Nonpharmacologic Neuraxial Interventions for Prophylaxis of Postdural Puncture Headache in the Obstetric Patient

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Postdural puncture headache due to accidental dural puncture during epidural catheter placement is a source of morbidity for new mothers. It can interfere with maternal-newborn bonding and increase the length of hospitalization. This evidence-based article examined the question: For obstetric patients experiencing an accidental dural puncture during epidural placement, which nonpharmacologic prophylactic neuraxial interventions safely and effectively decrease the incidence of postdural puncture headache?

A search of online databases revealed 4 systematic reviews with meta-analysis and a randomized controlled trial meeting the inclusion criteria. Three of the 4 systematic reviews used rigorous appraisal methods. Two systematic reviews included nonobstetric populations and 3 included additional interventions. Subgroup analyses allowed examination of the interventions of interest. Nonpharmacologic prophylactic neuraxial interventions included prophylactic epidural blood patch, epidural saline administration, and intrathecal catheter placement. There was a lack of standardization of interventions.

The evidence suggested there may be value in performing a prophylactic blood patch or placing an intrathecal catheter. The risk of the intervention must be carefully weighed with the benefits. Further rigorous studies are needed to help determine the best methods to decrease the incidence of postdural puncture headache in obstetric patients experiencing an accidental dural puncture during epidural placement.

**Keywords:** Anesthesia, complication, epidural, obstetric, postdural puncture headache.
cost-effective to initiate, but no substantial data support their use.10,11 Anesthesia providers use other prophylactic methods with varying frequency based on provider preference or belief. Nonpharmacologic neuraxial prophylactic interventions include the administration of a prophylactic epidural blood patch, administration of saline through the existing epidural catheter before removal, intrathecal placement of the catheter when ADP occurs for administration of continuous spinal anesthesia, administration of saline before intrathecal catheter removal, and maintaining the intrathecal catheter for a time after delivery.3 These interventions carry risks, and providers should be aware of these risks as well as potential benefits. This review examines if these nonpharmacologic neuraxial prophylactic interventions safely and effectively decrease the incidence of PDPH.

Materials and Methods

• The PICO Question. The PICO (patient, intervention, comparison, outcome) question12 guiding the literature search was “For obstetric patients with ADP during epidural placement (patient), which nonpharmacologic prophylactic neuraxial interventions (intervention) effectively and safely decrease the incidence of PDPH (outcome)?”

• Search Strategy. The literature search (1975 to 2014) was performed using the following databases: PubMed and The Cochrane Library. The search also included the following professional and governmental organization websites: American Association of Nurse Anesthetists, American Society of Anesthesiologists, American Society of Regional Anesthesia and Pain Medicine, and National Guideline Clearinghouse. The following search terms (and wildcards) were used alone or in combination: epidural, post dural puncture headache, accidental dural puncture, prophylaxis, parturient, pregnant, and obstetric. The search was limited to systematic reviews with and without meta-analysis and randomized controlled trials available in full-text from peer-reviewed English-language journals. Evidence-based clinical practice guidelines from professional and governmental organization websites were also included.

Potential evidence sources were sought from subject matter experts. PubMed’s “related links” section and the reference lists of all relevant articles were scrutinized for additional articles that met inclusion criteria.

Only evidence pertaining to prophylactic neuraxial techniques for PDPH due to ADP with an epidural needle in the obstetric population was included. To take advantage of higher-level evidence, evidence from systematic reviews was not individually appraised. Evidence sources included in more than 1 systematic review were noted.

Results

The search (Figure) yielded 4 systematic reviews1,7,13,14 and 1 randomized controlled trial15 (Table 1). One of these systematic reviews7 is now listed by Cochrane as “withdrawn” for being out of date and authors are no longer available to update it. We felt the information in this systematic review was sufficiently recent to warrant inclusion. Two systematic reviews1,7 included studies using nonobstetric samples; however, subgroup analyses in these systematic reviews were done on data solely from studies using obstetric samples (Tables 2 through 4). Two systematic reviews1,14 included randomized controlled trials along with nonrandomized controlled trials and descriptive studies. Three systematic reviews1,7,13 included studies examining additional interventions. The meta-analysis of subgroups in these systematic reviews1,7,13 allowed for exclusion of data not meeting our inclusion
criteria. Interventions were prophylactic epidural blood patch, epidural administration of saline, placement of intrathecal catheter for continuous spinal analgesia after ADP, and maintenance (leaving in place) of an intrathecal catheter for less than or greater than 24 hours.

Investigators\(^1,7,13-15\) did not specify studies that included obstetric patients who delivered vaginally, labored followed by cesarean delivery, or had a planned cesarean delivery. The method of delivery and the presence of labor may affect the incidence of PDPH and the impact of prophylactic intervention. Patients who experience labor after ADP likely experience increased CSF leakage through the dural defect.\(^1,14\)

Some studies\(^16-29\) were included in more than 1 systematic review. Specifically, this duplication occurred in the systematic reviews examining the use of prophylactic epidural blood patch\(^1,7,13\) and intrathecal catheter placement\(^1,13,14\) (noted in Tables 2 and 3). Studies appraised...

<table>
<thead>
<tr>
<th>Study</th>
<th>Subgroup</th>
<th>Total number of subjects</th>
<th>Comparison</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apfel et al,(^1) 2010(^b)</td>
<td>NA(^c)</td>
<td>17 (1,264)</td>
<td>No PEBP</td>
<td>PDPH</td>
<td>RR 0.32 (95% CI 0.10 to 1.03)</td>
</tr>
<tr>
<td>Boonmak &amp; Boonmak,(^7) 2010(^b)</td>
<td>Level I</td>
<td>9 (379)</td>
<td>Conservative treatment Sham procedure</td>
<td>OR 0.06 (95% CI 0.03 to 0.14)(^a)</td>
<td></td>
</tr>
<tr>
<td>Bradbury et al,(^13) 2013</td>
<td>Level I</td>
<td>40 (11,536)</td>
<td>任何头痛</td>
<td>OR 0.87 (95% CI 0.23 to 3.31)</td>
<td></td>
</tr>
<tr>
<td>Heesen et al,(^14) 2013</td>
<td>NA(^c)</td>
<td>9 (963)</td>
<td>Any headache Backache</td>
<td>OR 1.17 (95% CI 0.39 to 3.52)</td>
<td></td>
</tr>
<tr>
<td>Stein et al,(^15) 2014</td>
<td>Level II</td>
<td>1 (109)</td>
<td>Any headache</td>
<td>OR 0.04 (95% CI 0.01 to 0.19)(^a)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Any headache</td>
<td>OR 0.08 (95% CI 0.02 to 0.37)(^a)</td>
<td></td>
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Table 1. Evidence Examining Use of Nonpharmacologic Neuraxial Intervention as Prophylaxis for Postdural Puncture Headache Following Accidental Dural Puncture During Epidural Placement for Obstetric Anesthesia

Abbreviation: NA, not applicable.
\(^a\)From Melnyk and Fineout-Overholt\(^30\): Level I, systematic reviews or meta-analyses of all relevant randomized controlled trials or evidence-based clinical practice guidelines; Level II, well-designed relevant randomized controlled trial; Level III, well-designed controlled trials without randomization; Level IV, well-designed case-control and cohort studies; Level V, systematic reviews of descriptive and qualitative studies; Level VI, descriptive or qualitative study; and Level VII, opinion of authorities and/or reports of expert committees.
\(^b\)Contained studies examining nonobstetric as well as obstetric subjects; however, subgroup analyses were done on studies that included solely studies with obstetric samples.
\(^c\)These 2 systematic reviews did not specifically meet the criteria of Melnyk and Fineout-Overholt\(^30\) for Level I or V evidence because these systematic reviews included sources other than randomized controlled trials.

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</thead>
<tbody>
<tr>
<td>Apfel et al,(^1) 2010(^b)</td>
<td></td>
<td>173</td>
<td>No PEBP</td>
<td>PDPH</td>
<td>RR 0.32 (95% CI 0.10 to 1.03)</td>
</tr>
<tr>
<td>Boonmak &amp; Boonmak,(^7) 2010(^b)</td>
<td></td>
<td>88</td>
<td>Conservative treatment Sham procedure</td>
<td>OR 0.06 (95% CI 0.03 to 0.14)(^a)</td>
<td></td>
</tr>
<tr>
<td>Bradbury et al,(^13) 2013</td>
<td></td>
<td>173</td>
<td>No PEBP</td>
<td>PDPH</td>
<td>RD −0.48 (95% CI −0.88 to −0.086)(^a)</td>
</tr>
<tr>
<td>Stein et al,(^15) 2014</td>
<td></td>
<td>109</td>
<td>Conservative treatment</td>
<td>PDPH</td>
<td>RD −0.37 (95% CI −0.78 to 0.038)(^a)</td>
</tr>
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Table 2. Evidence Examining Epidural Blood Patch as Prophylaxis for Postdural Puncture Headache Following Accidental Dural Puncture During Epidural Placement for Obstetric Anesthesia

Abbreviations: CI, confidence interval; LOS, length of stay; OR, odds ratio; PDPH, postdural puncture headache; PEBP, prophylactic epidural blood patch; RCT, randomized controlled trial; RD, risk difference; RR, relative risk; TEBP, therapeutic epidural blood patch.
\(^a\)P < .05.
\(^b\)P < .0001.
by authors of the systematic reviews\textsuperscript{1,7,13,14} were not reviewed separately because the systematic review with meta-analysis is considered the highest level of evidence, able to overcome some weaknesses of individual studies.\textsuperscript{30} The evidence was appraised using the method proposed by Melnyk and Fineout-Overholt.\textsuperscript{30}

Authors of the systematic reviews\textsuperscript{1,7,13,14} described a broad search strategy detailing inclusion criteria. Systematic reviews included only randomized controlled trials\textsuperscript{7,13} or studies with a control group.\textsuperscript{1,14} Evidence may suggest publication bias toward small nonrandomized controlled trials with positive findings.\textsuperscript{1}

Three of the systematic reviews\textsuperscript{1,7,13} were rigorously conducted, using 2 to 3 authors to assess the methodologic quality of studies. Many of the studies suffered from insufficient blinding and randomization.\textsuperscript{13} Four studies were published only as abstracts and may not have reached publication standard for peer-reviewed journals\textsuperscript{18,22,31,32}.

The systematic review by Heesen et al\textsuperscript{14} did not discuss how validity was assessed for individual studies and described their lack of formal assessment as a study limitation. A large amount of heterogeneity existed among included studies. The systematic reviews used

### Table 3. Evidence Examining Intrathecal Catheter Placement as Prophylaxis for Postdural Puncture Headache Following Accidental Dural Puncture During Epidural Placement for Obstetric Anesthesia

<table>
<thead>
<tr>
<th>Study</th>
<th>Subgroup</th>
<th>Total number of subjects</th>
<th>Comparison</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apfel et al,\textsuperscript{1} 2010</td>
<td>ITC &gt; 24 hours: 3 Retrospective chart reviews\textsuperscript{22,24,27}</td>
<td>318</td>
<td>NO ITC</td>
<td>PDPH</td>
<td>RR 0.21 (95% CI 0.02 to 2.65)</td>
</tr>
<tr>
<td></td>
<td>ITC &lt; 24 hours: 5 Studies: 1 Non-RCT\textsuperscript{26} 3 Retrospective chart reviews\textsuperscript{24,27,29} 1 Prospective audit\textsuperscript{28}</td>
<td>306</td>
<td>No ITC</td>
<td>PDPH</td>
<td>RR 0.88 (95% CI 0.68 to 1.14)</td>
</tr>
<tr>
<td>Bradbury et al,\textsuperscript{13} 2013</td>
<td>1 RCT\textsuperscript{25}</td>
<td>115 (18 excluded)</td>
<td>Repeated epidural</td>
<td>PDPH</td>
<td>ITC 36 of 50 subjects</td>
</tr>
<tr>
<td>Heesen et al,\textsuperscript{14} 2013</td>
<td>9 Studies: 1 RCT\textsuperscript{25} 2 Non-RCTs\textsuperscript{26,31} 5 Retrospective chart reviews\textsuperscript{22,24,27,29,32} 1 Prospective audit\textsuperscript{28}</td>
<td>939</td>
<td>Repeated epidural or no treatment</td>
<td>PDPH</td>
<td>RR 0.82 (95% CI 0.67 to 1.01)</td>
</tr>
</tbody>
</table>

### Table 4. Evidence Examining Epidural Administration of Saline as Prophylaxis for Postdural Puncture Headache Following Accidental Dural Puncture During Epidural Placement for Obstetric Anesthesia

<table>
<thead>
<tr>
<th>Study</th>
<th>Subgroup</th>
<th>Total number of subjects</th>
<th>Comparison</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apfel et al,\textsuperscript{1} 2010</td>
<td>3 Studies: 2 Non-RCTs\textsuperscript{17,34} 1 Cohort\textsuperscript{35}</td>
<td>143</td>
<td>No epidural saline</td>
<td>PDPH</td>
<td>RR 0.65 (95% CI 0.40 to 1.05)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; ITC, intrathecal catheter; PDPH, postdural puncture headache; RCT, randomized controlled trial; RR, relative risk; TEBP, therapeutic epidural blood patch.\textsuperscript{a}P < .05.
various sensitivity analyses in an attempt to lessen the impact of heterogeneity during statistical analysis.

A randomized controlled trial published in 2014 was not included in the described systematic reviews. Subjects were randomly assigned to the control group (56 subjects) or the prophylactic epidural blood patch treatment group (60 subjects). The sample size was determined by power analysis based on the outcome of PDPH. Forty-three subjects were required in each group to detect 80% power and \( P \leq 0.05 \). All but 7 subjects in the control group completed the study as planned. These 7 subjects were not included because of a failure to randomly assign. A few methodologic weaknesses were identified. There was no mention of allocation concealment. Although the evaluator was blinded, subjects and providers were not. Additionally, subjects in the control group were assigned to receive nonstandardized conservative treatment. Several pharmacologic interventions were used based on provider preference.

Lack of standardization of the interventions was a possible source of bias across studies. For example, of the studies that examined prophylactic epidural blood patch, only randomized controlled trials standardized the intervention to a range of 15 to 20 mL of blood for the prophylactic epidural blood patch. The intervention saline injection via epidural catheter varied across studies in the amount of saline, length of duration of injection, and number of injections. The duration of maintenance of the intrathecal catheter was not clearly standardized, and failure to meet maintenance time protocol existed. The single randomized controlled trial examining 24-hour intrathecal catheter maintenance reported that only 18 of 55 subjects followed the 24-hour study protocol.

Lastly, outcomes used to measure the effectiveness of interventions varied. The most common outcome was PDPH. Any headache, severe PDPH, and PDPH that required treatment with therapeutic epidural blood patch were also used as outcome measures. Stein et al used the International Headache Society definition of PDPH to define outcome measurement; however, this was not the case for many other studies. Postdural puncture headache is distinct. The lack of clear differentiation between PDPH and any headache could have affected the validity of study results.

**Discussion**

The review of the evidence examining prophylactic epidural blood patch (see Table 2), epidural administration of saline (see Table 4), placement of an intrathecal catheter for continuous spinal analgesia after ADP (see Table 3), and maintenance of the intrathecal catheter for less than or greater than 24 hours did not indicate that any intervention was clearly effective. The evidence sources suffered from various methodologic problems, and some studies were included in more than 1 systematic review.

**Prophylactic Epidural Blood Patch.** The injection of autologous blood into the epidural space is thought to seal the dural defect created by the epidural needle and to increase pressure in the intraspinal space. This procedure increases the distribution of CSF intracranially. The redistribution of CSF increases intracranial pressure, mitigating the cause of the PDPH. Therefore, the use of a prophylactic epidural blood patch might prevent the outcome of PDPH and the further need for therapeutic epidural blood patch. Risks associated with prophylactic and therapeutic epidural blood patches include common transient complications such as backache and rare complications such as neurologic deficit or infection. The findings from a Cochrane review and 2 other systematic reviews did not conclusively support performing a prophylactic epidural blood patch. However, the finding of a more recent randomized controlled trial suggested this intervention might be effective.

The authors of the Cochrane review examined the intervention and the outcomes of PDPH, severe PDPH, any headache, and backache. Odds ratios with 95% or 99% confidence intervals were reported. Trials were broken into subgroups based on study quality. A subgroup of 2 randomized controlled trials with very low heterogeneity (\( I^2 = 5\% \)) and totaling 88 subjects, found a significant difference in PDPH following prophylactic epidural blood patch compared with conservative treatment. However, the results of a single randomized controlled trial with improved methods and 64 subjects did not achieve statistical significance for any of the 4 measured outcomes. The comparison group received a sham procedure to help differentiate the intervention from placebo effect.

Two other systematic reviews examined the efficacy of prophylactic epidural blood patch. These 2 systematic reviews examined the 4 randomized controlled trials that were included in the Cochrane review. The authors of 1 of the systematic reviews reported relative risk, and the other reported risk difference. The findings of these reviews differed, perhaps because of the difference in the weight assigned to the individual studies by their respective authors. Findings comparing prophylactic epidural blood patch with no blood patch for prevention of PDPH were close but did not meet significance. However, findings for the use of prophylactic epidural blood patch to avoid future treatment with therapeutic epidural blood patch were significant. The systematic review reporting risk difference weighted all 4 studies evenly. In this systematic review there was an overall statistically significant effect for the outcome PDPH. The number needed to treat was calculated as 2.1. Conversely, findings were no longer significant following a sensitivity analysis conducted to remove 1 randomized controlled...
A more recent randomized controlled trial included 109 subjects. The authors identified a statistically significant reduction in PDPH, with 11 of 60 subjects having PDPH who underwent a prophylactic epidural blood patch compared with 39 of 49 subjects who did not (P < .0001). Significance remained when PDPH was broken down by severity of the headache. Accompanying symptoms also were examined. A significant difference in the occurrence of nuchal rigidity and tinnitus was identified for subjects receiving prophylactic epidural blood patch instead of conservative treatment following ADP. Authors evaluated the length of hospital stay, emergency room visit after discharge, and need for repeated therapeutic epidural blood patch. No difference was found for these outcomes between the 2 groups. Subjects who received prophylactic epidural blood patch did not experience any adverse effects. Contrary to the findings of the systematic reviews, a meta-analysis of 3 studies containing a total of 143 subjects, epidural blood patch may be effective in preventing PDPH.

With the difference of these findings, the provider must carefully consider the risks and benefits of performing a prophylactic epidural blood patch.

- **Epidural Administration of Saline.** Saline injected into the epidural space may minimize the CSF leakage by equilibrating the pressure between the epidural and subarachnoid spaces temporarily. This may then allow fibrin to seal the dural defect. Only 1 systematic review, a meta-analysis of 3 studies (2 nonrandomized controlled trials and 1 cohort study) containing a total of 143 subjects, compared epidurally administered saline with “no epidural saline” to prevent PDPH and the need for therapeutic epidural blood patch after ADP in obstetric patients. The comparison reached significance for neither outcome. Only 1 of the studies achieved significance for the prevention of PDPH on its own. This was a small nonrandomized controlled trial consisting of only 33 subjects. The available evidence does not support the use of epidurally administered saline.

- **Intrathecal Catheter Placement.** The placement of an intrathecal catheter through the defect created in the dura by the epidural needle theoretically closes the defect and prevents CSF leakage. Some authors purport that the maintenance of the intrathecal catheter for up to 24 hours post partum creates a localized inflammatory response that will encourage closure of the dural defect. This intervention allows for immediate relief of labor pain and negates the risk of repeated dural puncture. The risk of cauda equina syndrome and infection with maintenance of intrathecal catheters is an important consideration. Three systematic reviews included the evaluation of intrathecal catheter placement for the prevention of PDPH after ADP in obstetric patients. Only 1 randomized controlled trial evaluated this intervention.

Bradbury et al found a single study examining intrathecal catheter placement. A Jadad score of 3 of 5 for methodologic quality was assigned to this randomized controlled trial because of the lack of blinding. Patients were randomly assigned to treatment groups using a crossover technique between hospitals, thus exposing the study to selection bias. This study was underpowered at 97 subjects, increasing the risk of Type II error. Of importance, many subjects did not complete the 24-hour intrathecal catheter maintenance protocol. The results of this randomized controlled trial were not significant.

Heesen et al examined the same randomized controlled trial with 8 other studies in a meta-analysis investigating the intervention of intrathecal catheter insertion in relation to the outcome of PDPH and therapeutic epidural blood patch. A sensitivity analysis done to exclude 1 study with a much larger effect size did not alter the statistical outcome. All studies were grouped for meta-analysis regardless of duration of intrathecal catheter maintenance. Findings were not significant for the prevention of PDPH. However, significant findings suggest that this intervention may decrease the need for a therapeutic epidural blood patch.

Another systematic review separated the intervention of intrathecal catheter into 2 groups: long-term (> 24-hour) and short-term (< 24-hour) catheter maintenance. Outcomes were PDPH and the need for therapeutic epidural blood patch. Three retrospective chart reviews were used to evaluate the intervention of long-term use of the intrathecal catheter compared with no intrathecal catheter. The 3 studies were heterogeneous. The results were not significant for both PDPH and therapeutic epidural blood patch. One large study was weighted heavily in comparison, with 222 subjects. Five studies were used to evaluate the intervention of short-term intrathecal catheter use vs no intrathecal catheter. For this short-term intrathecal catheter intervention, there was also no difference in PDPH between the groups. However, the results for prevention of therapeutic epidural blood patch were significant.

Two incidents of adverse events without detriment were described among the studies that evaluated intrathecal catheter placement following ADP. These were a single incident of high block that resulted in dyspnea, upper limb weakness, and hypotension and a single incident of paresthesia that resolved on removal of the intrathecal catheter.

These findings suggest intrathecal catheter placement does not significantly reduce the incidence of PDPH. However, this intervention may decrease the overall severity of PDPH and reduce the need for a therapeutic epidural blood patch.

**Conclusion**

The review of the evidence did not conclusively indicate
that any of the interventions were clearly effective in decreasing the incidence of PDPH. Only a single recent randomized controlled trial indicated that a prophylactic epidural blood patch was effective in preventing a PDPH. Intrathecal catheter placement does not prevent a PDPH but may decrease the need for a therapeutic epidural blood patch. The evidence suffered from many methodologic problems such as lack of the following: homogeneity, controls, randomization, and blinding. It is important to note that many studies were underpowered, increasing the risk of Type II error.

The decision to use these interventions is provider and patient dependent because these interventions are not without risk. Although no adverse effects due to administration of a prophylactic epidural blood patch were reported, a large sample is required to study rare side effects. The risk of an intervention must be carefully compared with the benefit for each patient.

Epidural anesthesia is very effective in relieving labor pain and is hugely popular among obstetric patients. Postdural puncture headache is a major source of morbidity for new mothers, with a potential impact on cost due to lengthened hospitalization. Further investigation into prevention of PDPH is warranted. Large multicenter randomized controlled trials with improved methods and risk-vs-benefit analysis are necessary to form conclusive recommendations.

REFERENCES


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DISCLOSURES
The authors have declared no financial relationships with any commercial interest related to the content of this activity. The authors did not discuss off-label use within the article.