A Systematic Review on the Effectiveness of Local Anesthetics and Intravenous Anesthetic Agents in Blunting the Hemodynamic Response to Skull-pin Insertion in Adult Patients for Craniotomy

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**Introduction:** Neurosurgery poses a challenge to the anesthesiologist because although much of cranial surgery is not particularly stimulating, certain aspects such as laryngoscopy, insertion of cranial or skull pins, incision and periosteal-dural contact induce noxious stimulation.

**Materials and Methods:** A systematic review was undertaken to determine the effectiveness of local anesthetics and intravenous anesthetic agents in blunting the hemodynamic response to skull pin insertion in adult patients for craniotomy. A computerized search of all published English journals between January 2000 to July 2010 was done from April to July 2010, using the following keywords: local anesthetic, bupivacaine, lidocaine, ropivacaine, intravenous, barbiturates, opioids, etomidate, propofol, benzodiazepines and ketamine. Appropriate measures were employed to minimize publication bias. Randomized control trials (RCTs) were the primary sources of data in this review with the following inclusion criteria, adult (≥ 18 years old), ASA I to III, undergoing elective craniotomy, requiring head fixation with the use of a Mayfield device. Initial search resulted to 183049 studies and upon applying the full criteria, seven studies were included and categorized as having good quality.

**Results:** Of the seven studies included, two RCTs investigated only local anesthetic as intervention, four RCTs investigated local anesthetic versus intravenous drugs, and one RCT investigated only intravenous drug as intervention. A narrative synthesis was done since data could not be pooled.

**Conclusion:** Studies included in this review present evidence that both interventions are effective, however, statistical evidence as to the best intervention to blunt this response is uncertain.

**Key words:** local anesthesia, intravenous anesthesia, skull-pin insertion, craniotomy

**INTRODUCTION**

Neurosurgical anesthesia requires understanding the effects of anesthetic agents on cerebral metabolism, blood flow, cerebrospinal fluid dynamics and intracranial volume and pressure. Patients undergo craniotomy for intracranial masses that may be congenital, neoplastic, infectious or vascular.\(^1\) Surgery on these patients poses a challenge to the anesthesiologist because although much of cranial surgery is not particularly stimulating, certain aspects such as laryngoscopy, insertion of cranial or skull pins, incision and periosteal-dural contact induce noxious stimulation.\(^2\)

The Mayfield device or head holder is used to stabilize the head, as head fixation is essential in cranial surgery. It is a clamp which consists of a C-shaped metal piece with three sharp interchangeable metal pins arranged triangularly to one another. These pins are forced through the layers of the skull, traversing the skin, galea and periosteum, lodging into the external lamina, by manually pushing the two arms of the clamp towards each other and tightening it with a calibrated pressure screw.\(^3,4\) Application is unaffected by operator technique or

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experience, and the force on the skull due to the pins is calibrated, resulting in a reproducible stimulus.\textsuperscript{5}

In patients with intracranial pathology, sudden increases in blood pressure can increase the blood flow and volume in intracranial blood vessels, and consequently increase intracranial pressure. Administration of drugs to attenuate this response may cause hypotension, and a sudden drop in mean arterial pressure below the lower autoregulatory margin will result in a lower cerebral perfusion pressure, and possibly cerebral ischemia. The response to placement of the Mayfield device, therefore, should be accompanied by minimal hemodynamic changes.\textsuperscript{6} Different anesthetic and pharmacologic techniques, including local anesthetics, narcotics, antihypertensives and deepening of anesthesia with inhalational anesthetics have been used with variable success.\textsuperscript{7}

**RESEARCH QUESTION**

The authors aimed to answer the following research questions: "What is the effectiveness of local anesthetics and intravenous anesthetic agents in blunting the hemodynamic response to skull pin insertion in adult patients for craniotomy?" and "What is the best intervention to blunt this response?"

**OBJECTIVE OF THE STUDY**

The objective of this systematic review is to find, assess and synthesize the latest evidence on the effectiveness of local anesthetics and intravenous anesthetic agents in blunting the hemodynamic response to skull pin insertion in adult patients for craniotomy.

**METHODOLOGY**

**Criteria for Considering Studies for this Review**

Randomized control trials (RCTs) were the primary sources of data in this review. Included studies were those whose participants are adults (\(\geq 18\) years old), ASA I to III, undergoing elective craniotomy, who require head fixation with the use of a Mayfield device. The intervention of interest in this review is any local anesthetic or intravenous anesthetic agent given with the aim of reducing or preventing the hemodynamic response from Mayfield device application. The main outcomes measured were elevations in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure.

**Search Strategy**

All published studies in the English language were searched from the period of January 2000 to July 2010 available in the databases of the Learning Resource Unit of the University of Santo Tomas Faculty of Medicine and Surgery was exhausted. Electronic research was also done at the University of the Philippines Manila College of Medicine Library. Unpublished studies were sought as well. Assessment for inclusion of foreign language publications was based on the English language extract, and if considered appropriate, an English translation was sought.

**Bibliographic Databases and Key words**

The databases searched included, Cochrane library, Google Scholar, EBSCOHost (MEDLINE and CINAHL), Ovid, PubMed and Science Direct. Studies identified during the database searches were assessed for relevance from a review of the title, abstract and descriptors of the study. A full text report was obtained for all studies deemed to be relevant.

The keywords used to search for studies included in this review are shown in Table I.

<table>
<thead>
<tr>
<th>Table I. Keywords used to search relevant studies for the review.</th>
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<tbody>
<tr>
<td><strong>Intervention</strong></td>
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<tr>
<td>Local anesthetics</td>
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<tr>
<td>Bupivacaine</td>
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<td>Lidocaine</td>
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<td>Mean arterial pressure</td>
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<td>Ropivacaine</td>
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<td>Intravenous anesthetics</td>
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<td>Barbiturates</td>
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<td>Opioids</td>
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<td>Etomidate</td>
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<td>Propofol</td>
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<td>Benzodiazepines</td>
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<td>Ketamine</td>
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Letters were sent to different medical institutions in the Philippines as to availability of any published or unpublished researches done relevant to the topic. Reference lists of all identified publications were searched for additional studies.

**Critical Appraisal**

All retrieved studies were screened by one author. Irrelevant studies were excluded at this point. Other studies that resulted from the search but excluded were used as references. The methodological quality of each RCT was assessed by two independent reviewers using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Experimental Studies.

The JBI tool consists of ten items, each requiring a yes/no response or unclear. One point was allocated with a yes response, and zero points with a no/unclear response. Studies that scored six or above on the JBI critical appraisal tool were categorized as good quality and were included in the review.

**JBI Critical Appraisal Critical Appraisal Checklist for Experimental Studies**

1. Was the assignment to the treatment groups truly random?
2. Were participants blinded to the treatment allocation?
3. Was allocation to treatment groups concealed from the allocator?
4. Were the outcomes of people who withdrew described and included in the analysis?
5. Were those assessing the outcomes blind to the treatment allocation?
6. Were the control and treatment groups comparable at entry?
7. Were groups treated identically other than for the named interventions?
8. Were outcomes measured in the same way for all groups?
9. Were outcomes measured in a reliable way?
10. Was appropriate statistical analysis used?

**RESULTS**

Initial search resulted to 183049 number of studies. Upon applying the full criteria, a total of seven studies were categorized as good quality and were included in this systematic review. Six criteria obtained a yes response in all seven studies included in this review. All studies employed randomization and had blinded participants, since all were under general anesthesia when the treatment was administered. In all studies, outcomes were measured the same way and measured reliably, since all patients were hooked to standard monitors. All studies used appropriate statistical analysis.

The criteria most often answered with a no or unclear response, were those which concern blinding of allocator and assessor. Some studies were only single blinded and some were not blinded at all. Criterion 3, was allocation to treatment groups concealed from the allocator, is feasible. However, criterion 5, were those assessing the outcomes blind to the treatment allocation, is difficult or sometimes impossible, due to the obvious nature of the interventions investigated.

Of the seven studies included, two RCTs investigated only local anesthetic as intervention, four RCTs investigated local anesthetic versus intravenous drugs, and one RCT investigated only intravenous drug as intervention.

**Local Anesthetic**

Two methods of delivering local anesthetic came out in the search, namely local infiltration and scalp block.
Table II. Rating of included studies based on the JBI Critical Appraisal Checklist for Experimental Studies. (Legend: Yes, X No, U unclear)

<table>
<thead>
<tr>
<th>Author</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>Mathieu, et al.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>U</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>9</td>
</tr>
<tr>
<td>Geze, et al.</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>9</td>
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<tr>
<td>Uyar, et al.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<td>Ozkose, et al.</td>
<td>✓</td>
<td>✓</td>
<td>U</td>
<td>✓</td>
<td>U</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>8</td>
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<tr>
<td>Yildiz, et al.</td>
<td>✓</td>
<td>✓</td>
<td>U</td>
<td>✓</td>
<td>U</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<td>10</td>
</tr>
<tr>
<td>Smith, et al.</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>8</td>
</tr>
<tr>
<td>Gazoni, et al.</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>7</td>
</tr>
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</table>

Mathieu, et al. compared local infiltration with 0.5% bupivacaine and placebo. No significant increase in blood pressure was observed in the group of patients who received bupivacaine after application of the head holder. One minute after pin insertion, there was a statistically significant rise in arterial pressure in the group of patients who received placebo (a mean rise of 10mmHg in systolic pressure [P = 0.003], 7mm Hg in diastolic pressure [P = 0.02], and 9mmHg in mean arterial pressure [P = 0.004]). A slight decrease in heart rate (a mean of four beats/minute) occurred in patients in both groups (bupivacaine P = 0.01; placebo P = 0.02) following pin insertion. This study concluded that infiltration of the skin and pericranium before securing the Mayfield head holder can effectively blunt the hemodynamic response associated with that stimulus.4

Geze, et al. compared scalp block with 0.5% bupivacaine (S), local infiltration with 0.5% bupivacaine (L) and control (C). There was no significant increase in heart rate or mean arterial pressure by repeated measurement intervals after pin insertion for group S, but in the groups L and C, heart rate was increased significantly at the 1st, 2nd and 3rd minute after pin insertion (P<0.05). When heart rate and mean arterial pressure were compared between groups, the increase in heart rate was also significant for groups L and C when compared with group S during head pinning and the 1st and 2nd minute after pinning (P<0.05). This increase in mean arterial blood pressure was higher in group C for the 1st and 2nd minute after pin insertion when compared with group L (P<0.05) and group S (P<0.01). This study demonstrated that scalp block is more effective than local anesthetic infiltration in controlling hemodynamic response to skull pin insertion.4

Intravenous

Uyar, et al. compared dexmedetomidine at 1mcg/kg bolus and placebo. Before skull-pin insertion, dexmedetomidine significantly decreased heart rate and mean arterial pressure compared with the baseline value and also compared with the placebo group (P<0.05). Although heart rate and mean arterial pressure might have been in the baseline level after the skull pinning, they were significantly increased compared with the situation just before skull pinning in the dexmedetomidine group (P<0.05). Pin attachment significantly increased heart rate and mean arterial pressure in the placebo group compared with both the baseline and the dexmedetomidine group at 1 and 5 minutes after pin insertion (P<0.05). Although heart rate and mean arterial pressure values were similar to baseline in the placebo group, they were significantly decreased in the dexmedetomidine group from 10 to 60 minutes after pin insertion. This study concluded that preoperative administration of a single bolus dose of dexmedetomidine attenuates increases in heart rate and mean arterial pressure during skull pin insertion.7
Local Anesthetic versus Intravenous

Ozkose, et al. compared intravenous fentanyl (F), local infiltration with 1% lidocaine (L) and intravenous fentanyl combined with local infiltration (FL). In group F, placement of the pins resulted in increases of mean arterial pressure and heart rate significantly above baseline levels (MAP: 103.7±9.2 vs. 89.8±8.9 mmHg, *P*<0.05; HR: 101.9±7.5 vs. 82.1±9.8, *P*<0.05). In group F, 3 minutes after Mayfield head holder placement, the average mean arterial pressure and heart rate were significantly higher than baseline (P<0.05 in both cases). In contrast, groups L and FL had no significant differences vs. baseline values (group L: MAP 96.3±6.3 vs. 92.5±8.9, HR 94.4±6.9 vs. 86.7±5.4; group FL: MAP 87.6±8.8 vs. 88.1±7.5, HR 86.5±7.4 vs. 82.6±7.8). In group FL, there was no significant increase in mean arterial pressure or heart rate at any time of the recordings. However, in group L, during placement of the Mayfield head holder, there was a significant increase in mean arterial pressure and heart rate compared to group FL (P<0.05). During and after Mayfield head holder placement, mean arterial pressure and HR were significantly higher in group F than in groups L and FL (P<0.05 in both cases). This study concluded intravenous fentanyl at 2 mcg/kg with local infiltration of lidocaine is effective in reducing the hemodynamic response to skull pin insertion.

Yildiz, et al. compared intravenous fentanyl (F) and intravenous fentanyl combined with local infiltration with 0.25% bupivacaine (FB). Heart rate at 5 minutes after skull pin insertion in group F and at one and 5 minutes after skull pin insertion in group FB, significantly decreased in comparison to the baseline values (P<0.05). In both groups, heart rate at one and 5 minutes after skull pin insertion were significantly lower than that of just before skull pin insertion (P<0.05). There were significant differences in the mean arterial pressure at one and 5 minutes after skull pin insertion between the groups (P<0.05). In group FB, the mean arterial pressure at one and 5 minutes after skull pin insertion were significantly lower than that in group F (P<0.05). In both groups, all mean arterial pressure values after baseline were significantly lower than that of baseline (P<0.05). This study concluded that scalp block is significantly more effective in attenuating blood pressure response to skull pin insertion.

Gazoni, et al. compared scalp block with 0.5% ropivacaine and remifentanil infusion. Patients in the scalp block group did not have a significant increase in blood pressure or heart rate associated with pinning. The control group had a significant increase in mean arterial blood pressure, systolic blood pressure and diastolic blood pressure with pinning, despite the ability of the anesthesiologist to titrate the remifentanil infusion as needed. There was no significant increase in heart rate in either group. Despite the fact that remifentanil was associated with a significant change
in BP during pinning, whereas a skull block was not, the mean change in BP and HR was not different between the groups. The results of this study support the suggestion that a scalp block is no more effective than remifentanil in reducing the hemodynamic response to skull pin insertion.10

DISCUSSION

In the studies reviewed comparing local anesthetics, evidence showed that scalp block is effective in blunting the hemodynamic response to skull pinning, followed by local infiltration, then by placebo.

A scalp block involves regional anesthesia to the nerves that innervate the scalp, including the greater and lesser occipital nerves, supraorbital and supratrochlear nerves, the zygomaticotemporal nerves and the greater auricular nerves.6 According to some authors, it is easy to learn, reproducible and has a high success rate. It also has an advantage over local infiltration in that the neurosurgeon has an opportunity to reposition the pins without the need for further infiltration.2,4 However, other authors disagree, saying skull block requires skill to perform, carries a risk of failure and consumes time under anesthesia.9

Local infiltration of pin insertion sites has been an accepted method of blunting the hemodynamic response to skull pinning because it is simple and can be performed by either anesthesiologist or neurosurgeon.9 It may not always be effective because the exact position of the pins may not match the infiltrated skin areas, and the dose of the local anesthetic may be inadequate.3

There was only one study evaluating the use of intravenous anesthetic agents. This study used dexmedetomidine as intervention and demonstrated its effectiveness.

In the studies reviewed comparing local anesthetic versus intravenous anesthetic agents, evidence was difficult to synthesize. Though the studies had comparable participants at entry and had same outcome measures evaluated, the protocol had a few dissimilarities. Two studies compared intravenous anesthetic agents versus local infiltration, one used lidocaine and the other used bupivacaine. One study concluded that intravenous plus local infiltration is more effective, while the other concluded that intravenous is more effective and local infiltration has no added benefit. Two studies compared scalp block versus intravenous anesthetic agents and had contradicting results. This inconclusive evidence may be the reason why there is no standard intervention at present. Both local anesthetics and intravenous agents are accepted in clinical practice and the decision as to what intervention to use depends on the preference and experience of the anesthesiologist or on the institution of practice.

The National Health and Medical Research Council (NHMRC) of the Australian Government has developed a process for assessing the body of evidence and formulating recommendations that should assist guideline developers and help ensure that these guidelines are consistent in their development of evidence-based recommendations. The overall grade of recommendation is based on a summation of the grading of the individual components of the body of evidence assessment.11 (Table III)

Table III. NHMRC Assessing the Body of Evidence Form.

<table>
<thead>
<tr>
<th>Volume of evidence</th>
<th>A- Excellent</th>
<th>The study design of all the papers included in this systematic review are Level II in the hierarchy, or randomized controlled trials, with low risk of bias.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consistency</td>
<td>C- Satisfactory</td>
<td>Evidence from the studies included in this systematic review is conflicting. Inconsistent findings can be explained by differences in the route, concentration and dose of the intervention investigated by each study.</td>
</tr>
<tr>
<td>Clinical impact</td>
<td>C - Satisfactory</td>
<td>Given that the evidence from some of studies included are conflicting, this systematic review has only moderate clinical impact.</td>
</tr>
<tr>
<td>Generalizability</td>
<td>A- Excellent</td>
<td>Though evidence from the studies included are inconclusive, the populations studied in the body of evidence are the same as the target population.</td>
</tr>
</tbody>
</table>
CONCLUSION

This systematic review aims to determine the effectiveness of local anesthetics and intravenous anesthetic agents in blunting the hemodynamic response to skull pin insertion in adult patients for craniotomy. Studies included in this review present evidence that both interventions are effective, however, evidence as to the best intervention to blunt this response is uncertain. The authors recommend further studies be done on this topic. Future RCTs should be conducted using a standardized protocol so that pooling of data and appropriate statistical analysis could be done.

REFERENCES


