Controlled hypotension and blood loss during frontoorbital advancement

Clinical article

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Object. Controlled hypotension is routinely used during open repair of craniosynostosis to decrease blood loss, although this benefit is unproven. In this study the authors analyzed the longitudinal relationships between intraoperative mean arterial pressure (MAP) and calculated blood loss (CBL) during frontoorbital advancement (FOA) for craniosynostosis.

Methods. The authors reviewed the records of infants with craniosynostosis who had undergone primary FOA between 1997 and 2009. Anesthesia records provided preoperative and serial intraoperative MAP. Interval measures of CBL had been determined during the course of the operation. The longitudinal relationships between MAPmean, MAP_change, and CBL_change were assessed over the same time interval and compared between adjacent time intervals to determine the directionality of associations.

Results. Ninety infants (44 males and 46 females) underwent FOA at a mean age and weight of 10.7 ± 12.9 months and 9.0 ± 7.0 kg, respectively. The average intraoperative MAP was 56.1 ± 4.8 mm Hg, 22.6 ± 12.1% lower than preoperative baseline. A negative correlation was found between CBL_change and MAP_mean over the same interval (r = -0.31, p < 0.05), and an inverse relationship was noted between CBL_change of the previous interval and MAP_change of the next interval (r = -0.07, p < 0.05). Finally, there was no significant association between MAP_change of the previous interval and CBL_change of the next interval.

Conclusions. Calculated blood loss demonstrated a negative correlation with MAP during FOA. Directionality testing indicated that MAP did not affect intraoperative blood loss; instead, blood loss drove changes in MAP. Overall, these findings challenge the benefit of controlled hypotension during open craniofacial repair.

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KEY WORDS • controlled hypotension • frontoorbital advancement • craniosynostosis • blood loss • postural ischemia • bone perfusion pressure • congenital defect

Open cranial remodeling procedures remain the standard treatment for craniosynostosis. One of the greatest concerns during these operations is blood loss, which can range from 20% to 500% of total blood volume as a result of the extensive exposure and bony osteotomies.25,26 Moreover, these operations are routinely performed in infants with low circulating blood volumes, and even low levels of blood loss can result in life-threatening hypotension and cardiac arrest.25 In a recent analysis of more than 8000 major craniofacial procedures, 50% of all intracranial deaths were reported to be the direct result of excessive blood loss.19 In response to blood loss, infants are often aggressively resuscitated with allogenic blood transfusions that pose risks of disease transmission, hemolytic reactions, acute lung injury, graft versus host disease, immunomodulation, circulatory overload, and coagulopathic complications.30,64,66 The risk of an adverse outcome from transfusion in an infant is nearly 3 times that in an adult,37 and increased blood loss has also been associated with extended hospitalizations.63 Thus, numerous techniques to control blood loss and/or reduce the need for blood transfusion have been proposed.

Some authors advocate controlled hypotension to reduce blood loss during open treatment of craniosynostosis. First introduced by Cushing in 1917,2 controlled hypotension is defined as a reduction in systolic blood pressure to 80–
90 mm Hg, a reduction in MAP to 50–65 mm Hg, or a 30% reduction from baseline MAP. Proposed benefits include 1) reduced intraoperative blood loss, 2) improved surgical visualization, 3) shortened operative time, and 4) decreased use of and exposure to blood products. The efficacy and safety of this technique have been studied in general plastic surgery, neurosurgery, orthopedic surgery, maxillofacial surgery, general surgery, otolaryngology, burn surgery, and obstetrics and gynecology. Only 1 study has investigated the use of hypotensive anesthesia in the open repair of craniosynostosis. Diaz and Lockhart compared 12 normotensive infants (mean systolic blood pressure 83.8 mm Hg) with 18 hypertensive infants (mean systolic blood pressure 65.0 mm Hg) undergoing open repair of largely sagittal synostosis and observed a significant reduction in estimated blood loss from 111 to 89 ml. However, they found no difference in CBL between the groups.

The purpose of this study was to investigate the longitudinal relationships between intraoperative MAP and CBL during FOA for craniosynostosis. The primary goal was to determine whether changes in blood pressure drove intraoperative blood loss or vice versa.

Methods

An institutional review board–approved retrospective review was performed in patients who underwent FOA for craniosynostosis at our institution between 1997 and 2009. Only those with complete medical records who had undergone primary FOA were included in the study.

Standard Intraoperative Protocol

The standard intraoperative protocol includes the following. All procedures are performed jointly by a neurosurgeon and a plastic surgeon. The infant is placed supine, with a slight head-up tilt. Perioperative antibiotics and steroids are used, as is scalp infiltration with a local anesthetic (0.5% lidocaine and 1:400,000 parts epinephrine) prior to incision. Under the care of a single pediatric anesthesia team, controlled systemic hypotension (target MAP 55–60 mm Hg) is initiated using one or more inhalational anesthetic agents (sevoflurane, desflurane, or isoflurane). The cranial vault is accessed through a standard coronal incision; hemostatic sutures or clips are not used in the process. A subgaleal dissection is then performed, with preservation of the pericranium. The frontal bones and supraorbital bandeau are removed using bone wax as necessary to control bleeding at the cut bony edges and bipolar cautery along the dural vessels. The supraorbital bandeau is remodeled using partial osteotomies at the midline. Absorbable hardware is used on the interior surface to maintain the newly contoured shape. The re-shaped supraorbital bandeau is stabilized to the calvarial foundation with absorbable hardware. The remodeled frontal bone is secured to the bandeau. Subgaleal drains are then placed in a bilateral fashion, followed by a layered soft tissue closure.

Data Collection

Chart and electronic medical records were accessed to obtain patient demographics and clinical information. Anesthesia records provided data on operative time (duration from incision to closure), baseline MAP, serial measures of intraoperative MAP, interval amounts of CBL, and an overall measure of CBL. Baseline MAP was calculated using preoperative systolic and diastolic pressures, which were available in 73 of 90 patients. Intraoperative MAP was determined using the systolic and diastolic blood pressures recorded every 5 operative minutes. Serial measures of MAP were averaged across the entire operation for an overall MAP mean. Based on surgical time, the operation was divided into 3 equal time periods. An MAP mean was then determined for the first third, middle third, and last third of the operation by averaging serial measures of MAP for each of the respective tertiles. This provided an opportunity to capture the degree of controlled hypotension during 3 critical periods of the procedure: 1) cranial vault access, 2) frontoorbital removal and remodeling, and 3) closure. While cranial vault access, remodeling, and closure may not necessarily be executed in the same exact amount of time, tertile analysis afforded the best window to capture these 3 epochs.

Calculated blood loss was determined using the formula developed by Gross and described by Faberowski et al. The formula corrects for the dilutional effects from the concurrent administration of crystalloid while simultaneously factoring intraoperative blood transfusions:

$$\text{CBL} = \frac{\left| (Hb_T - Hb_i) \times ABV \times Wt \right| + iRCT}{Wt}$$

where $Hb_T$ is baseline hemoglobin, per preoperative labs; $Hb_i$ is interval hemoglobin, per intraoperative or immediate postoperative labs; ABV is average blood volume (infants = 80 ml/kg); Wt is patient weight in kg; and iRCT is volume (ml) of red blood cells transfused intraoperatively.

Hemoglobin values were periodically available during the procedure and divided an operation into multiple intervals. An “interval” was defined as the time period from one hemoglobin measure to the next, with preoperative hemoglobin considered to be the first measure. For each interval, 3 parameters were calculated: 1) MAP mean, the average of serial measures of MAP within the interval; 2) MAP change, equal to MAP_T2 − MAP_T1, where T2 is the end and T1 is the start of the interval; and 3) CBL change, equal to CBL_T2 − CBL_T1, an interval measure of blood loss. An immediate postoperative level of hemoglobin provided a total CBL, an overall measure of blood loss.

Blood loss volume (ml) was converted to percent estimated blood volume (%EBV), which was done by dividing volume (ml) by the total EBV (ABV × Wt) and multiplying by 100. This provided a better opportunity to observe relationships between factors and outcomes while accounting for patient weight.

Statistical Analysis

Both simple and multiple linear and logistic regression models were used to evaluate the hemodynamic relationships. These models controlled for patient demographics (for example, surgical age and weight) and intraoperative factors (for example, operative time), which were previously found to be related to blood loss during FOA. First, the gross relationship between blood loss
and blood pressure was evaluated by plotting total measures of CBL against overall MAP\textsubscript{mean}. Second, the relationship between specific periods of controlled hypotension (that is, cranial vault access, frontoorbital removal and remodeling, or closure) and overall blood loss was investigated by graphing MAP\textsubscript{mean} for the first, middle, and last tertiles in relation to total CBL. Third, the longitudinal relationships between MAP\textsubscript{mean}, MAP\textsubscript{change}, and CBL\textsubscript{change} were compared over the same interval and between adjacent intervals (staggered analysis) to determine the directionality of associations between blood pressure and blood loss. A p value < 0.05 was considered significant.

**Results**

Ninety infants (44 males and 46 females) underwent FOA at a mean age and weight of 10.7 ± 12.9 months and 9.0 ± 7.0 kg, respectively. Indications for the procedure included metopic (36 patients), unicoronal (32 patients), and bicoronal (22 patients) synostoses. Approximately 13.3% of patients had an associated syndrome: Saethre–Chotzen (4 patients), Apert (4 patients), Pfeiffer (2 patients), Crouzon (1 patient), and Noonan (1 patient) syndrome. The average operative time was 4.2 ± 0.8 hours, and the intraoperative MAP was 56.1 ± 4.8 mm Hg, which was 22.6% ± 12.1% lower than preoperative baseline.

The mean CBL was 259.3 ml or 39.3% of EBV. From the perspective of the operation as a whole, CBL negatively correlated with MAP\textsubscript{mean} (r = -0.19, p < 0.05). The relationship between MAP\textsubscript{mean} and total CBL was then stratified by surgical age: < 6 months (28 patients), 6–12 months (41 patients), and > 12 months (21 patients). As shown in Table 1, a significantly inverse relationship was maintained between MAP\textsubscript{mean} and total CBL specifically for the 6- to 12-month age group. No significant correlation was found between MAP\textsubscript{mean} and total CBL for the < 6 months or > 12 months surgical age groups.

 Associations between specific periods of controlled hypotension and total CBL were next investigated. As shown in Table 2, an inverse relationship was maintained between total CBL and MAP\textsubscript{mean} for the first, middle, and last thirds of the operation. Only the association between total blood loss and blood pressure for the last tertile approached statistical significance (r = -0.18, p = 0.09).

Longitudinal relationships between blood pressure and blood loss were explored over the same interval and between adjacent intervals of the operation. As shown in Fig. 1, a negative correlation was found between CBL\textsubscript{change} and MAP\textsubscript{mean} (r = -0.31, p < 0.05) over the same interval. On staggered analysis, a significantly inverse relationship was maintained between CBL\textsubscript{change} of the previous interval and MAP\textsubscript{mean} of the next interval (r = -0.07, p < 0.05; Fig. 2). Finally, no significant association was found between MAP\textsubscript{change} of the previous interval and CBL\textsubscript{change} of the next interval (r = -0.28, p = 0.12).

**Discussion**

Although first proposed by Cushing in 1917,\textsuperscript{9} controlled hypotension was implemented into clinical practice nearly 30 years later by Gardner.\textsuperscript{24} Hypotension was induced during resection of an olfactory meningioma by cannulating the dorsalis pedis artery and withdrawing 1600 ml of blood. Gardner noted that reduced bleeding led to improved visualization, and he attributed these findings to peripheral vasoconstriction rather than to a reduction in blood pressure. Earlier that year, Page\textsuperscript{49} had demonstrated that peripheral vasoconstriction was an early and constant accompaniment of shock.

In 1948, Griffiths and Gillies\textsuperscript{25} pioneered the concept of total spinal analgesia as a safer alternative to arterial bleeding for inducing hypotension. Preganglionic sympathetic blockade promoted arteriolar dilation, which lowered peripheral resistance and produced systemic hypotension. By preserving capillary bed and venous tone, this technique of “neurogenic shock” maintained end-organ gas exchange and metabolism to a better degree than the method of “oligemic shock” by arteriotomy.\textsuperscript{27} Induced neurogenic shock has largely formed the basis for contemporary techniques of controlled hypotension.

In the pediatric population, primary methods include the use of inhalational anesthetic agents (halothane, sevoflurane, isoflurane, or enfurane) or direct-acting vasodilators (sodium nitroprusside or nitroglycerin). While the medical literature provides data supporting the efficacy

**TABLE 1:** Total CBL versus MAP\textsubscript{mean} for different surgical age groups

<table>
<thead>
<tr>
<th>MAP\textsubscript{mean}</th>
<th>Total CBL</th>
<th>r Coefficient</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 mos</td>
<td></td>
<td>0.12</td>
<td>0.54</td>
</tr>
<tr>
<td>6–12 mos</td>
<td></td>
<td>-0.39</td>
<td>0.01</td>
</tr>
<tr>
<td>&gt;12 mos</td>
<td></td>
<td>-0.15</td>
<td>0.50</td>
</tr>
</tbody>
</table>

**TABLE 2:** Total CBL versus MAP\textsubscript{mean} for each operative tertile

<table>
<thead>
<tr>
<th>MAP\textsubscript{mean}</th>
<th>Total CBL</th>
<th>r Coefficient</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>first tertile</td>
<td></td>
<td>-0.16</td>
<td>0.12</td>
</tr>
<tr>
<td>middle tertile</td>
<td></td>
<td>-0.14</td>
<td>0.18</td>
</tr>
<tr>
<td>last tertile</td>
<td></td>
<td>-0.18</td>
<td>0.09</td>
</tr>
</tbody>
</table>

![Graph showing the relationship between CBL change and MAP mean](image)
of induced hypotension in the adult patient population, there is relatively limited experience with this technique in the pediatric age group.

The application of controlled hypotension in the pediatric population during open craniofacial procedures is of special interest, as it might protect against certain causes of perioperative mortality. Admittedly, controlled hypotension would not prevent the mortality due to acute exsanguination from a torn venous sinus or due to indolent sequestration of blood under the scalp in the postoperative period. Nevertheless, controlled hypotension could curtail the mortality arising from severely acidic states in the setting of steady oozing of blood from raw bone edges.

A principle finding in this study is that blood loss negatively correlated with blood pressure, regardless of the operative period studied. We previously demonstrated a general inverse relationship between total blood loss and blood pressure averaged over the entire operation, but results of the present study show that this observation holds true for every time period of the operation (that is, cranial vault access, frontoorbital removal and remodeling, or closure). We sought to determine the directionality of this finding; that is, was the lower MAP increasing blood loss or did the higher blood loss reduce MAP? Either scenario could lead to hemodynamic instability, placing the patient at higher risk for life-threatening hypotension or cardiovascular collapse. In the former case, the institution of hypotensive anesthesia would actually worsen with hypotensive anesthesia.

Our findings must be interpreted in the light of several limitations. These include the study’s retrospective design, relatively low study power, and the fact that our findings are not generalizable to other types of open craniofacial repair. With regard to the study design, we performed a retrospective review of the senior author’s (R.F.K.) practice of controlled hypotension during FOA for craniosynostosis. During the study period, controlled hypotension was considered a critical part of the standard of care to limit blood loss. No effort was made to deliberately maintain patients at normotension for the purposes of comparison, as doing so could have placed patients at risk for severe blood loss and/or hemodynamic collapse. In the absence of a true control arm, the relative effectiveness of hypotensive anesthesia was assessed by looking at the correlation between the degree of hypotension and the extent of blood loss. The retrospective design also limited our ability to determine causality; however, staggered interval analysis did provide an opportunity to evaluate the temporal relationship between blood pressure and blood loss.

One could also argue that some of our patients were not in the therapeutic zone of controlled hypotension. Based on an absolute definition (MAP 50–65 mm Hg), controlled hypotension was achieved in 93.3% of patients. However, from a relative perspective (30% or more MAP reduction), an absolute definition (MAP 50–65 mm Hg), controlled hypotension was achieved in 93.3% of patients. However, from a relative perspective (30% or more MAP reduction), only 26.7% of patients underwent controlled hypotension. To determine whether our patients were undertreated from a relative standpoint, we evaluated the relationship between

![Graph showing the relationship between CBL change of the previous interval and MAP change of the next interval.](image-url)

\[r = -0.07, p < 0.05\]

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MAP reduction from baseline and blood loss. We found no association between the MAP decrease and CBL, as previously reported. Going a step further, we analyzed the relationship between MAP and total CBL for the subset of patients meeting the criteria for both absolute and relative hypotension. An inverse relationship was once again observed between blood pressure and blood loss, although the relation did not reach statistical significance ($r = -0.17$, $p = 0.31$). Low study power may explain the lack of significance, as only 23 patients, or 25.6% of the study population, met both criteria.

With data supporting the inability of controlled hypotension to curtail blood loss, one wonders whether controlled hypotension is protective against blood product use and exposure. While this question was not the focus of this report, we took an opportunity to look at the degree of red blood cell transfusion. With the exception of 3, all patients received a red blood cell transfusion during their hospital stay, for an average of 48.4% EBV. Furthermore, a significant inverse relationship was found between MAP and total red blood cell transfusion ($r = -0.32$, $p = 0.002$). Thus, from the standpoint of blood product use and exposure, controlled hypotension was also not protective.

Conclusions

In this study of controlled hypotension during FOA, CBL demonstrated an inverse relationship with MAP. Directionality testing indicated that MAP did not affect intraoperative blood loss; instead, blood loss drove changes in MAP. Overall, these findings caution against the use of controlled hypotension during complex open craniofacial repair.

Disclosure

The authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Seruya. Acquisition of data: Seruya. Analysis and interpretation of data: Keating, Seruya, Oh, Rogers. Drafting the article: Seruya. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Keating. Administrative/technical/material support: Boyajian, Yaun. Study supervision: Keating, Oh, Rogers. Drafting the article: Seruya. Critically revising the article: all authors. Approved the final version of the manuscript on behalf of all authors: Keating. Administrative/technical/material support: Boyajian, Yaun. Study supervision: Keating, Oh, Rogers. Drafting the article: Seruya. Critically revising the article: all authors. Approved the final version of the manuscript on behalf of all authors: Keating.


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