Anesth Pain Med. 2021 October; 11(5):e119674. doi: 10.5812/aapm.119674.

Published online 2021 November 14. **Methods Article**

Aminophylline for Prevention and/or Treatment of Post-Dural Puncture Headache: A Systematic Review and Meta-Analysis Study Protocol

Ali Reza Safarpour [1], Manoosh Mehrabi [2,*], Firoozeh Tarkesh [1], Hadis Ashrafizadeh [3], Abbasali Keshtkar [4], Hassan Askari [1], Danya Abazari [5], Afshin Amini [6] and Reza Barati-Boldaji [1]

[1] Gastroenterohepatology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[2] Department of E-Learning, Virtual School, Shiraz University of Medical Sciences, Shiraz, Iran
[3] Department of Nursing, School of Nursing and Midwifery, Student Research Committee, Ahvaz Jundishapur University of Medical Science, Ahvaz, Iran
[4] Department of Health Sciences Education Development, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[5] Department of Cellular & Physiological Sciences & the Brain Research Center, University of British Columbia, Vancouver, Canada
[6] Department of Anesthesiology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

[*] *Corresponding author*: Department of E-Learning, Virtual School, Shiraz University of Medical Sciences, Shiraz, Iran. Email: mehrabi.manoosh@gmail.com

Received 2021 September 17; **Revised** 2021 October 18; **Accepted** 2021 October 26.

Abstract

Objectives: Post-dural Puncture Headache (PDPH) is prevalent among individuals undergoing lumbar punctures. The non-invasive effect of some drugs, such as aminophylline on PDPH has been investigated in several clinical studies. As there is no comprehensive systematic review and meta-analysis about the preventive and therapeutic effects of aminophylline on PDPH in the literature, the clinical effectiveness of this drug on the prevention and/or treatment of PDPH will be assessed in this study.

Methods: PubMed/MEDLINE, Embase, WoS (Clarivate Analytics), the Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL Complete, Scopus, and Google Scholar as electronic databases will be precisely searched for clinical studies that assessed the effect of aminophylline on PDPH. Studies between 01-01-1980 and 30-06-2020 will be evaluated in this study, and there will not be any language restrictions. Contradictions between the reviewers within any phase of the study (screening, selecting, quality assessment, and data extraction) will be resolved by consensus; in case of unsolved disagreements, a third reviewer will eventually decide. The combination method will be applied according to the methodological resemblance in the selected articles using the Random Effect Model or the Fixed Effect Model. Also, for the included articles, forest plots will be drawn. For assessing statistical heterogeneity, the I^2 statistic and the Q-statistic test will be applied. In addition, funnel plots will be used for assessing non-significant study effects and potential reporting bias. Furthermore, Egger's and Begg's tests will be done, and publication bias will be indicated by significant findings ($P < 0.05$).

Conclusions: It is expected that the results of this study will be of benefit to researchers and clinicians for managing PDPH, and will be reported in conferences and publications.

Keywords: Aminophylline, Post-Dural Puncture Headache, Lumbar Puncture

1. Background

Lumbar puncture is an invasive technique mainly performed for sampling Cerebrospinal Fluid (CSF) or injecting medications such as anesthetics (1-3). Post-dural Puncture Headache (PDPH) is prevalent among individuals undergoing lumbar puncture (4, 5). This type of headache can be accompanied by hearing loss, tinnitus, etc. (6-9). Moreover, patients and their families incur enormous health costs as a result of various types of headaches (10-13).

The incidence of PDPH has been estimated between 1% and 40% based on the gauge and orientation of needles, the operator proficiency, etc. (14, 15). The incidence rate of PDPH can also be associated with the type of lumbar puncture; for example, less than 10% of cases with spinal anesthesia and 36% of cases with diagnostic lumbar puncture can experience PDPH (6, 15).

The pathophysiology of this type of headache has not been fully comprehended (16). According to several studies, making a dural puncture can result in CSF leakage from the subarachnoid space, and it eventually leads to a decrease in the pressure and volume of CSF (17). The loss of CSF volume can affect pain-sensitive structures, followed by a headache. On the other hand, the lost CSF volume trig-

gers an increment in blood flow, vasodilation, and PDPH (18). Moreover, some studies hypothesized the association between a low substance P concentration and a higher risk of PDPH (19).

There are several interventions to relieve different types of pain (7, 20). Also, various interventions are recommended to be performed before, throughout, or promptly after the procedure of lumbar puncture in order to prevent PDPH (21). For example, some limitations in patients' mobility, such as lying down and drinking plenty of fluids are usually advised by doctors after a lumbar puncture. However, in two Cochrane systematic reviews, Arevalo-Rodriguez et al. and April et al. could not demonstrate the effectiveness of bed rest or fluid supplementation after lumbar puncture for preventing PDPH (22, 23).

Several pharmacological options have also been assessed for preventing PDPH; however, their clinical effectiveness needs more investigation (24). Basurto Ona et al. in a systematic review examined studies using drug options for the prevention of PDPH through searching in the Cochrane Central Register of Controlled Trials, MEDLINE, MEDLINE in Process, EMBASE, and CINAHL (6). The results of this study showed that aminophylline, a methylxanthine drug that is an active metabolite of theophylline, could decrease the number of patients with PDPH in comparison with the control group among women experiencing elective cesarean sections (6). Along with this finding, Sadeghi et al., in a double-blinded randomized study reported the clinical effectiveness of a single dose of intravenous aminophylline for preventing PDPH in cesarean section (25).

Based on several studies, PDPH can be relieved by bed rest, the prone position, hydration, caffeine, analgesics, and the invasive technique of epidural blood patch (18, 26). There is also some research that has investigated the efficacy of therapeutic drugs on relieving PDPH; for example, the effectiveness of methylxanthine derivatives for treating PDPH has been assessed in several studies (25). Basurto Ona et al. designed a systematic review to examine the safety and effectiveness of pharmacological drugs administered for the treatment of PDPH; studies until 2014 were evaluated in this systematic review. They searched in the Cochrane Central Register of Controlled Trials, EMBASE, CINAHL, and MEDLINE, and MEDLINE in Process. Basurto Ona et al. reported that Gabapentin, theophylline, and hydrocortisone could reduce pain severity scores. Additionally, the results showed that administrating theophylline compared to conventional therapy increased the percentage of participants who reported improved pain scores (18).

In a randomized clinical trial, Wu et al. reported the safety and clinical effectiveness of the early administration of aminophylline for decreasing pain intensity compared to the placebo treatment (1); these findings were in line with a previous multicenter clinical study performed by this research group (27).

Despite that the therapeutic mechanism of aminophylline on PDPH is not fully described yet (16), some studies suggest that it might be responsible for blocking adenosine receptors, constricting blood vessels, and blocking pain transmission. It also seems that aminophylline can increase the intracellular levels of cyclic adenosine monophosphate. Furthermore, calcium uptake by the endoplasmic reticulum of endothelial cells might be suppressed with the administration of aminophylline; this process induces CSF secretion.

Although several randomized controlled studies have reported the preventive and therapeutic effects of aminophylline on PDPH, these effects have not been investigated in a comprehensive systematic review and meta-analysis to rule out the unrepresentative statistical results and confirm the potential advantages. Therefore, this study will be conducted to better comprehend the effect of aminophylline on preventing and/or treating PDPH. It should be noted that two systematic reviews about the preventive and curative effects of different drugs on PDPH searched the relevant studies until 2012 and 2014, respectively (6, 18); however, we will search more recent studies until 30-06-2020 and a higher number of electronic databases. This paper can inspire subsequent practice guidelines, and clinicians might derive benefit from the results of this comprehensive study.

2. Objectives

2.1. Primary Objective

Investigating the effect of aminophylline on the prevention and/or treatment of PDPH is the primary target of this study.

2.2. Secondary Objectives

1- Estimating the effect of aminophylline on prevention and/or treatment of PDPH by age group.

2- Estimating the effect of aminophylline on prevention and/or treatment of PDPH by gender.

3- Evaluating potential heterogeneity and finding its sources.

3. Methods

The study protocol of this systematic review and meta-analysis was written based on the Cochrane Handbook guidelines and reiterated (PROSPERO registration number:

CRD42020211990). The process of selecting studies will be reported based on the Preferred Reporting Items for Systematic review and Meta-analysis Protocols (PRISMA-P) 2015 (28-30). Moreover, the planned start and end dates for the study are 30 October 2020 and 31 December 2021, respectively; however, these dates may change due to reviewers' comments and also the editor's final decision.

3.1. Patient and Public Involvement

No patient will be involved.

3.2. Inclusion and Exclusion Criteria

3.2.1. Study Types

All the trial designs, such as one group before and after, two groups before and after, and sequential analysis trials that examined the preventive and/or therapeutic effects of aminophylline on PDPH would be included in this study. This study will not use case reports, case series, observational studies, non-randomized trials, cross-sectional studies, review articles, and protocol papers.

3.2.2. Types of Participants

All the participants (male, female, or both) undergoing lumbar puncture before surgery (including all surgeries) whose anesthesia was induced by an anesthesiologist will be considered in this study.

3.3. Intervention

To be analyzed in this study, interventions must have aimed to prevent and/or ameliorate PDPH using intravenously administered aminophylline.

3.4. Comparator

Comparator arms of the included studies might be groups of participants that did not administer aminophylline to prevent and/or ameliorate PDPH.

3.5. Outcomes

The assessment of PDPH will be the outcome measure of this study, assessed based on the Visual Analog Scale (VAS) score, which is considered a continuous variable. The VAS is a validated, subjective measure for acute and chronic pain. Scores are recorded by making a handwritten mark on a 10-cm line that represents a continuum between "no pain" and "worst pain". The effect size is the Standardized Mean Difference, which is defined as the difference between the two means of the VAS score before and after the intervention. The data of PDPH prevention and treatment will be extracted and analyzed separately; in other words, the treatment and prevention of PDPH will be considered as two different outcomes. All studies that had reported PDPH as a categorical variable will be excluded.

3.6. Sampling Method

The sampling process would be performed through a random method (simple, systematic, stratified, cluster, or a mixture of the mentioned types) in the preliminary studies that meet the inclusion criteria of this study; the preliminary studies that have not used any random sampling method or public calls will be ruled out.

3.7. Selection Phase Examining (pilot)

A pilot phase will be initially performed on a few articles for the selection process. Within this stage, the reliability of authors (FT and HA) in comprehending the eligibility criteria will be examined. Additionally, the mentioned pilot phase will be useful for verifying the clarity degree of the inclusion criteria.

3.8. Search Strategy Components

In order to reach the most inclusive search, the PICO (Patient, Intervention, Comparison/Control, and Outcome) framework will be applied for developing search terms related to the intervention (aminophylline) and outcome (PDPH) components.

Key search terms are written in Table 1. The relevant formatting would be applied for each database. Thesaurus systems that include Medical Subject Headings (MeSH) and Emtree, the free text method, related papers, and experts' views will be used to obtain the equivalents of components. The other methods to find relevant studies are mentioned in the following.

3.9. Electronic Database Search

Computerized searches would be conducted in the electronic databases of Scopus, Embase (Embase.com), PubMed/MEDLINE, Google Scholar, WoS (Clarivate Analytics), the Cochrane Central Register of Controlled Trials (CENTRAL), and CINAHL Complete.

3.10. Main Journals and Reference Lists of Relevant Studies

In key journals, a manual search would be meticulously conducted. These journals would be chosen according to the analysis of search outcomes of databases. Another search will be done in order to find journals with the largest pool of available sources relevant to the topic of the study; this search would be according to the described eligibility criteria. Moreover, another search would be manually performed in the reference lists of the finally included papers chosen for quality assessment. The reference lists of the previous review articles will be checked for any probable missed-out paper.

Table 1. Search Strategies Used in PubMed/MEDLINE Between 01-01-1980 and 30-06-2020

	Search terms
1	((Headache AND Post-Dural Puncture) OR (Headaches AND Post-Dural Puncture) OR "Post Dural Puncture Headache" OR "Post-Dural Puncture Headaches" OR "Postdural Puncture Headache" OR (Headache AND Postdural Puncture) OR (Headaches AND Postdural Puncture) OR "Postdural Puncture Headaches" OR "Post-Lumbar Puncture Headache" OR (headache AND lumbar puncture) OR "lumbar puncture headache" OR "lumbar puncture headaches" OR "post lumbar puncture headache" OR "post lumbar puncture headaches" OR "postlumbar puncture headache" OR "postlumbar puncture headaches")
2	("Theophylline Ethylenediamine" OR (Ethylenediamine AND Theophylline) OR Theophyllamine OR Phyllotemp OR Mundiphyllin OR "Theophyllamin Jenapharm" OR "Theophyllin EDA-ratiopharm" OR "Theophyllin EDA ratiopharm" OR "Theophyllin EDAratiopharm" OR Truphylline OR Afonilum OR Carine OR Eufilina OR Euphyllin OR Aminodur OR Aminophyllin OR "Aminophylline DF" OR Cardophyllin OR Clonofilin OR Corophyllin OR Diaphyllin OR Drafilyn OR Duraphyllin OR "Eufilina Venosa" OR "Euphyllin Retard" OR Euphylline OR Godafilin OR Mini-Lix OR "Mundiphyllin Retard" OR Novophyllin OR Phyllocontin OR Somophyllin OR Tari-Dog OR "afi phyllin" OR allenfillina OR "amino phylline" OR "aminocardol" OR aminofilina OR aminomal OR "aminomal r" OR aminophelline OR aminophyl OR aminophylline OR "aminophylline dye free" OR "aminophylline in sodium chloride" OR aminoserp OR ammophyllin OR ammophylline OR androphyllin OR anephyllin OR anpillin OR asiphylline OR asthcontin OR biophylline OR cardiofillina OR cardiofilma OR cardiomin OR cardiophyllin OR cardiophylline OR cardofilina OR cardophylin OR cardophyllin OR carena OR carine OR corophyllin OR corphyllamin OR corphyllamine OR corphyllin OR diaphyllin OR diaphylline OR diophyllin OR diurophylline OR diuxanthine OR "drafilyn z" OR dyspnein OR emphylline OR enphylline OR escophyllin OR ethophylline OR "etilen xantisan" OR eudiamin OR eufilin OR eufilina OR "eufilina mite" OR "eufilina retard" OR euphylline OR "euphylline la" OR filotempo OR genophyllin OR godafilin OR grifomin OR grofomin OR inophyline OR inophylline OR kyophyllin OR leofillina OR lixaminol OR lyphomed OR metaphyllin OR metaphylline OR methaphyllin OR minaphil OR miofilin OR miofyllin OR miophylline OR optophyllin OR "paediatric asthcontin for children sr" OR paralon OR "pediatric asthcontin for children sr" OR peterphyllin OR phylcardin OR phyllindon OR phyllocontin OR "phyllocontin continus" OR phyllocormin OR phyllotemp OR "phyllotemp retard" OR "purophyllin laevosan" OR "rectalad aminophylline" OR schiwaphyllin OR somophyllin-df OR stenovasan OR suppophylline OR syntophyllin OR syntophylline OR tefamin OR teofylamin OR teofyllamin OR theoaethamin OR theodrox OR theofyllamin OR theolamine OR theolone OR theophylamin OR theophylamine OR theophyldine OR theophyllamin OR theophyllamine OR "theophylline ethylenediamine" OR theosumman OR thephyldine OR thilophyllin OR truphylline OR unifilin OR "v 37" OR variaphylline OR vasophylline)
3	1 OR 2
4	1980/01/01:2020/06/30 [dp]
5	3 AND 4

3.11. Grey Literature

Theses relevant to the study topic will be found using electronic databases of Scopus and ProQuest plus contacting the authors. Furthermore, electronic databases will be used for finding proceedings and conference papers.

3.12. Contacting Experts

For unpublished papers and theses (for example, non-significant result studies or studies conducted without publication in peer review journals), the experts will be asked to share their studies related to the topic of this study. In addition, papers will be included if they are acceptable in terms of relevant data and quality analysis.

3.13. Publication Date

All available relevant studies published between 01-01-1980 and 30-06-2020 would be considered in this study.

3.14. Publication Language

There would not be any language limitations in the present study. The studies written in a non-English language, which will be included in the finally selected studies, should have been initially translated by Google Translate. After that, an official translator will recheck them.

3.15. Constructing the Search Syntax

As can be seen in Table 1, 'Intervention (aminophylline)' and 'Outcome (PDPH)' are the components that will be searched for extracting relevant studies. This search strategy is predicted to provide the largest possible number of clinical studies within the electronic databases by carrying out a comprehensive search. This search syntax would be appropriate for being used in other electronic databases. The thorough search syntax for using in PubMed has been presented in Table 1. All the search steps will be detailed, and the final report will document them. Eventually, all the searches performed in different databases will be entered into the Endnote software.

3.16. Study Screening and Selection

One contributor outside the group of authors was employed for examining the subjects' correct perception of the eligibility criteria throughout the screening stage. This contributor exerted the corresponding criteria on two output files, The mentioned procedure was performed before registering the protocol on the PROSPERO.

The process of searching will be performed based on the written syntax relevant to each electronic database. Two authors (ARS and MM) will assess the titles and abstracts of papers according to a previously prepared checklist considering the eligibility criteria within the screening stage; articles relevant to the study subject will be found and extracted.

If a study does not meet any of the eligibility criteria, it will be eliminated at this point. Although papers with deficient information in one or some of the eligibility criteria would be firstly included, the final determination will be made after reading the full texts of these papers.

Within the selection phase, two of the contributors (ARS and HA) will precisely review the full texts of studies obtained from the screening stage; they will independently select the final studies.

If any disagreement occurs within the mentioned phases, it will be resolved by consensus. If the disagreement remains unsolved, the third expert's opinion (AK) will be considered.

3.17. Risk of Bias Assessment

Assessing the methodological quality of clinical trials will be performed by using the Cochrane Collaboration's tool for assessing the risk of bias (31). The Cochrane tool considers random sequence generation, allocation sequence concealment, insufficient outcome data, blinding of personnel, participants, and outcome assessors, selective outcome reporting, and other possible causes of bias. The overall risk of bias within each included study will be ranked as "high", "low", or "unclear".

This assessment will be independently done by two authors (ARS and MM), and any discordance will be unanimously obviated by consensus, or the third expert's view (AK) will be sought to resolve the case.

3.18. Data Extraction

Three authors (FT, DA, and HAS) will independently complete a predefined data extraction form for all the included papers. Any disagreement will be discussed to reach an agreement, or a third expert's opinion (AA) will be regarded.

The following information will be documented in the data extraction form: first author's name, publication year, study country, journal name, study design, study location, participants' gender and age, study duration, sample size, the quality scores of papers, the type of operation, the type of headache scale, aminophylline dosage, the type of comparison arm, mean (SD) of pain score in both groups in the studies..

If the included studies contain incomplete statistical data, the authors will independently calculate the required data, or they will make contact with the study authors to collect data; the paper will be excluded after three times of failing to respond to the study authors.

3.19. Data Synthesis and Analysis

Brief information on each included study will be provided in a table. This table will contain the first author's name, publication year, study design, participants' characteristics, and the number of participants in both intervention and comparison groups.

3.20. Statistical Analysis

Stata V.13.1 software (StataCorp, USA) will be applied for the statistical analysis in this study.

3.21. Assessment of Heterogeneity

In order to investigate the statistical heterogeneity of the PDPH score in the intervention and comparison groups of the included studies, the I^2 statistic and Q-statistic test and their corresponding 95% Confidence Intervals (CIs) shall be applied. Heterogeneity values of 0%-40%, 30%-60%, 50%-90%, and 75%-100% will be considered as 'perhaps not important', 'moderate heterogeneity', 'substantial heterogeneity', and 'considerable heterogeneity', respectively. For the Q-test, $P < 0.05$ will be considered statistically significant (32).

3.22. Subgroup Analysis

For the evaluation of the source of statistical heterogeneity, we will perform subgroup analysis according to the type of the evaluated outcomes (treatment or prevention) and the age or gender of the participants.

3.23. Assessment of Publication Bias

Carrying out the most inclusive search at the beginning of the study process is the first approach to address publication bias. Furthermore, funnel plots will be drawn to evaluate the non-significant study effect and potential reporting bias. Egger's test and Begg's test will additionally be executed; significant results ($P < 0.05$) can reveal publication bias; then, the non-parametric 'trim and fill' method will be applied to adjust for this type of bias.

3.24. Sensitivity Analysis

A sensitivity analysis will be done for assessing the methodological quality, data analysis considerations, limitations of the study design, effect of missing data, and the study sample size. The sensitivity analysis will be done according to the one-out remove method. In this method, the other papers will be combined, and they will be compared with each other with one of the papers excluded each time.

3.25. Quality Analysis

Regarding quality analysis, the association between the methodological quality index of the included studies and their outcomes will be completely investigated.

In case of considerable variances between the outcomes of studies with high-quality methodology and the outcomes of studies with poor-quality methodology, a mixture of studies with a minimum acceptable quality shall be considered as a valid and reliable estimation of the combination of these included papers.

3.26. Missing Data

Regarding probable missing data of the final papers, we would try to find the contact information of the corresponding authors to be in correspondence with them and complete the data. Failing to contact the authors will make us eliminate their studies.

4. Conclusions

The present systematic review and meta-analysis will assess the efficacy of aminophylline for the prevention and/or treatment of PDPH. Researchers and clinicians are expected to benefit from the results of this study since they will be able to use the findings of the study to manage PDPH. The results of this study will be reported in publications and presentations at conferences.

5. Strengths and Limitations of this Study

•This study will combine data and assess the value and causes of possible heterogeneity.

•The data reporting will adhere to the Preferred Reporting Items for Systematic reviews and Meta-Analyses Protocols.

•This study uses an inclusive search based on thesaurus systems, including Emtree and MeSh, and carries out its search in large databases, such as Scopus, WOS, MEDLINE/PubMed, Embase, Google Scholar, and ProQuest, with a long time span.

•Methodological biases in the primary studies included may cause uncertainty in the results of the present study.

•One limitation of this study is that the authors are only fluent in Persian and English. Therefore, a translator will be required when the papers are published in other languages.

Acknowledgments

The authors wish to declare their gratefulness to Professor Abbas Rezaianzadeh, the Vice-Chancellor for Research at Shiraz University of Medical Sciences, for his support of systematic review and meta-analysis projects.

Footnotes

Authors' Contribution: As the senior author, ARS took care of the process of preparing this study protocol. All the authors were involved in the conception and design of this study protocol and the authors' contributions are as follows. ARS contributed to the formulation of the research question, topic refinement, study selection forms, review design, analysis plan, and writing the manuscript. Additionally, ARS wrote the search syntax under the supervision of AA and AK. AK, MM, and AA worked on the formulation of the research question, topic refinement, review design, and gave pivotal feedback on the content of the manuscript. ARS will supervise the data extraction phase. In addition, RBB, MM, FT, HA, HAS, and DA will be responsible for database management and performing the literature handle/search. All the individuals in the author team read the final paper and approved it.

Conflict of Interests: The authors declare that they have no conflict of interest.

Ethical Approval: As patient information will be collected from previously published papers, there is no necessity for obtaining ethical approval. The findings of this study will be available in a peer-reviewed journal and presented at conferences related to the topic. If any deviation from the protocol occurs, it will be completely recorded in the final report.

Funding/Support: This research did not receive any specific grant from any funding agency in the commercial, public, or not-for-profit sectors.

References

1. Wu C, Guan D, Ren M, Ma Z, Wan C, Cui Y, et al. Aminophylline for treatment of postdural puncture headache: A randomized clinical trial. *Neurology*. 2018;**90**(17):e1523–9. eng. doi: 10.1212/wnl.0000000000005351. [PubMed: 29572284].
2. Sievänen H, Kari J, Halonen S, Elomaa T, Tammela O, Soukka H, et al. Real-time detection of cerebrospinal fluid with bioimpedance needle in paediatric lumbar puncture. *Clin Physiol Funct Imaging*. 2021;**41**(4):303–9. eng. doi: 10.1111/cpf.12697. [PubMed: 33682245]. [PubMed Central: PMC8251608].
3. Jane LA, Wray AA. *Lumbar Puncture*. Treasure Island (FL): StatPearls Publishing; 2021.
4. Cognat E, Koehl B, Lilamand M, Goutagny S, Belbachir A, de Charentenay L, et al. Preventing Post-Lumbar Puncture Headache. *Ann Emerg Med*. 2021;**78**(3):443–50. eng. doi: 10.1016/j.annemergmed.2021.02.019. [PubMed: 33966935].

5. de Almeida SM, Shumaker SD, LeBlanc SK, Delaney P, Marquie-Beck J, Ueland S, et al. Incidence of post-dural puncture headache in research volunteers. *Headache*. 2011;**51**(10):1503–10. eng. doi: 10.1111/j.1526-4610.2011.01959.x. [PubMed: 21797856]. [PubMed Central: PMC3217171].
6. Basurto Ona X, Uriona Tuma SM, Martínez García L, Solà I, Bonfill Cosp X. Drug therapy for preventing post-dural puncture headache. *Cochrane Database Syst Rev*. 2013;**2013**(2):Cd001792. eng. doi: 10.1002/14651858.CD001792.pub3. [PubMed: 23450533]. [PubMed Central: PMC8406520].
7. Hadianfard MJ, Aminlari A, Daneshian A, Safarpour AR. Effect of Acupuncture on Pain and Quality of Life in Patients with Lumbar Spinal Stenosis: A Case Series Study. *J Acupunct Meridian Stud*. 2016;**9**(4):178–82. eng. doi: 10.1016/j.jams.2015.11.032. [PubMed: 27555222].
8. O'Shaughnessy SM, Fitzgerald CWR, Katiri R, Kieran S, Loughrey JPR. Permanent hearing loss and tinnitus following epidural analgesia complicated by accidental dural puncture. *Int J Obstet Anesth*. 2020;**43**:9–12.
9. Shivan M, Smita P, Parul M, Keshaban M. Effect of reinsertion of the spinal needle stylet after spinal anaesthesia procedure on post dural puncture headache in women undergoing caesarean delivery. *Indian J Anaesth*. 2020;**64**(11):971–8. eng. doi: 10.4103/ija.IJA_1080_20. [PubMed: 33487683]. [PubMed Central: PMC7815016].
10. Namjoo S, Seirafi M, Assarzadegan F, Borjali A. Cognitive Processing Styles and Mindfulness on Pain Intensity Prediction in People with Primary Headache. *Anesth Pain Med*. 2018;**8**(6). eng. e82470. doi: 10.5812/aapm.82470. [PubMed: 30719414]. [PubMed Central: PMC6347729].
11. Namjoo S, Borjali A, Seirafi M, Assarzadegan F. The Role of Mindfulness in Predicting Pain Interference in Patients with Primary Headache. *Anesth Pain Med*. 2019;**9**(4). eng. e88340. doi: 10.5812/aapm.88340. [PubMed: 31750092]. [PubMed Central: PMC6820068].
12. Namjoo S, Borjali A, Seirafi M, Assarzadegan F. Use of Mindfulness-based Cognitive Therapy to Change Pain-related Cognitive Processing in Patients with Primary Headache: A Randomized Trial with Attention Placebo Control Group. *Anesth Pain Med*. 2019;**9**(5). eng. e91927. doi: 10.5812/aapm.91927. [PubMed: 31903329]. [PubMed Central: PMC6925538].
13. Amighi D, Majedi H, Tafakhori A, Orandi A. The Efficacy of Sphenopalatine Ganglion Block and Radiofrequency Denervation in the Treatment of Cluster Headache: A Case Series. *Anesth Pain Med*. 2020;**10**(6). eng. e104466. doi: 10.5812/aapm.104466. [PubMed: 34150572]. [PubMed Central: PMC8207843].
14. Weji BG, Obsa MS, Melese KG, Azeze GA. Incidence and risk factors of postdural puncture headache: prospective cohort study design. *Perioper Med (Lond)*. 2020;**9**(1):32. eng. doi: 10.1186/s13741-020-00164-2. [PubMed: 33292510]. [PubMed Central: PMC7650180].
15. Meshram S, Deshmukh P, Sabale P, Bankar N, Chandak VC. Incidence of Post Dural Puncture Headache in Our Set Up with Quincke Spinal Needle: An Observational Crossectional Study. *Indian J Forensic Med Toxicol*. 2020;**14**(4).
16. Abate SM, Ahmed S, Anbese GM, Basu B. Efficacy and safety of prophylactic intrathecal normal saline for prevention of Post Dural Puncture Headache among women undergoing cesarean section under spinal anesthesia: A randomized controlled trial. *Int J Surg Open*. 2021;**35**:100396.
17. Bezov D, Lipton RB, Ashina S. Post-dural puncture headache: part I diagnosis, epidemiology, etiology, and pathophysiology. *Headache*. 2010;**50**(7):1144–52. eng. doi: 10.1111/j.1526-4610.2010.01699.x. [PubMed: 20533959].
18. Ona XB, Osorio D, Cosp XB. Drug therapy for treating post-dural puncture headache. *Cochrane Database Sys Rev*. 2015;(7). doi: 10.1002/14651858.CD007887.pub3. [PubMed: 26176166]. [PubMed Central: PMC6457875].
19. Clark JW, Solomon GD, Senanayake PD, Gallagher C. Substance P concentration and history of headache in relation to postlumbar puncture headache: towards prevention. *J Neurol Neurosurg Psychiatry*. 1996;**60**(6):681–3. eng. doi: 10.1136/jnnp.60.6.681. [PubMed: 8648338]. [PubMed Central: PMC1073955].
20. Farahmand S, Shafazand S, Alinia E, Bagheri-Hariri S, Baratloo A. Pain Management Using Acupuncture Method in Migraine Headache Patients; A Single Blinded Randomized Clinical Trial. *Anesth Pain Med*. 2018;**8**(6). eng. e81688. doi: 10.5812/aapm.81688. [PubMed: 30666295]. [PubMed Central: PMC6334036].
21. Zangouei A, Zahraei SAH, Sabertanha A, Nademi A, Golafshan Z, Zangoue M. Effect of Low-Dose Intravenous Ketamine on Prevention of Headache After Spinal Anesthesia in Patients Undergoing Elective Cesarean Section: A Double-Blind Clinical Trial Study. *Anesth Pain Med*. 2019;**9**(6). eng. e97249. doi: 10.5812/aapm.97249. [PubMed: 32280620]. [PubMed Central: PMC7118677].
22. Arevalo-Rodriguez I, Ciapponi A, Roqué i Figuls M, Muñoz L, Bonfill Cosp X. Posture and fluids for preventing post-dural puncture headache. *Cochrane Database Syst Rev*. 2016;**3**(3):Cd009199. eng. doi: 10.1002/14651858.CD009199.pub3. [PubMed: 26950232].
23. April MD, Long B. Does Bed Rest or Fluid Supplementation Prevent Post-Dural Puncture Headache? *Ann Emerg Med*. 2018;**71**(5):e55–7. eng. doi: 10.1016/j.annemergmed.2017.12.011. [PubMed: 29342423].
24. Urits I, Schwartz R, Smoots D, Koop L, Veeravelli S, Orhurhu V, et al. Peripheral Neuromodulation for the Management of Headache. *Anesth Pain Med*. 2020;**10**(6). eng. e110515. doi: 10.5812/aapm.110515. [PubMed: 34150578]. [PubMed Central: PMC8207880].
25. Sadeghi SE, Abdollahifard G, Nasabi NA, Mehrabi M, Safarpour AR. Effectiveness of single dose intravenous aminophylline administration on prevention of post dural puncture headache in patients who received spinal anesthesia for elective cesarean section. *World J. Med. Sci*. 2012;**7**(1):13–6.
26. Patel R, Urits I, Orhurhu V, Orhurhu MS, Peck J, Ohuabunwa E, et al. A Comprehensive Update on the Treatment and Management of Postdural Puncture Headache. *Curr Pain Headache Rep*. 2020;**24**(6):24. eng. doi: 10.1007/s11916-020-00860-0. [PubMed: 32323013].
27. Wu C, Lian Y, Guan D, Wang L, Miao Y, Xie N, et al. A Multicenter Clinical Study on Treating Post-Dural Puncture Headache with an Intravenous Injection of Aminophylline. *Pain Physician*. 2016;**19**(5):E761–5. eng. [PubMed: 27389119].
28. Dissemination CFRA. *Systematic reviews: CRD's guidance for undertaking reviews in healthcare*. York: University of York NHS Centre for Reviews & Dissemination; 2009.
29. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *Jama*. 2000;**283**(15):2008–12. eng. doi: 10.1001/jama.283.15.2008. [PubMed: 10789670].
30. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;**6**(7). eng. e1000097. doi: 10.1371/journal.pmed.1000097. [PubMed: 19621072]. [PubMed Central: PMC2707599].
31. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev*. 2019;**10**:Ed000142. eng. doi: 10.1002/14651858.Ed000142. [PubMed: 31643080].
32. Safarpour AR, Mehrabi M, Keshtkar A, Edjtehadi F, Bagheri Lankarani K. Systematic review and meta-analysis of the incidence and prevalence and 30-year trend of inflammatory bowel diseases in Asia: a study protocol. *BMJ Open*. 2019;**9**(11). eng. e031854. doi: 10.1136/bmjopen-2019-031854. [PubMed: 31748306]. [PubMed Central: PMC6886900].