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Neuroanesthesia Abstracts



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Comparison of heated and humidified high flow nasal cannula and traditional facemasks on patient comfort and gas exchange in adult patients undergoing awake craniotomy—a pilot, prospective, randomized controlled study

Submission ID

120

AUTHORS

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INTRODUCTION

Patients undergoing awake craniotomy are exposed to non-humidified, non-warmed oxygen/air mix via face masks for prolonged duration with the inherent limitation of being unable to move due to fixation of the head on a frame with neurosurgical pins. This potentially causes discomfort, inadequate tidal volumes, poor gas exchange, and perioperative lung atelectasis.^{1,2} Improvement of patient comfort by heated and humidified oxygen may result in better breathing, contributing to lesser atelectasis and improved gas exchange.^{3,4} High flow nasal cannula (HFNC) oxygen therapy (OptiflowTM THRIVE [Fisher & Paykel Healthcare]) is an air-oxygen blender, providing high flow (up to 70 L·min⁻¹) of warmed (36 °C) and humidified gas mixture, allowing tighter control of F_1O_2 from 0.2 to 1.0. This pilot, single-centre, prospective, open-labeled, parallel-group, randomized controlled clinical study aimed to evaluate the impact of HFNC oxygen therapy on patient comfort and pulmonary function by providing heated and humidified air-oxygen mixture at reliable F_1O_2 settings.

METHODS

After obtaining ethics approval and written informed consent, 20 consecutive adult patients undergoing awake craniotomy for epilepsy surgery were randomized to either HFNC therapy (starting at 40 L·min⁻¹ at 40% F_IO2) or standard oxygen mask at 6 L·min⁻¹ flow. Sedation was administered using a combination of dexmedetomidine/propofol/remifentanil infusions, titrated to the Richmond Agitation Sedation Score (RASS).⁵ The primary objective of this pilot study was to test the feasibility of study methods for a possible future larger-scale study. Secondary outcomes were patient comfort, dryness of mouth/nose, brain exposure conditions, and preventing postoperative atelectasis. Patient comfort was assessed on a scale of 1 to 5 (1quite dissatisfied, 5-very satisfied) at six times (preoperative, start of anesthesia, start of surgery, before and after awake neurosurgical testing, and at arrival in postanesthetic recovery unit (PACU). Dryness of mouth and nose were assessed as yes/no. The neurosurgeon assessed brain exposure score (1-excellent with no swelling, 4-swelling needing treatment) after dural opening. Anesthetic management was at the discretion of the attending anesthesiologist. Lung ultrasound was performed in PACU to detect signs of atelectasis (A and B lines, pulse sign, air bronchogram, lung sliding, irregular pleural line) in anterior, lateral and posterior regions on both sides of the chest.

RESULTS

Among 20 patients enrolled, (HFNC group, n = 10; facemask group, n = 10), demographics were comparable between both groups (Fig. 1a). The RASS scores to assess level of sedation (P = 0.934) were comparable between both groups (Fig. 1b). Patient comfort scores were similar across all time points (median 4; IQR 1; P = 0.151; Fig. 1c). Fewer patients in the HFNC group reported episodes of dry mouth (80%) than facemask group (100%), though this difference was not statistically significant (P = 0.474). Dry nose was less frequent in the HFNC group (10%) compared to facemask group (60%) (P = 0.057). Brain exposure scores were comparable in both groups (median, 1.5; IQR, 1; P = 0.97) with only 1 patient in the facemask group needing treatment (Fig. 1d). On ultrasound examination, findings suggestive of atelectasis were reported only on the left lateral chest region in the facemask group in one patient, while the HFNC group exhibited no significant abnormalities.

DISCUSSION

Heated humidified HFNC oxygen therapy was found to be safe and effective for the conduct of awake craniotomies. However, patient comfort, oxygenation, ventilation, lung atelectasis, and brain exposure conditions were similar to standard oxygen therapy. This could be attributed to the small sample size and pilot design, limiting the generalizability of our findings. Considering a change of 2 points on the comfort score as clinically significant, 124 patients would have been required for 80% power with an alpha of 0.05. High flow nasal cannula use in awake craniotomies may need individualization for specific situations with high risk of lung collapse, like morbid obesity.⁴

REFERENCES

1. Sokhal N, Rath GP, Chaturvedi A, Dash HH, Bithal PK, Chandra PS. Anaesthesia for awake craniotomy: a retrospective study of 54 cases. Indian J Anaesth 2015; 59: 300–5. https://doi.org/10.4103/0019-5049.156878

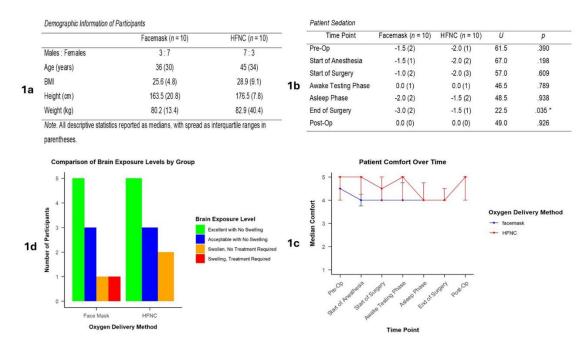
2. *Kumar P, McGinlay M, Kelly C, Farling PA, Mullan B*. High-flow nasal oxygenation: a new tool to increase patient safety during awake craniotomy. J Neurosurg Anesthesiol 2017; 29: 368–9. https://doi.org/10.1097/ana.00000000000312

3. *Cuquemelle E, Pham T, Papon JF, Louis B, Danin PE, Brochard L.* Heated and humidified high-flow oxygen therapy reduces discomfort during hypoxemic respiratory failure. Respir Care 2012; 57: 1571–7. https://doi.org/10.4187/respcare.01681

4. *Wong JW, Kong AH, Lam SY, Woo PY*. High-flow nasal oxygen in patient with obstructive sleep apnea undergoing awake craniotomy: a case report. A A Case Rep. 2017; 9: 353–6. https://doi.org/10.1213/xaa.00000000000615

5. *Sessler CN, Gosnell MS, Grap MJ*. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med 2002; 166: 1338–44. https://doi.org/10.1164/rccm.2107138

Figure Figure showing (clockwise from top left) a) demographic information for the study, b) table showing Richmond Agitation Sedation Scores in both groups at various times, c) graph showing patient comfort scores at various times, and d) comparison of brain exposure levels in both groups



BMI = body mass index; HFNC = High Flow Nasal Cannula

Effect of blood pressure threshold on adverse outcomes in patients with acute spinal cord injury: a systematic review and meta-analysis

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55

AUTHORS

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INTRODUCTION

Spinal cord injury (SCI) is a prevalent issue worldwide, with the World Health Organization (WHO) estimating around 15.4 million people living with SCI in 2021.¹ Hypotension, a common complication in patients with SCI, has been found to precipitate secondary injury, due to ischemia and hypoxia, leading to worse clinical outcomes.² The 2024 AO Spine & Praxis guidelines recommend maintaining mean arterial pressure (MAP) to at least 75–80 mm Hg, but not exceeding 90–95 mm Hg, for the first 3–7 days to optimize spinal cord perfusion in acute traumatic SCI.³ However, the quality of evidence supporting this recommendation is very low, and the strength of the recommendation is weak. There is a lack of quantitative analyses examining the effect of hypotension on outcomes for patients sustaining SCI. Thus, this study analysis aimed to review relevant literature and synthesize existing evidence pertaining to the impact of hypotension on adverse outcomes in patients with SCI.

METHODS

A literature search of studies examining outcomes after hypotension in patients with SCI was conducted using MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, CINAHL, Web of Science, and Scopus. Eligibility criteria included: adult patients presenting with traumatic or non-traumatic SCI, any type of blood pressure threshold, and reported outcomes. Only primary research articles were included. Exclusion criteria include studies discussing controlled or induced hypotension, case series, case reports, and reviews. Reviewers independently conducted initial title and abstract screening followed by full-text review for eligibility using Covidence. Data was extracted using a standardized data collection spreadsheet, including study characteristics, patient characteristics, outcomes, and study quality. The primary outcome of interest was adverse outcomes following hypotension in SCI patients. Secondary outcomes included: length of hospital and/or intensive care unit stays, and vasopressor usage. Subgroup analyses were conducted to compare different blood pressure types, and SCI at different anatomic spinal levels. The effect of hypotension was quantified using pooled odds ratios (OR) estimated using meta-analysis of individual study effect estimates. Heterogeneity was quantified using I². Sensitivity analyses were also performed using the leave-one-out method to assess robustness of findings. This protocol has been registered in PROSPERO.

RESULTS

Our search identified 16,366 records, of which 38 studies met the eligibility criteria. Metaanalysis of 12 studies with 20 data points (n = 2,179) revealed that suboptimal blood pressure management significantly increased the odds of adverse outcomes. The overall unadjusted odds ratio (uOR) was 2.55 (95% confidence interval [CI], 2.13 to 3.05), with MAP thresholds showing a stronger association (uOR, 2.81; 95% CI, 2.27 to 3.48) compared to systolic blood pressure (SBP) thresholds (uOR, 2.00; 95% CI, 1.41 to 2.84) (Figure). After adjusting for confounders, the overall adjusted odds ratio (aOR) was 1.04 (95% CI, 1.03 to 1.06) with minimal heterogeneity (I^2 = 0.02%). Subgroup analyses of adjusted results showed that SBP thresholds (aOR, 1.88; 95% CI, 1.22 to 2.90) had a stronger association with adverse outcomes than MAP thresholds (aOR, 1.04; 95% CI, 1.03 to 1.06). Cervical injuries (uOR, 2.64; 95% CI, 2.04 to 3.40; aOR, 1.03; 95% CI, 0.66 to 1.62) had similar results compared to all other spinal levels (uOR, 2.55; 95% CI, 2.13 to 3.05; aOR, 1.04; 95% CI, 1.03 to 1.06).

DISCUSSION

This systematic review and meta-analysis demonstrates that suboptimal blood pressure management is associated with adverse outcomes in SCI, although the aOR suggests a modest effect. This finding was consistent with Jiang *et al.* 2019, a study included in the meta-analysis, which found that the association between blood pressure thresholds and functional outcomes was significant in unadjusted analysis but was lost after accounting for confounders.⁴ This suggests that other factors play a significant role in functional recovery after SCI. Future research should focus on identifying additional factors influencing outcomes and refining blood pressure targets to enhance recovery strategies for SCI patients.

REFERENCES

1. World Health Organization: WHO. (2024, April 16). Spinal cord injury.

https://www.who.int/news-room/fact-sheets/detail/spinal-cord-injury

2. *Gaudin XP, Wochna JC, Wolff TW, et al.* Incidence of intraoperative hypotension in acute traumatic spinal cord injury and associated factors. Journal of Neurosurgery: Spine 2019; 32: 127–32. <u>https://doi.org/10.3171/2019.7.spine19132</u>

3. *Kwon BK, Tetreault LA, Martin AR, et al.* A clinical practice guideline for the management of patients with acute spinal cord injury: recommendations on hemodynamic management. Global spine journal 2024; 14: 1875–211. <u>https://doi.org/10.1177/21925682231202348</u>

4. *Jiang F, Jaja BN, Kurpad SN, et al.* Acute adverse events after spinal cord injury and their relationship to long-term neurologic and functional outcomes: analysis from the North American Clinical Trials Network for 2019.

Figure Forest plot summarizing the unadjusted (left) and adjusted (right) odds ratios for adverse outcomes associated with blood pressure thresholds in acute SCI. Subgroup analyses are presented for mean arterial pressure, systolic blood press, and spinal cord perfusion pressure. Overall pooled estimates and heterogeneity (I²) are shown for each group.

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					Random-effects ML model			

MAP = mean arterial pressure; SBP = systolic blood pressure; SCPP = spinal cord perfusion pressure

Effect of ketamine on intraoperative motor evoked potentials: a systematic review and meta-analysis

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INTRODUCTION

Intraoperative motor-evoked potentials (MEPs) are an important monitoring modality used to detect and prevent neurological deficits during surgery. The choice of anesthetic regimen significantly impacts MEP signal reliability, with propofol-based total intravenous anesthesia (TIVA) being the preferred approach for optimal signal acquisition. However, challenges in signal acquisition, particularly in pediatric patients and those with preexisting neurological deficits, have led to an ongoing search for adjuvants that could facilitate MEP monitoring.

Reports suggesting that ketamine may amplify MEP signal amplitudes have generated interest in its potential as an adjunct to standard anesthetic regimens.¹ However, literature presents mixed findings—some studies report improved amplitudes,² while others show no significant benefit.³

This systematic review aims to evaluate the impact of ketamine on MEP amplitudes compared to regimens without ketamine. By analyzing available evidence, we aim to determine whether ketamine-based regimens enhance and preserve MEP signals, improving signal acquisition and contributing to better patient outcomes.

METHODS

We conducted a comprehensive search of databases (EMBASE, Scopus, Web of Science, MEDLINE, Cochrane Library, CINAHL, PsycINFO), gray literature including clinical trial registries (ClinicalTrials.gov, WHO ICTRP), and dissertations and theses (Proquest). Reference lists of relevant articles were reviewed to identify additional studies. We identified 1,580 studies and removed 650 duplicates (23 manually, 627 via Covidence). After screening 930 studies by title and abstract, 16 full-text articles were assessed for eligibility, with 6 studies excluded due to wrong design (n = 3), wrong patient population (n = 2), and unavailability of full-text (n = 1). Ten studies met the inclusion criteria, and data from a total of 369 participants were included in the final review.

Two independent reviewers conducted screening, full-text review, data extraction, and risk of bias assessment using the Cochrane Risk of Bias 2 (ROB2) tool. Discrepancies were

resolved by a third reviewer. Meta-analysis was performed (using a random/fixed effects model as appropriate) to estimate pooled effect sizes with 95% confidence intervals (CIs) and assess heterogeneity using the I² statistic. Sensitivity analysis was performed. Publication bias was evaluated using Egger's test. The certainty of evidence was evaluated using the GRADE assessment.

RESULTS

Of the 10 included studies, 2 studies assessed the effect of a ketamine bolus on MEP amplitudes, while eight evaluated ketamine infusions. However, only 6 studies provided MEP amplitude data at comparable time points, enabling meta-analysis. Two sets of data were analyzed: baseline MEP values before surgical incision (6 studies; 232 patients) and MEP data after \geq 2 hours of anesthetic infusion (4 studies; 172 patients). Meta-analysis of baseline data showed no significant difference in MEP amplitudes between ketamine and comparator groups (Cohen's d, -0.15; 95% CI, -0.41 to 0.12), with high heterogeneity (I² = 75.19%) and low certainty of evidence. In contrast, after \geq 2 hours of anesthetic infusion, significantly higher amplitudes were observed in the ketamine group (Cohen's d, 1.22; 95% CI, 0.88 to 1.55), with low heterogeneity (I² = 10.33%) and moderate certainty of evidence. No single study disproportionately influenced the results (sensitivity analysis), and Egger's test indicated no significant publication bias (Figure).

DISCUSSION

Our systematic review and meta-analysis indicated that adding ketamine does not significantly impact MEP amplitudes at baseline. However, after ≥ 2 hours of infusion, significantly higher amplitudes were observed with ketamine, compared to propofol-based regimens. This suggests ketamine may mitigate the suppressive effects of prolonged propofol infusion, improving MEP signal acquisition during extended surgeries. However, the GRADE assessment highlights the need for cautious interpretation due to concerns related to imprecision and indirectness, particularly in baseline measurements. Future randomized controlled trials using the target-controlled infusions, trials in pediatric patients and/or those with neurological deficits, are needed to explore ketamine's potential benefits and clinical applications.

REFERENCES

 Erb TO, Ryhult SE, Duitmann E, Hasler C, Luetschg J, Frei FJ. Improvement of motorevoked potentials by ketamine and spatial facilitation during spinal surgery in a young child. Anesth Analg 2005; 100: 1634–6. https://doi.org/10.1213/01.ane.0000149896.52608.08
 Kalkman CJ, Drummond JC, Patel PM, Sano T, Chesnut RM. Effects of droperidol, pentobarbital, and ketamine on myogenic transcranial magnetic motor-evoked responses in humans. Neurosurgery 1994; 35: 1066–71. https://doi.org/10.1227/00006123-199412000-00008

3. *Inoue S, Kawaguchi M, Kakimoto M, et al.* Amplitudes and intrapatient variability of myogenic motor evoked potentials to transcranial electrical stimulation during ketamine/N₂O-

and propofol/ N_2O -based anesthesia. J Neurosurg Anesthesiol 2002; 14: 213–7. https://doi.org/10.1097/00008506-200207000-00007

Figure Figure showing A) baseline characteristics of included studies including risk of bias assessment, B) forest and funnel plots for baseline data (presurgical incision), and C) forest and funnel plots for post \geq 2 hours of infusion data

