Atraumatic versus conventional lumbar puncture needles: a systematic review and meta-analysis protocol (international prospective register of systematic reviews, PROSPERO registration number: CRD42016047546)

Introduction

Lumbar puncture is one of the oldest and most commonly performed procedures in modern medicine, used to both diagnose and treat disease. Headache secondary to cerebrospinal fluid (CSF) leak into the epidural space following lumbar puncture remains a frequent complication, which may cause significant patient discomfort, requiring narcotic analgesia or invasive therapy.[1] Needle tip design has been postulated to affect the incidence of headache post lumbar puncture, with pencil point 'atraumatic' needles thought to reduce its incidence in comparison to conventional bevelled 'traumatic' needles.[2] In vitro studies suggest that atraumatic needles dilate and spread apart dural fibres during puncture, leaving behind a small pinpoint opening, whereas conventional needles have been observed to tear through dural tissues, creating irregular lacerations.[3] Therefore, atraumatic needles are postulated to reduce the incidence of headache following lumbar puncture by limiting CSF leak into the epidural space.

Despite development of atraumatic needles nearly 70 years ago, their use remains significantly limited. In fact, only a fraction of surveyed clinicians report awareness of the existence of atraumatic needles and evidence describing their safety and efficacy has failed to reach consensus.[4,5] This meta-analysis will aim to systematically examine atraumatic needles in comparison to the conventional type.

Methods

The current protocol:

- Is developed in accordance with the preferred reporting items for systematic reviews and meta-analysis protocols (PRISMA-P).[6]
- Is registered with the international prospective register of systematic reviews (PROSPERO), registration number: CRD42016047546.

Our systematic review and meta-analysis will be conducted in accordance with:

- Preferred reporting items for systematic reviews and meta-analysis (PRISMA).[7,8]
- Cochrane handbook for systematic reviews of interventions.[9]

Literature search

We will conduct a detailed search of the following 13 electronic databases:

1. Medline
2. Embase
3. Web of Science
4. CINAHL
5. Cochrane CENTRAL
6. Cochrane DSR
7. LILACS
8. ClinicalTrials.gov
9. WHO Clinical Trials Database
10. Google Scholar

11. WangFangData
12. CQVIP
13. CNKI

We will use keyword and medical subject heading (MeSH) terms related to needle type (atraumatic or conventional) and clinical outcomes. Search strategies will be developed collaboratively in consultation with librarians with expertise in systematic reviews and academic clinicians from diverse specialties worldwide. The search strategy employed for the Medline database is provided in table a1. The search will be supplemented by manually screening the references of relevant articles, reviewing the proceedings of pertinent meetings, and contacting clinical experts in the field. Our search will be conducted without publication type, language, or time restrictions.

Study selection

A multidisciplinary research team consisting of librarians and clinical experts from diverse specialties worldwide will independently evaluate studies for eligibility. Disagreements between the team will be resolved collegially through discussion and consensus, including an impartial reviewer, and contacting the study authors. Our inclusion criteria shall be:

- *Study design:* randomised controlled trials (including cluster trials and pilot studies) comparing atraumatic and conventional lumbar puncture needles, with no publication type, time, or language restrictions. We will include fully published trials and proceeding abstracts in the grey literature. Conference abstracts will be included if they fit our inclusion criteria and if no follow-up study has been published.
- *Population:* patients of any age group and demographic undergoing lumbar puncture as a part of their clinical care.
- *Intervention:* lumbar puncture with an atraumatic needle.
- *Control:* lumbar puncture with a conventional or 'traumatic' needle.
- *Outcomes:* clinical outcomes such as the incidence of post dural puncture headache as well as any headache, backache, hearing disturbance, nerve root irritation, traumatic tap, severity of post dural puncture headache, need for intravenous fluid or controlled analgesia, need for epidural blood patch, failure rate, mean number of attempts, and rate of success on first attempt.

For studies published more than once (duplicates), we will include only the report with the most informative and complete data. Studies evaluating combined spinal anaesthesia (epidural and dural puncture) will be included and post puncture outcomes will be evaluated. We will exclude:

- Observational studies
- Reviews
- Correspondences
- Letters to the editor
- Randomised trials examining atraumatic and conventional needles where no dural puncture was performed (epidural injections)
- Randomised trials examining atraumatic needles without a comparative conventional needle control group

Data management and collection

Literature search results will be exported from all relevant databases as .ris files or .ciw files containing the complete reference. EndNote X8 software will be used for reference management. The research team will develop and pilot screening questions and forms based on the eligibility criteria. Prior to data abstraction, complete articles of all eligible studies will be retrieved. For studies not published in English, the full article will be translated into English and a medical expert fluent in the original language of the article will be involved in data management. Where necessary, we will contact authors of relevant studies to obtain additional information, article texts, and resolve questions about eligibility.

Data from selected studies will be abstracted independently by the research team. We will gather information from eligible articles using data abstraction forms that include fields for:

- Study first author
- Year of publication
- Journal of publication
- Language
- Study design
- Included centres
- Included countries
- Number of patients
- Number of males and females
- Inpatients or outpatients
- Recruitment period
- Eligibility criteria
- Method of randomisation
- Purpose of lumbar puncture
- Specialty of clinician performing lumbar puncture
- Patient position
- Atraumatic and conventional needle specific type
- Atraumatic and conventional needle gauge
- Procedure for follow-up
- Scale used to assess headache
- Treatment of headache
- Number of patients in atraumatic and conventional groups
- Age of patients in atraumatic and conventional groups
- Body mass index (BMI) of patients in atraumatic and conventional groups
- Number of patients in atraumatic and conventional groups given prophylactic intravenous fluids
- Number of patients in atraumatic and conventional groups instructed bedrest
- Characteristics of headache reported
- Number of patients with postural headache in atraumatic and conventional groups
- Number of patients with non-postural headache in atraumatic and conventional groups
- Number of patients with both postural and non-postural headaches in atraumatic and conventional groups
- Severity of headaches in atraumatic and conventional groups

- Duration of headaches in atraumatic and conventional groups
- Number of patients with backache in atraumatic and conventional groups
- Number of patients treated with epidural blood patch for headache in atraumatic and conventional groups
- Success on first attempt with atraumatic and conventional needles
- Number of traumatic taps with atraumatic and conventional needles
- Failure rate of atraumatic and conventional needles
- Number of attempts required to obtain CSF with atraumatic and conventional needles
- Cross overs (atraumatic-to-conventional and conventional-to-atraumatic)
- Number of patients with nerve root irritation in atraumatic and conventional groups
- Number of patients with hearing disturbance in atraumatic and conventional groups
- Number of patients with serious complications (eg, persistent CSF leak, nerve damage) in atraumatic and conventional groups
- Ease of use of needles as reported by authors

Definition of outcomes

- *Primary outcome – post dural puncture headache:*
    - Headache fulfilling the international classification of headache disorders (ICHD) III criteria:[10] an orthostatic headache occurring within 5 days of lumbar puncture, secondary to CSF leak into the epidural space; usually accompanied by neck stiffness as well as subjective hearing symptoms that remits spontaneously within 2 weeks or after sealing of the puncture site with an autologous epidural blood patch.
    - There are 4 diagnostic criteria defined by the ICHD for post dural puncture headache as follows:[10]
        1. Headache is secondary to CSF leakage
        2. Dural puncture was performed
        3. Headache developed within 5 days of dural puncture
        4. All other causes of headache were excluded
    - For studies that do not explicitly list the above criteria, we will search for terminology that satisfies these criteria without them being entirely stated. In cases where we are unable to assess whether headaches fit the ICHD III definition, we will contact study authors for clarification.
    - Severity of post dural puncture headache will be classified using the visual analogue scale (VAS) and the required treatment regimen:
        - *Mild:* VAS score 1–3; responds to over-the-counter analgesics and bedrest.
        - *Moderate:* VAS score 4–7; responds to controlled analgesia or intravenous fluid.
        - *Severe:* VAS score 8–10; requires epidural blood patch.
- *Additional outcomes:*
    - *Any headache:* incidences of post dural puncture headache and non-specific headaches. Non-specific headaches will be those not in line with the ICHD III definition for post dural puncture headache and those secondary to anaesthetics.

- *Mild headache:* post dural puncture headache that is classified as having a VAS score of 1–3 and responds to over the counter analgesics and bedrest.
- *Severe headache:* post dural puncture headache that is classified as having a VAS score of 8–10 and requires epidural blood patch.
- *Backache:* any pain in the lumbar region post puncture.
- *Nerve root irritation:* radicular pain radiating to lower limbs.
- *Hearing disturbance:* hearing loss at any frequency or tinnitus.
- *Traumatic tap:* presence of blood in the CSF upon visual inspection.
- *Need for intravenous fluid/controlled analgesia:* for headache treatment.
- *Need for epidural blood patch:* for headache treatment.
- *Failure rate:* all instances in which a puncture attempt was made but CSF could not be obtained.
- *Rate of success on first attempt:* CSF obtained on the first puncture.
- *Mean number of attempts:* average number of lumbar punctures.

Risk of bias in individual studies

The research team will independently assess all included studies using the Cochrane assessment tool. Each domain will be judged as low, unclear, or high. If there is insufficient information provided to make a judgement, we will categorise that domain as unclear and the original study authors will be contacted for further information. We will evaluate studies across the following domains:[9,11]

- Random sequence generation (selection bias)
  - *Low:* the study states randomisation and its method is determined to be unpredictable (eg, computerised random number block, minimisation, coin toss).
  - *High:* the study does not state randomisation or states randomisation but the method is predictable (eg, hospital admission number, date of birth, day of visit).
  - *Unclear:* the study does not state the randomisation method, but mentions explicitly that randomisation occurred or the study describes allocation concealment but does not discuss the method of randomisation.
- Allocation concealment (selection bias)
  - *Low:* the study states how the integrity of randomisation was maintained and the method is determined to be difficult to circumvent (eg, central computer server, sealed opaque envelopes).
  - *High:* the study states how the integrity of randomisation was maintained and the method is determined to be relatively easy to circumvent (eg, unsealed, translucent envelopes, use of personal computer for random sequence generation, paper records stored in shared office).
  - *Unclear:* the study does not state the method used to maintain the integrity of randomisation or the study describes randomisation method without discussing how allocation concealment was maintained.
- Blinding of participants and personnel (performance bias)
  - *Low:* the study discusses that blinding occurred either explicitly or implicitly (eg, the outcome assessor was unaware of the needle type used for puncture). Blinding of personnel performing puncture is not possible as the needle tip is visible while performing the procedure. Patient blinding will be determined by

either explicitly stating that patients were blinded, or mentioning the study involved blinding.
    - *High:* the study does not discuss blinding either implicitly or explicitly.
- Blinding of outcome assessment (detection bias)
    - *Low:* the study discusses that blinding occurred either explicitly or implicitly (eg, the outcome assessor was unaware of the needle type used for puncture). Single-blinded studies will be assumed to have blinding of the outcome assessor unless a study specifies that it is a 'patient-blinded' study as blinding of the practitioner performing puncture is not possible.
    - *High:* the study does not implicitly or explicitly discuss blinding.
    - *Unclear:* the study discusses that blinding occurred but does not mention blinding of the outcome assessor or patients, or states that it is 'patient-blinded'. In both scenarios, the study will be classified as low risk of bias for performance bias, and unclear risk for detection bias.
- Incomplete outcome data (attrition bias)
    - *Low:* fewer than 10% of patients dropped out from the study.
    - *High:* greater than 10% of patients dropped out from the study.
    - *Unclear:* applies to abstracts as they do not normally discuss the flow of patients through the trial in detail.
- Selective reporting bias (reporting bias)
    - *Low:* the study clearly defines post dural puncture headache or provides criteria for post dural puncture headache. The study must state that post dural puncture headache was evaluated in either the methods or results sections.
    - *High:* the study offers no description of post dural puncture headache in any section and discusses only 'headache'. Studies that report on a primary outcome that is not post dural puncture headache (eg, hearing disturbance) and do not assess post dural puncture headache as an additional outcome will also be categorised as high risk for reporting bias.
    - *Unclear:* the study discusses post dural puncture headache or its criteria in the introduction or discussion but discusses only 'headache' in the methods and results sections without providing post dural puncture headache definition or criteria.
- Other sources of bias
    - *Low:* the study presents no discrepancies in numerical data across tables and the text. The study is well written and formatted.
    - *High:* there are significant discrepancies between the data presented in figures and tables and data reported in the text. There are issues with the study that cannot be categorised into other domains.
    - *Unclear:* abstracts will be evaluated as unclear for other sources of bias as they provide a summary of the trial and do not disclose complete methodology and data.
- Overall risk of bias
    - *High:* a study evaluated as having one or more high risk domains will be judged as having an overall high risk of bias.

- *Low:* a study evaluated as having no high risk domains will be categorised as overall low risk of bias.

Disagreements will be resolved through discussion, consensus, and if necessary, including an impartial reviewer and contacting the trial investigators.

Data synthesis

Analyses for all outcomes will be conducted on an intention-to-treat basis. Relative risks (RR) with associated 95% confidence intervals (CI) will be used to summarise our findings. For continuous variables, such as the mean number of attempts, we will calculate the weighted mean difference (MD) and corresponding 95% CI. Random-effects meta-analysis for all outcomes will be performed using the DerSimonian and Laird model.[12] Weights of included studies will be calculated using the inverse variance method. The number needed to treat to prevent harm will be calculated using the following equation:[9]

$$\text{Number needed to treat to prevent harm} = \left| \frac{1}{\text{Assumed control risk} \times (1 - \text{RR})} \right|$$

The threshold of type I error for statistical significance shall be α=0.05. Between study heterogeneity will be evaluated using Cochran's Q test and measured by the I^2 statistic, with I^2 values exceeding 25%, 50%, and 75% being judged as low, moderate, and high heterogeneity, respectively.[13] Publication bias will be assessed by visual inspection of the symmetry of funnel plots and quantitatively by calculation of Begg-Mazumdar's,[14] and Egger's tests.[15] The quality of evidence for outcomes will be rated using the grading of recommendations assessment, development, and evaluation (GRADE) approach.[16]

Prespecified subgroup analyses will be conducted to examine if covariates exist and to explore potential heterogeneity for the primary outcome of post dural puncture headache. We will examine 8 key subgroups pertaining to:

- Patient age (<18 *vs* ≥18 years)
- Patient sex (male *vs* female)
- Bedrest post puncture
- Needle gauge (20–22 *vs* 23–26 *vs* >26)
- Indication for lumbar puncture (spinal anaesthesia *vs* diagnostic *vs* myelography)
- Use of prophylactic intravenous fluid
- Patient position (sitting *vs* lateral)
- Specialty of clinician performing lumbar puncture (anaesthesiologist *vs* neurologist *vs* radiologist)

We will conduct 3 sensitivity analyses adjusting for:

- *Cochrane risk of bias assessment tool:* low *vs* high.
- *Meta-analysis models:* random- *vs* fixed-effects.
- *Trial sequential analysis:* to account for the risk of type I error secondary to sparse data by performing cumulative significance testing.[17] A diversity (D^2) adjusted information size, where D^2 is the relative variance when the meta-analysis model is changed from random to fixed-effects will be calculated for each outcome. D^2 values will be used to determine whether required information sizes were reached.[18] Monitoring boundaries for benefit or futility will be constructed using the conventional test and O'Brien-

Fleming test boundaries.[19] Trial sequential analyses will be conducted using Trial Sequential Analysis version 0.9.5.5beta (Copenhagen Trial Unit, Copenhagen, Denmark) with an intention to maintain an overall 5% risk of type I error and 80% power.[20]

All statistical analyses will be conducted using:

- R version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria)
- Stata version 14 (StataCorp LLC, College Station, Texas, USA)

References

1 Thomas SR, Jamieson DR, Muir KW. Randomised controlled trial of atraumatic versus standard needles for diagnostic lumbar puncture. *BMJ* 2000; **321**: 986–90.

2 Arendt K, Demaerschalk BM, Wingerchuk DM, Camann W. Atraumatic lumbar puncture needles: after all these years, are we still missing the point? *Neurologist* 2009; **15**: 17–20.

3 Celleno D, Capogna G, Costantino P, Catalano P. An anatomic study of the effects of dural puncture with different spinal needles. *Reg Anesth* 1993; **18**: 218–21.

4 Moisset X, Ruet A, Brochet B, et al. Who performs lumbar puncture, how many do they perform, how and why? A retrospective study of 6,594 cases. *Eur Neurol* 2016; **76**: 8–11.

5 Birnbach DJ, Kuroda MM, Sternman D, Thys DM. Use of atraumatic spinal needles among neurologists in the United States. *Headache* 2001; **41**: 385–90.

6 Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015; **350**: g7647.

7 Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; **339**: b2535.

8 Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009; **339**: b2700.

9 Higgins JP, Green S, eds. Cochrane handbook for systematic reviews of interventions. Version 5.1.0. Oxford: The Cochrane Collaboration, 2011. http://handbook-5-1.cochrane.org/ (accessed Aug 4, 2015).

10 Headache Classification Committee of the International Headache Society. The international classification of headache disorders, 3rd edition (beta version). *Cephalalgia* 2013; **33**: 629–808.

11 Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011; **343**: d5928.

12 DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**: 177–88.

13 Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; **327**: 557–60.

14 Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994; **50**: 1088–101.

15 Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; **315**: 629–34.

16 Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; **336**: 924–26.
17 Wetterslev J, Thorlund K, Brok J, Gluud C. Trial sequential analysis may establish when firm evidence is reached in cumulative meta-analysis. *J Clin Epidemiol* 2008; **61**: 64–75.
18 Wetterslev J, Jakobsen JC, Gluud C. Trial sequential analysis in systematic reviews with meta-analysis. *BMC Med Res Methodol* 2017; **17**: 39.
19 O'Brien PC, Fleming TR. A multiple testing procedure for clinical trials. *Biometrics* 1979; **35**: 549–56.
20 Thorlund K, Engstrøm J, Wetterslev J, Brok J, Imberger G, Gluud C. User manual for trial sequential analysis (TSA). Copenhagen Trial Unit, Centre for Clinical Intervention Research, Copenhagen, Denmark. 2011. p. 1–115. Available from http://ctu.dk/tsa (accessed Mar 30, 2017).

Database	Search terms	
Medline	1	spinal puncture/
	2	(spinal adj2 (puncture* or tap or taps)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
	3	lumbar punctur*.mp.
	4	dural punctur*.mp.
	5	spine punctur*.mp.
	6	((spine or spinal or lumbar or subarachnoid) adj2 block*).mp.
	7	spinal drain*.mp.
	8	spinal fluid drain*.mp.
	9	cerebrospinal fluid drain*.mp.
	10	anesthesia, spinal/
	11	anesthesia, obstetrical/
	12	anesthesia/
	13	an?esthe*.mp.
	14	myelography/
	15	myelography.mp.
	16	(spinal epidural adj2 (combined or block* or an?esthes* or technique* or procedure* or method*)).mp.
	17	(continuous spinal adj2 (combined or block* or an?esthes* or technique* or procedure* or method*)).mp.
	18	or/1-17
	19	atraumatic needle*.mp.
	20	sprotte.mp.
	21	whitacre.mp.
	22	((non cutting or noncutting or non-cutting or pencil point* or pencil-point*) adj2 needle*).mp.
	23	pencan.mp.
	24	gertie marx.mp.
	25	zimmon.mp.
	26	traumatic needle*.mp.
	27	quincke.mp.
	28	cutting needle*.mp.
	29	knife needle*.mp.
	30	standard needle*.mp.
	31	conventional needle*.mp.
	32	greene.mp.
	33	(green adj2 needle*).mp.
	34	spinal needle*.mp.
	35	lumbar puncture needle*.mp.
	36	tuohy.mp.
	37	crawford.mp.
	38	eldor.mp.
	39	hustead.mp.
	40	weiss.mp.
	41	wagner.mp.
	42	cheng.mp.
	43	crawley.mp.
	44	foldes.mp.
	45	bell.mp.
	46	brace.mp.
	47	huber.mp.
	48	scott.mp.
	49	"needle through needle".mp.
	50	or/19-49
	51	18 and 50

Table a1: **Search strategy for the Medline database using the Ovid interface**