τ^2=0.34; χ^2=12.19, df=4 (*P*=0.02); I^2=67%						
Test for overall effect: *Z*=1.99 (*P*=0.05)						
Total (95% CI)		**505**		**741**	**100.0%**	**0.68 (0.53, 0.87)**
Total events	219		480			
Heterogeneity: τ^2=0.15; χ^2=69.75, df=16 (*P*=0.00001); I^2=77%						
Test for overall effect: *Z*=3.09 (*P*=0.002)						

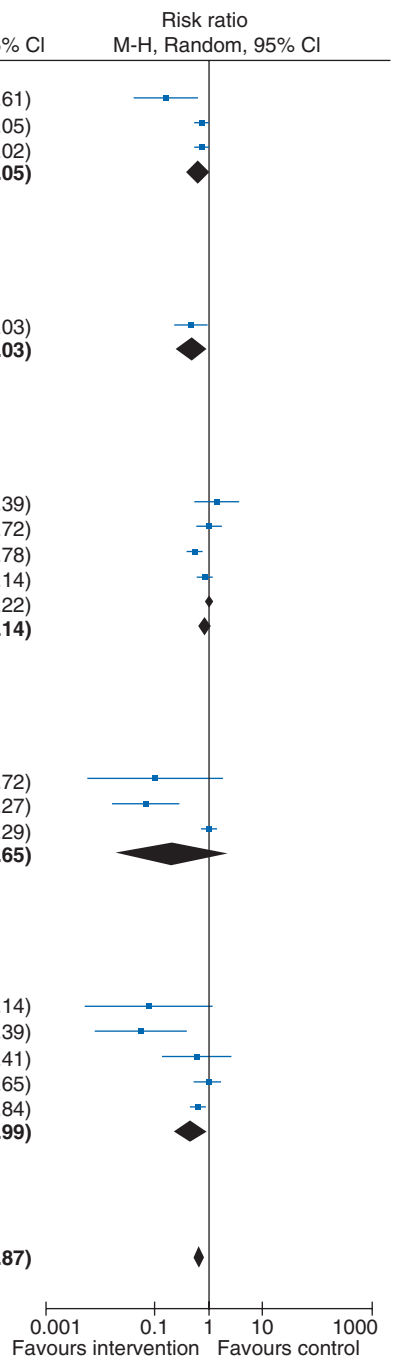
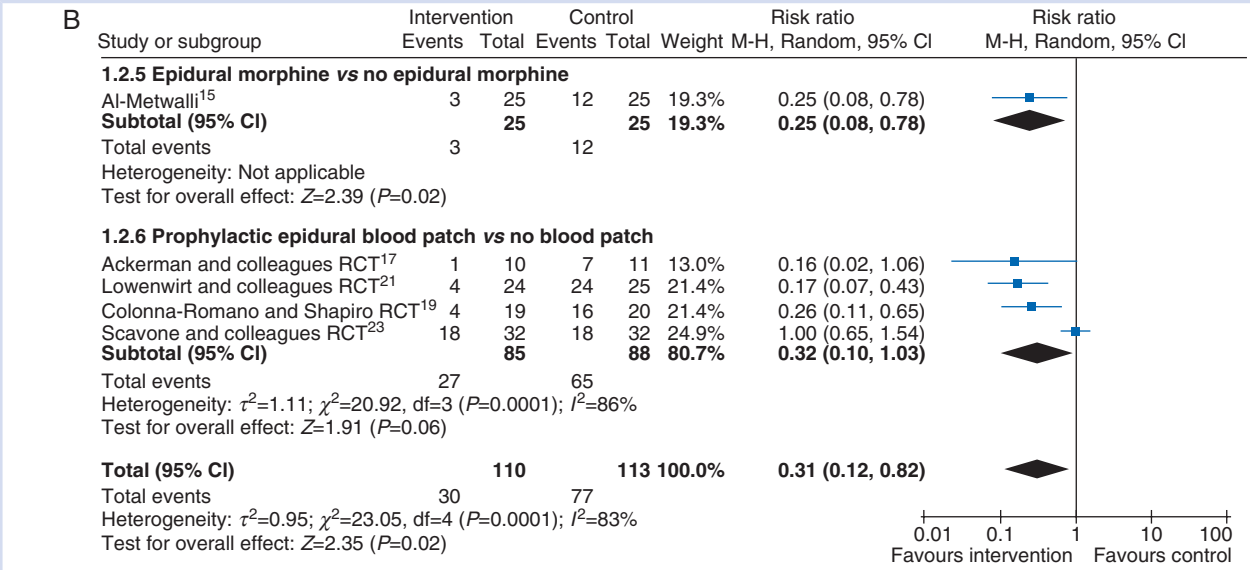


Fig 1 (A) PDPH non-RCT for headache; (B) PDPH RCT for headache.



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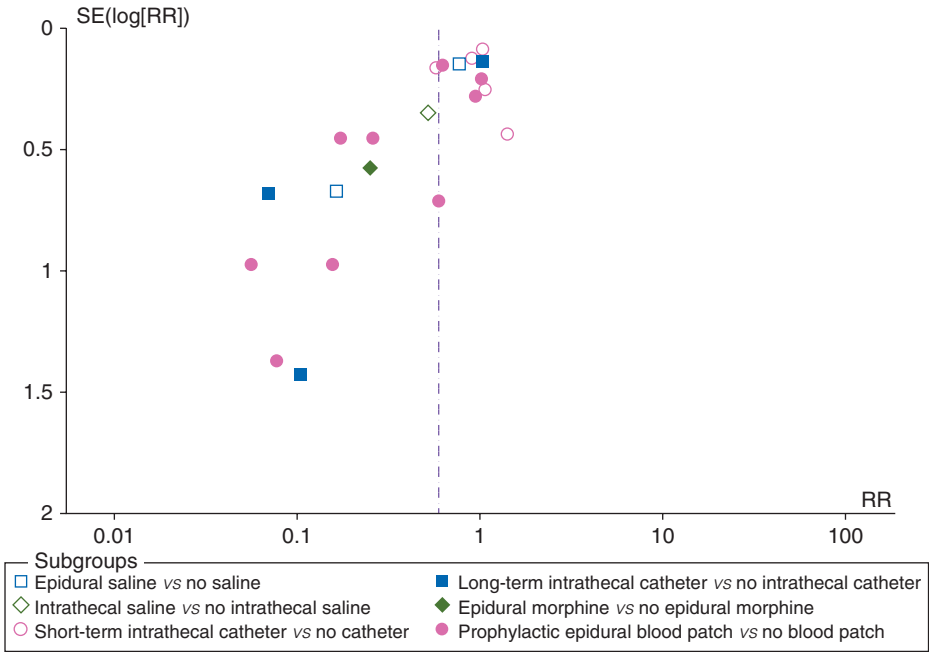

Fig 2 PDPH funnel plot of all prophylactic measures versus conservative treatment.

Volumes between 7.5 and 30 ml are commonly used in clinical practice to perform epidural blood patching, but 5–20 ml was used in the studies analysed here.[3] If all studies were taken together, the RR for PDPH after PEBP was 0.41 (0.24–0.71). At first glance, these findings support the proposed mechanism for the PEBP: that coagulation of the injected blood will clog the dural tear and stop the leakage of CSF. However, because efficacy results showed significant heterogeneity across the studies ($P<0.001$), we conducted a sensitivity analysis dependent on whether the studies were randomized or not. As a consequence, the pooled results from the non-RCTs remained statistically significant whereas those of the four RCTs were no longer statistically significant.[17 19 21] Interestingly, the first three RCTs showed a clear reduction in PDPH but had methodological limitations, while the largest and most thoroughly conducted trial found the same incidence

Table 2 RRs and 95% CIs (RR <1 favours the intervention whereas RR >1 favours the control group) for the primary outcome (PDPH) and secondary outcome (TEBP). PDPH, postdural puncture headache; TEBP, therapeutic epidural blood patch; CI, confidence intervals

Type of intervention	Study design	Outcome	RR (%) (95 CI)
Epidural saline	Non-randomized	PDPH	0.65 (0.40, 1.05)
		TEBP	0.72 (0.48, 1.06)
Intrathecal saline	Non-randomized	PDPH	0.51 (0.26, 1.03)
		TEBP	0.11 (0.01, 0.77)
Short-term intrathecal catheter	Non-randomized	PDPH	0.88 (0.68, 1.14)
		TEBP	0.58 (0.42, 0.80)
Long-term intrathecal catheter	Non-randomized	PDPH	0.21 (0.02, 2.65)
		TEBP	0.19 (0.02, 2.37)
Epidural morphine	Randomized	PDPH	0.25 (0.08, 0.78)
		TEBP	0.11 (0.01, 1.96)
PEBP	Randomized	PDPH	0.32 (0.10, 1.03)
		TEBP	0.33 (0.14, 0.78)
	Non-randomized	PDPH	0.48 (0.23, 0.99)
		TEBP	0.63 (0.28, 1.46)
	Overall	PDPH	0.41 (0.24, 0.71)
		TEBP	0.47 (0.26, 0.85)

of PDPH (18/32) in both the prophylactic and placebo groups.[23] In addition, a recently updated Cochrane Review of the epidural blood patch for preventing and treating PDPH also found conflicting results on the efficacy of the PEBP and concluded that there is insufficient evidence to recommend its use.[38] However, it should be noted that the Cochrane Review was not focused on the typically more severe and frequently occurring headache that develops after inadvertent epidural puncture with the large and sharp needles that are used for the placement of epidural catheters. As a result, it may have been the limited number of symptomatic patients and consequently low power that made it impossible to more confidently quantify the potential benefit of the PEBP.

The failure of a prophylactic blood patch to reduce PDPH appears consistent with a retrospective analysis from the late 1970s that described a 71% failure rate of a therapeutic blood patch when applied within 24 h after puncture, as opposed to only a 4% failure rate when applied later than 24 h.[39] With this in mind, a more recent paper is considered to provide additional evidence of an early blood patch leading to a higher failure rate.[40] However, while a delay in applying the therapeutic blood patch of <4 days was associated with a higher failure rate, the failure rate was only about 10% when given within the first 2 days. Moreover, taking failure and incomplete relief together, the failure rate was generally more than 30%, irrespective of the time of administration. Therefore, there is limited evidence that the efficacy of an epidural blood patch is markedly influenced by the timing of application.

There are several theories as to how *intrathecal catheters* can prevent PDPH. One hypothesis is that the large-bore intrathecal catheter plugs the dural tear, thereby lessening or stopping the CSF leak from the subarachnoid space and maintaining the intrathecal volume.[26 41] Another possibility was inspired by pathological findings in cats, which showed an inflammatory response within the spinal cord when a catheter was left in place for at least 5 days.[42] Together with the observation of a low incidence of PDPH after continuous spinal anaesthesia for an extended period of time, it was hypothesized that an inflammatory reaction in the dura surrounding the puncture site may facilitate sealing of the hole and prevent leakage of the CSF.[43] However, in one study, we analysed the catheters that remained in place for only 5 h, so it is unclear whether the low incidence can be explained by the inflammation theory or is better explained by the type of surgery. For instance, the mechanics of orthopaedic surgery are less likely to be associated with a leak of the CSF compared with expulsive efforts of a vaginal delivery in obstetrics.

The RR reduction of PDPH was not significant in the short-term catheter group, in which the catheter was left in place for <24 h and usually removed immediately after delivery. Two non-RCTs examining the effects of long-term catheters reported strong preventative effects, with one reporting a reduction of PDPH from more than 90% to <10% when the catheter was left in place for at least 24 h.[27] However, a subsequent analysis of a much larger data set was unable to detect any benefit, causing the pooled results of long-term catheters to fail statistical significance.[20] Given the heterogeneity of the study results, the long-term intrathecal catheter might still be a treatment option, beneficial to our patients. However, the direct or indirect evidence is insufficient to provide a strong recommendation.

The injection of *saline* solution into the epidural space is believed to temporarily equilibrate the pressure, which should minimize the leakage of CSF through the dural tear long enough for a fibrin seal to block the aperture.[44]

However, the pooled RR reduction from this intervention failed significance, with only a non-randomized study[25] having a statistically significant result. The other two studies[18 24] failed to produce significant findings. A possible cause for the heterogeneity in the findings is that the non-randomized study[25] injected 60 ml of saline through the catheter on two occasions, immediately after delivery and also the next morning, compared with a single prophylactic saline patch of 40–60 ml.[24] This inconsistency is mirrored in the other study[18] where some patients received bolus injections of 40–60 ml every 6 h for 24 h whereas others received an epidural infusion of 1.5–2 litre over 24 h. Either way, neither of these strategies significantly reduced the risk of headache.

A non-randomized study examined the effects of injecting 10 ml of *saline intrathecally* immediately after accidental dural puncture.[26] The hypothetical mechanism behind this approach is that the increased CSF pressure results in approximation of the dura and arachnoid at the puncture site, which seals the aperture and limits the loss of CSF volume. While the risk was cut by almost half in patients who received the 10 ml saline, this did not reach statistical significance and one can only speculate that injection of a larger volume of saline may have been more effective. However, the study did find that the need for therapeutic epidural blood patch was significantly reduced, suggesting that the intervention at the very least reduced the severity of the headaches.

There are some limitations to our analysis. Because accidental dural puncture is a rare complication, it is inherently difficult to conduct well-powered RCTs and it is not surprising that the majority of studies were non-RCTs. Therefore, we conducted sensitivity analyses for RCTs and non-RCTs only where appropriate, which turned out to be only the case for the PEBP. In addition, efficacy measures were mostly heterogeneous across studies, that is, differences in efficacy measures across the studies cannot be explained by random effects (chance) only. We constructed a funnel plot and found that the treatment effect was inversely related to the standard error of the study (Fig. 2). This means that there is evidence of a significant publication bias towards smaller trials being published if their results are positive. In fact, PEBP appeared highly effective in small trials but less (or not) effective in a larger and well-designed RCT.[23] Similarly, long-term intrathecal catheter appeared to be quite effective in two smaller trials but was found to be less (or not) effective in a much larger study.[20]

Given that accidental dural puncture may lead to PDPH in at least 50% of cases, we believe that prophylactic action is justified to prevent any possible morbidity that may occur in the obstetric patient. Since the headaches can be severe enough to prevent the mother from taking care of her newborn and can increase the cost of health care by lengthening hospital stay, it might be more prudent to take a proactive approach by administering preventative measures rather than waiting to begin treatment once the symptoms appear. However, it is important that the prophylactic procedure itself is not associated with significant risks, a consideration worth incorporating into future risk/benefit analyses.

Although study results for both PEBP and intrathecal catheters were heterogeneous, several studies did have promising results. However, the strong evidence for a publication bias among the clinical trials included in this meta-analysis necessitates a cautious interpretation of these results. To avoid the potential downfalls related to a meta-analysis of small RCTs, a properly designed RCT with sufficient power is needed to gain a better understanding of various preventive measures for PDPH.

The results of this meta-analysis have given us the best available evidence for the efficacy of individual interventions for PDPH prevention. Future clinical trials should focus on rigorously comparing the more substantially supported treatment and prophylaxis options, for example, intrathecal catheter, epidural blood patch, or morphine. In addition to providing direction for PDPH research, the results of this study may also be used for the sample size analyses of future studies. It will also be of great interest to compare proactive preventative measures with reactive symptomatic treatment options, a comparison that has the potential to provide valuable information to generate firm PDPH management guidelines.

In conclusion, we have summarized all available evidence for the prevention of PDPH. The largest effect was seen in a single RCT using epidural morphine as a preventative measure. However, these results need to be repeated before firm recommendations can be made. Data on long-term intrathecal catheters and epidural blood patch show potential, but the results are too heterogeneous to make firm recommendations. In addition, there is strong evidence of a publication bias that necessitates a cautious interpretation of these results. A large, well-designed, double-blind, randomized controlled multicentre trial is recommended to provide clinical evidence for the effectiveness of the most promising treatment options, for example, intrathecal catheter, epidural blood patch, and morphine.

Conflict of interest

None declared.

Funding

The study was conducted and internally funded by the Department of Anesthesia at the University of California San Francisco, San Francisco, CA, USA. The authors involved in this study and preparation of the manuscript received no external funding.

References

1 Gaiser R. Postdural puncture headache. *Curr Opin Anaesthesiol* 2006; **19**: 249–53

2 Smedstad KG. Dealing with post-dural puncture headache—is it different in obstetrics? *Can J Anaesth* 1998; **45**: 6–9

3 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**: 110–4

4 Gleeson CM, Reynolds F. Accidental dural puncture rates in UK obstetric practice. *Int J Obstet Anesth* 1998; **7**: 242–6

5 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

6 Stride PC, Cooper GM. Dural taps revisited. A 20-year survey from Birmingham Maternity Hospital. *Anaesthesia* 1993; **48**: 247–55

7 Choi PT, Galinski SE, Takeuchi L, Lucas S, Tamayo C, Jadad AR. PDPH is a common complication of neuraxial blockade in parturients: a meta-analysis of obstetrical studies. *Can J Anaesth* 2003; **50**: 460–9

8 Cook TM, Mihai R, Wildsmith JA. A national census of central neuraxial block in the UK: results of the snapshot phase of the Third National Audit Project of the Royal College of Anaesthetists. *Anaesthesia* 2008; **63**: 143–6

9 Cook TM, Counsell D, Wildsmith JA. Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists. *Br J Anaesth* 2009; **102**: 179–90

10 Carbaat PA, van Crevel H. Lumbar puncture headache: controlled study on the preventive effect of 24 hours' bed rest. *Lancet* 1981; **2**: 1133–5

11 Allen C, Glasziou P, Del MC. Bed rest: a potentially harmful treatment needing more careful evaluation. *Lancet* 1999; **354**: 1229–33

12 Baraz R, Collis RE. The management of accidental dural puncture during labour epidural analgesia: a survey of UK practice. *Anaesthesia* 2005; **60**: 673–9

13 Harrington BE, Schmitt AM. Meningeal (postdural) puncture headache, unintentional dural puncture, and the epidural blood patch: a national survey of United States practice. *Reg Anesth Pain Med* 2009; **34**: 430–7

14 Harrington B, Schmitt A. Management of accidental dural puncture in obstetrics: survey of current US practice. *Anesthesiology* 2007: A1768

15 Al-Metwalli RR. Epidural morphine injections for prevention of post dural puncture headache. *Anaesthesia* 2008; **63**: 847–50

16 Ackerman WE, Colclough GW. Prophylactic epidural blood patch: the controversy continues. *Anesth Analg* 1987; **66**: 913

17 Ackerman WE, Juneja MM, Kaczorowski DM. Prophylactic epidural blood patch for the prevention of postdural puncture headache in the parturient. *Anesthesiology* 1990; **71**: 45–9

18 Brownridge P. The management of headache following accidental dural puncture in obstetric patients. *Anaesth Intensive Care* 1983; **11**: 4–15

19 Colonna-Romano P, Shapiro BE. Unintentional dural puncture and prophylactic epidural blood patch in obstetrics. *Anesth Analg* 1989; **69**: 522–3

20 Kaul B, Sines D, Vallejo MC, Derenzo J, Waters J. A five year experience with post dural puncture headaches. *Anesthesiology* 2007: A1762

21 Lowenwirt I, Cohen S, Zephyr J, Hamer R, Hronkova B, Rovner JS. Can prophylactic epidural blood patch reduce the incidence and severity of postpartum dural puncture headache in obstetrics? *Anesth Analg* 1998; **86**: 378S

22 Palahniuk RJ, Cumming M. Prophylactic blood patch does not prevent post lumbar puncture headache. *Can Anaesth Soc J* 1979; **26**: 132–3

23 Scavone BM, Wong CA, Sullivan JT, Yaghmour E, Sherwani SS, McCarthy RJ. Efficacy of a prophylactic epidural blood patch in preventing post dural puncture headache in parturients after inadvertent dural puncture. *Anesthesiology* 2004; **101**: 1422–7

24 Trivedi NS, Eddi D, Shevde K. Headache prevention following accidental dural puncture in obstetric patients. *J Clin Anesth* 1993; **5**: 42–5

25 Craft JB, Epstein BS, Coakley CS. Prophylaxis of dural-puncture headache with epidural saline. *Anesth Analg* 1973; **52**: 228–31

26 Charsley MM, Abram SE. The injection of intrathecal normal saline reduces the severity of postdural puncture headache. *Reg Anesth Pain Med* 2001; **26**: 301–5

27 Ayad S, Demian Y, Narouze SN, Tetzlaff JE. Subarachnoid catheter placement after wet tap for analgesia in labor: influence on the risk of headache in obstetric patients. *Reg Anesth Pain Med* 2003; **28**: 512–5

28 Cohen S, Amar D, Pantuck EJ, Singer N, Divon M. Decreased incidence of headache after accidental dural puncture in caesarean delivery patients receiving continuous postoperative intrathecal analgesia. *Acta Anaesthesiol Scand* 1994; **38**: 716–8

29 Norris MC, Leighton BL. Continuous spinal anesthesia after unintentional dural puncture in parturients. *Reg Anesth* 1990; **15**: 285–7

30 Paech M, Banks S, Gurrin L. An audit of accidental dural puncture during epidural insertion of a Tuohy needle in obstetric patients. *Int J Obstet Anesth* 2001; **10**: 162–7

31 Rutter SV, Shields F, Broadbent CR, Popat M, Russell R. Management of accidental dural puncture in labour with intrathecal catheters: an analysis of 10 years' experience. *Int J Obstet Anesth* 2001; **10**: 177–81

32 Morewood GH. A rational approach to the cause, prevention and treatment of postdural puncture headache. *Can Med Assoc J* 1993; **149**: 1087–93

33 Morley-Forster PK, Singh S, Angle P, Littleford J, Currin M, Halpern SH. The effect of epidural needle type on postdural puncture headache: a randomized trial. *Can J Anaesth* 2006; **53**: 572–8

34 Norris MC, Leighton BL, DeSimone CA. Needle bevel direction and headache after inadvertent dural puncture. *Anesthesiology* 1989; **70**: 729–31

35 Richardson MG, Wissler RN. The effects of needle bevel orientation during epidural catheter insertion in laboring parturients. *Anesth Analg* 1999; **88**: 352–6

36 Boskovski N, Lewinski A. Epidural morphine for the prevention of headache following dural puncture. *Anaesthesia* 1982; **37**: 217–8

37 Thangathurai D, Bowles HF, Allen HW, Mikhail MS. Epidural morphine and headache secondary to dural puncture. *Anaesthesia* 1988; **43**: 519

38 Boonmak P, Boonmak S. Epidural blood patching for preventing and treating post-dural puncture headache (Review). *Cochrane Database Syst Rev* 2010; **1**: CD001791

39 Loeser EA, Hill GE, Bennett GM, Sederberg JH. Time vs. success rate for epidural blood patch. *Anesthesiology* 1978; **49**: 147–8

40 Safa-Tisseront V, Thormann F, Malassine P *et al.* Effectiveness of epidural blood patch in the management of post-dural puncture headache. *Anesthesiology* 2001; **95**: 334–9

41 Dennehy KC, Rosaeg OP. Intrathecal catheter insertion during labour reduces the risk of post-dural puncture headache. *Can J Anaesth* 1998; **45**: 42–5

42 Yaksh TL, Noueihed RY, Durant PA. Studies of the pharmacology and pathology of intrathecally administered 4-anilinopiperidine analogues and morphine in the rat and cat. *Anesthesiology* 1986; **64**: 54–66

43 Denny N, Masters R, Pearson D, Read J, Sihota M, Selander D. Postdural puncture headache after continuous spinal anesthesia. *Anesth Analg* 1987; **66**: 791–4

44 Rice GG, Dabbs HC. The use of peridural and subarachnoid injections of saline solution in the treatment of severe postspinal headache. *Anesthesiology* 1950; **11**: 17–23