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doi: 10.1016/j.bja.2020.10.002
Advance Access Publication Date: 26 October 2020

Use of sphenopalatine ganglion block in patients with postdural puncture headache: a pilot meta-analysis

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Keywords: epidural blood patch; headache; nasal trauma; postdural puncture headache; sphenopalatine ganglion block

Editor—We read with great interest the article by Jespersen and colleagues,[1] who reported no significant difference in pain relief between postdural puncture headache (PDPH) patients with sphenopalatine ganglion block treatment and those without.[1] However, sphenopalatine ganglion block has been found to be an effective intervention for PDPH in a case series,[2] and a retrospective study has shown better effectiveness of sphenopalatine ganglion block against PDPH compared with epidural blood patch.[3] Because of these conflicting results, we wished to perform a pilot meta-analysis to investigate whether sphenopalatine ganglion block is superior to conventional treatment (e.g. epidural blood patch or analgesic treatment) in patients with PDPH in terms of analgesic efficacy and safety.

This meta-analysis was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines. The databases of PubMed, Medline, Google Scholar, Embase, and the Cochrane controlled trials register were searched using the keywords 'postdural puncture headache', 'postdural puncture headache', 'dural puncture', 'epidural blood patch', 'PDPH', 'sphenopalatine ganglion block', 'transnasal local anaesthetic', 'sphenopalatine', 'SPGB', 'SGB', and their synonyms to identify studies that compared the analgesic effect of sphenopalatine ganglion block with that of other conventional methods from inception to May 30, 2020. We conducted our search by combining these keywords and the Boolean operators 'AND' and 'OR'. The full PubMed search strategy is available in Supplementary Table S1. No limits were applied for language and year of publication. The inclusion criteria were (1) studies that compared the analgesic effect of sphenopalatine ganglion block with that of placebo or other interventions and (2) those that reported incidence of headache relief as an outcome in patients with PDPH. Exclusion criteria were (1) case reports, case series, abstracts, or conference presentations and (2) unavailability of information regarding outcomes.

Two authors independently examined eligible studies, from which data were extracted. In the event of discrepancy, the third author was consulted. The primary outcome was the success rate in headache relief according to the criteria of each trial at 30 min after sphenopalatine ganglion block or other therapeutic interventions. We adopted headache relief 30 min after sphenopalatine ganglion block as the primary outcome because previous studies have identified rapid headache relief after sphenopalatine ganglion block.[4,5] The secondary outcome was the incidence of adverse events. The risk of bias was assessed for RCTs using criteria outlined in *Cochrane Handbook for Systematic Reviews of Interventions*. For non-RCTs or retrospective studies, the risk of bias was not analysed. Cochrane Review Manager (RevMan 5.3; Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for data synthesis and analysis. A random effects model was used for analysis because of anticipated clinical between-study heterogeneity. For dichotomous outcomes, we calculated odds ratios (ORs) with 95% confidence intervals (CIs). The Mantel–Haenszel (MH) method was used to pool dichotomous data and to compute pooled OR with 95% CIs. The I^2 statistic was used for heterogeneity assessment, whereas inconsistency was quantified by defining 0–50%, 51–75%, and 76–100% as low, moderate, and high heterogeneity, respectively. To assess the impact of individual studies on the overall results of the present meta-analysis, we removed one study at a time to re-evaluate the changes in effect size, with significance set at $P<0.05$ for all analyses.

A total of 181 records were identified. After excluding duplicate records ($n=70$) and other reports by title and abstract ($n=108$), three full-text articles including 139 participants

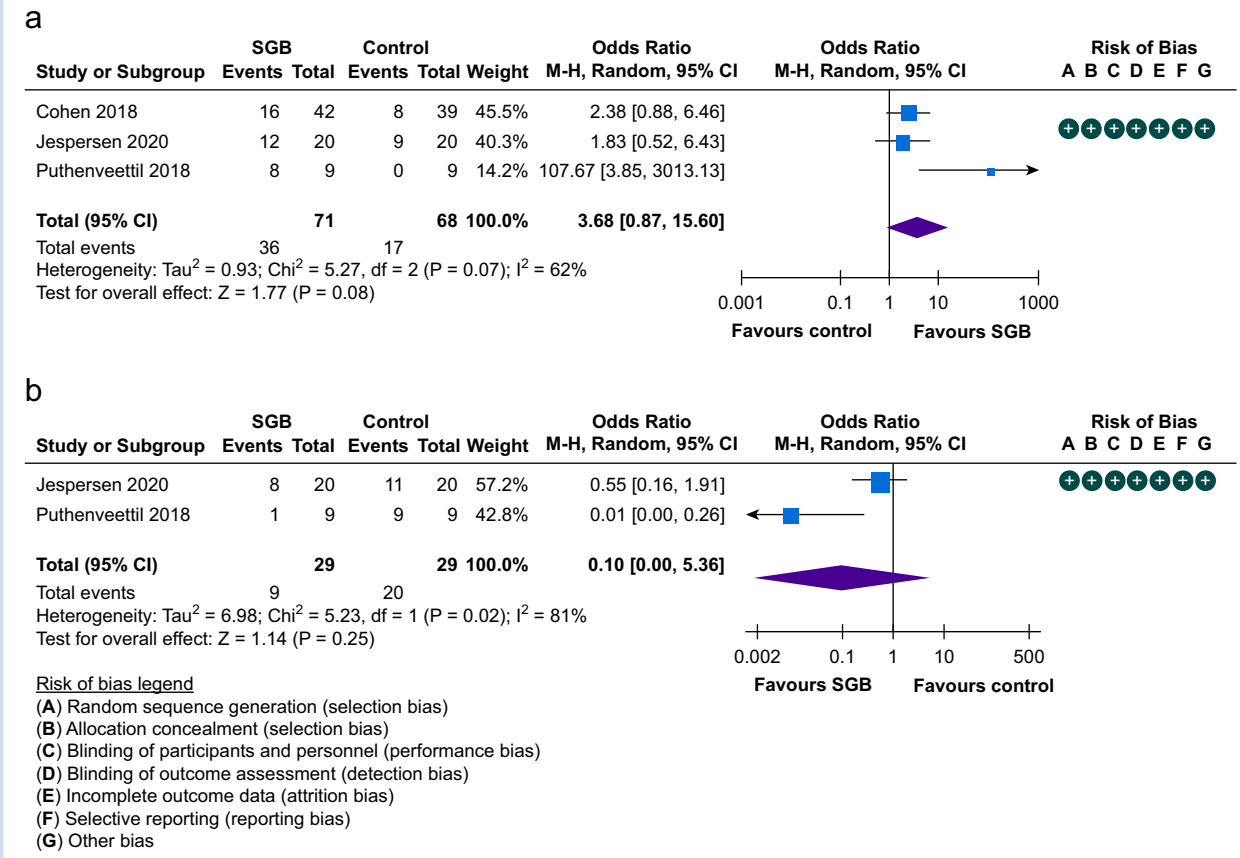

Fig 1. Forest plots for comparison of (a) success rate of pain relief at 30 min and (b) adverse events between sphenopalatine ganglion block (SGB) and control groups. M-H, Mantel–Haenszel; OR, odds ratio; CI, confidence interval.

published from 2018 to 2020 were considered relevant and were read in full (see Supplementary Fig. S1 for flowchart).[1,3,6] The characteristics of the included studies are shown in Supplementary Table S2. Two studies focused on obstetric patients,[3,6] whereas the study by Jespersen and colleagues[1] focused on patients who developed PDPH within 3 days after an intended or accidental dural puncture. The primary outcome was reported in all studies,[1,3,6] whereas the secondary outcome was available in two studies.[1,3] A forest plot regarding the success rate in headache relief at 30 min after intervention is presented in Fig. 1a, indicating no significant difference in success rate in headache relief between sphenopalatine ganglion block and other interventions (pooled OR=3.68; 95% CI, 0.87–15.60; P=0.08). After removing the trial using normal saline as control,[1] our results showed no significant difference in therapeutic benefit between sphenopalatine ganglion block and the two conventional treatments (epidural blood patch or paracetamol) (OR=11.46; 95% CI, 0.28–477.08; P=0.20), suggesting no significant therapeutic advantage of sphenopalatine ganglion block over these approaches. There was also no significant difference in the incidence of adverse events in patients receiving sphenopalatine ganglion block compared with those undergoing other treatments (OR=0.10; 95% CI, 0.00–5.36, P=0.25) (Fig. 1b).

The major limitation in the current meta-analysis was that the limited number of patients as well as the differences in definition of pain relief and study design (e.g. retrospective study *vs* randomised controlled studies) may contribute to a high heterogeneity among the included studies, which reduced the strength of our findings. Moreover, differences in therapeutic interventions (e.g. repeating sphenopalatine ganglion block for inadequate pain relief) and local anaesthetics used (e.g. lidocaine 2%[6] *vs* 4 %[1,3]) (Supplementary Table S2) in the included studies may also affect our results. Although the impact of sphenopalatine ganglion block on physical function, quality of life, and the length of hospital stay would also be of interest as secondary outcomes for the current analysis, relevant information was unavailable from the included studies.

Although most retrospective studies have demonstrated effectiveness of sphenopalatine ganglion block against PDPH, our investigation showed that it offered no significant therapeutic advantage over conventional approaches. This finding is consistent with that of the only randomised clinical trial included showing no significant difference in pain relief in patients with PDPH undergoing sphenopalatine ganglion block with local anaesthetics compared with those receiving placebo, which may reflect the actual clinical scenario. Our results should prompt clinicians to conduct large-scale prospective studies to elucidate the therapeutic benefit of sphenopalatine ganglion block in this clinical setting.

Acknowledgements

We pay tribute to the chief librarian of E-Da Hospital, Su-Ying Chiu, for professional assistance in retrieving the full text of the eligible articles for literature appraisal and also confirming the completeness of our search.

Declaration of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.10.005.

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doi: 10.1016/j.bja.2020.10.005
Advance Access Publication Date: 31 October 2020

Immunoglobulin E cross-linking or MRGPRX2 activation: clinical insights from rocuronium hypersensitivity

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Keywords: allergy; hypersensitivity; immunoglobulin E; mast cell; MRGPRX2; rocuronium; skin test

Editor—Mast cell activation via the MRGPRX2 receptor provides a novel paradigm in our knowledge of immunoglobulin E (IgE)/high-affinity IgE receptor (FcεRI)-independent immediate drug hypersensitivity reactions (IDHRs). However, current evidence for activation of the MRGPRX2 receptor comes from animal or *in vitro* studies, and translation of these findings into clinical relevance in humans is difficult and should be critically interpreted.[1–5]

Based on current models, the MRGPRX2-activating potency of neuromuscular blocking agents (NMBAs) is different and does not correspond to their potency to activate the mouse orthologue. For example, rocuronium is ~12 times less potent at the MRGPRX2 receptor in humans than in mice.[1,3] Consequently, many questions remain unanswered, and speculation and controversy, including suggestions to reclassify hypersensitivity reactions to NMBAs, are emerging.[6,7] However, we think that such a generalised mechanistic reclassification with focus on MRGPRX2 activation is premature and likely unjustified. Specifically, it could entail a significant risk for patients, as it has been suggested that in MRGPRX2-dependent reactions, one could consider re-administration with reduced speed or lower dose.[7]