Evaluation of Acute Normovolemic Hemodilution and Autotransfusion in Neurosurgical Patients Undergoing Excision of Intracranial Meningioma

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ABSTRACT

Background: Several blood conservation strategies have been tried with the purpose of reducing homologons blood transfusion.

Patients & Methods: In a prospective randomized study, the potential benefits of acute normovolemic hemodilution (ANH) with autologous transfusion were investigated as a blood conservation technique in surgical excision of intracranial meningioma. Over a period of 2 years, 40 patients undergoing excision of intracranial meningioma were randomly assigned to two groups of 20 patients each. Group I (Control Group) received conventional homologous blood intraoperatively and were not subjected to ANH. In Group II (ANH Group), Acute Normovolemic Hemodilution was initiated to a target hematocrit of 30% after induction of anesthesia. Parameters studied included changes in hemoglobin, hematocrit and hemodynamic parameters.

Results: The mean value of blood withdrawn in ANH group was 802.5 ± 208 ml. This was replaced simultaneously with an equal volume of 6% Hydroxyethyl starch to maintain normovolemia. There was no statistically significant variation in mean hemoglobin levels between the two groups at various stages of study. Hematocrit decreased significantly in both the groups at various stages as compared to preoperative values , the decrease being more but insignificant in group II. Changes in heart rate and mean blood pressure were similar and without statistically significant differences in either group at various stages of study. The amount of surgical blood loss in group I was 835.29 ± 684.37 ml, as compared to 865 + 409.78 ml in group II. The difference was statistically insignificant ($p>0.05$). The mean volume of homologous blood transfused in group I was 864.71 ± 349.89 ml, as compared to 165 ± 299.6 ml in group II which was statistically significant ($p<0.05$). In group II (ANH Group) only 5 patients (25%) required homologous blood whereas in group I all patients (100%) needed homologous blood.

Conclusion: We conclude that acute normovolemic hemodilution up to a target hematocrit of 30% is safe and effective in reducing the need for homologous blood in neurosurgical patients undergoing excision of intracranial meningioma.

KEYWORDS: Surgery: Neurosurgery; Transfusion: Autologous, Homologous; Technique: Normovolemic hemodilution; Diluent: 6% hydroxyethyl starch

Blood for blood is an ancient dictum being still followed perioperatively throughout the world. The extensive surgical procedures associated with major blood loss requiring large amount of blood are becoming more and more frequent and continue to increase the need for intra and post-operative replacement of whole blood and its components. In neurosurgery, a major problem during excision of intracranial meningioma is the extensiveness of the surgical procedure associated with significant amount of blood loss due to its high vascular nature. Moreover the hemostasis also is sometimes very difficult, especially in deep-seated meningiomas, often requiring intraoperative blood transfusion. However, the use of homologous blood to replace intraoperative losses has been questioned during recent years because of an increasing awareness of the potential risks for the recipient.[1] It is now realized that transfusion of homologous blood carries with it a very high risk of transmission of infectious diseases such as hepatitis B, C, D and F[2] and human immunodeficiency virus.[3] Immunological complications may also occur ranging from allergic reaction to an anaphylactic shock and even suppression of immune system.[4] The functional quality of blood progressively deteriorates with duration of storage. There is gradual fall in pH, rise in free plasma hemoglobin due to red cell lysis, rise in potassium, lactic acid and ammonia levels. Functional platelets are almost absent beyond 24 hours of collection and there is fall in levels of factor V & VII along with depletion of ATP & 2-3 DPG.

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Several blood conservation strategies have been introduced with the aim of reducing homologous blood transfusion. Messmer and Sunder-Plassman laid the foundation of a large number of blood conservation techniques involving autologous blood withdrawal.[5] Autologous transfusion by either preoperative autologous blood donation, acute normovolemic hemodilution (ANH) or intraoperative blood salvage have been definitely useful in reducing the use of homologous blood in surgical patients but failure of widespread acceptance is presumably a reflection of effort and cost.

Acute normovolemic hemodilution with autologous transfusion significantly reduces the requirement of homologous blood during and after surgery. It provides the only source of fresh whole autologous blood for transfusion and unlike preoperatively donated autologous units, blood drawn during hemodilution does not undergo biochemical alterations associated with blood storage. Platelet function is preserved and hypothermia associated with refrigerated blood administration is avoided because of its storage at room temperature.[6] This practice also eliminates the possibility of any clerical error that could lead to an ABO incompatible blood transfusion and death.

Our study was designed to evaluate the safety of acute normovolemic hemodilution and its efficacy in reducing the need for homologous blood transfusion in neurosurgical patients undergoing excision of meningioma.

PATIENTS & METHODS

After obtaining approval from the Institutional Ethics Committee, forty adult patients of either sex belonging to ASA grade I or II, scheduled for excision of intracranial meningioma were selected for the study. Patients with hemoglobin level of less than 11gm/dl and those with history of ischemic heart disease, coagulation disorders or anticoagulant medication, hepatic and renal disease were excluded from the study. The patients were randomly allocated to two groups of twenty patients each. Group I (Control Group) received conventional homologous blood for replacement intraoperatively, depending on the blood loss and were not subjected to hemodilution. In Group II (ANH Group), patients were bled while maintaining normovolemia with 6% hydoxyethyl starch and autologous blood collected in CPD-A bags for retransfusion later.

All patients received a standardized general anesthetic technique. Patients were premedicated with alprozolam 0.25 mg orally, the night before surgery and injection glycopyrolate 5 microgram per kg intramuscularly one hour before induction of anesthesia. General anesthesia was induced with propofol 2mg kg^{-1} followed by succinylcholine 2mg kg^{-1} to facilitate endotracheal intubation. Anesthesia was maintained with 50% nitrous oxide in oxygen and 0.5-1% halothane. Analgesia was provided with morphine 0.1mg kg^{-1} and muscle relaxation achieved with vecuronium bromide 0.1mg kg^{-1}. Ventilation was controlled to maintain mild hypocarbia. At the end of the surgery, residual neuromuscular block was reversed with neostigmine (0.05mg kg^{-1}) and atropine (0.02mg kg^{-1}).

Immediately after induction of anesthesia, arterial and central venous catheterization was performed for continuous measurement of arterial and central venous pressures. Surgery was allowed to proceed in Group I, and homologous blood transfused when blood loss was estimated to be 300ml or more. In Group II, acute normovolemic hemodilution (ANH) was performed to a target hematocrit of 30% before the start of surgery. Patients were bled from arterial or venous cannula with simultaneous infusion of 6% hydoxyethyl starch in the contralateral arm so as to maintain normovolemia. Blood was collected into standard blood collection bags containing 49ml of CPDA. The volume of the blood collected was determined by the following formula (7):

$$V = EBV \times \frac{Hi - Hf}{Hav}$$

Where V = Volume of blood collected,

EBV = Patient's estimated blood volume (70ml kg^{-1}),

Hi = Patients initial Hematocrit,

Hf = Patient's final (Desired) Hematocrit after hemodilution (30%), and

Hav = Average of initial and final Hematocrit.

The bags were sequentially labeled and stored at room temperature. Retransfusion was started once the main resection of tumor was over and hemostasis achieved, however in the event of excessive blood loss, autologous transfusion was started early and if the blood loss exceeded the autologous blood donation, homologous blood was also given. The autotransfusion was performed in reverse order of collection i.e. first unit collected was transfused last.

During surgery, monitoring included ECG, heart rate, arterial blood pressure, central venous pressure, oxygen saturation, temperature, urine output and blood loss by gravimetric method. Blood collected in suction bottles and drapes was also included in the total calculated blood loss. Arterial blood gas and serum electrolytes were measured hourly during surgical procedure. Preoperative hemoglobin, hematocrit, electrolytes were recorded as baseline values. These were measured again after blood drainage, hemodilution, at maximum surgical blood loss and after retransfusion in group II, whereas in group I, same parameters were measured at maximum surgical blood loss and after transfusion of homologous blood.

The results were analyzed statistically using student's't' test for inter group comparison and analysis of variance test (ANOVA) for intra group comparison. A p value of < 0.05 was considered significant whereas a p value of > 0.05 was considered insignificant.

RESULTS

The groups were statistically comparable with respect to age, weight, sex and duration of surgery [Table 1]. The amount of surgical blood loss in group I was 835.29 ± 684.37 ml, whereas in group II, 865±409.78 ml of blood was lost during surgery. Difference in blood loss between group I and group II was statistically insignificant (p>0.05). The mean volume of homologous blood transfused in group I patients (Control Group) was 864.71±349.89 ml, compared to 165±299.6 ml in group II (ANH Group). Reduction in homologous blood used in group II was statistically significant (p<0.05). The amount of autologous blood withdrawn and retransfused in group II was 802.5±208 ml. All patients (100%) in group I received homologous blood, 13 patients (65%) requiring more than 2 units of blood. In group II, only 5 (25%) patients received homologous blood, with just one patient requiring more than 2 units of blood.

The hematological and hemodynamic changes in two groups are summarized in Table 2 and 3. The baseline (Preop) hemoglobin value averaging 12.61±1.16 gm/dl in group I and 13.35±1.40 gm/dl in group II, were statistically comparable. When compared to baseline values, a significant fall in Hb was observed in both the groups during

Table 1
Demographic Data in the two groups. (Mean ± SD)

	Group I	Group II
Age (Years)	42.94 ± 11.79	47.35 ± 6.31
Weight (kgs)	58.76 ± 12.45	56.90 ± 9.35
Sex (M:F)	10:10	8:12
Duration of Surgery (Hrs)	5.147 ± 0.931	5.150 ± 1.182
Blood loss (ml)	835.29 ± 684.37	865 ± 409.78
Homologous blood used (ml)	864.71 ± 349.89	165 ± 299.61*
Autologous Blood Used (ml)	——	802.5 + 208

* Significant (p< 0.05)

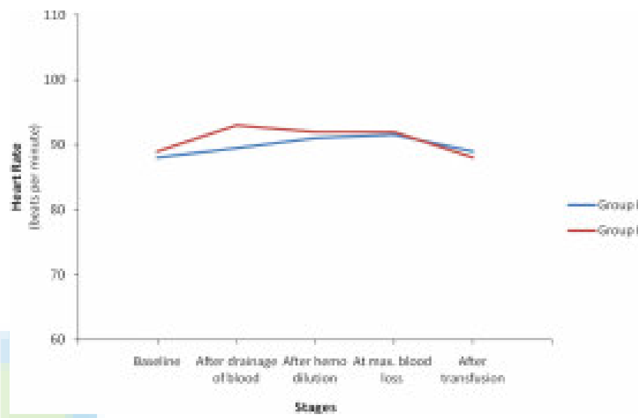

Figure 1
Changes in Heart Rate at various Stages in two Groups

Table 2
Hematological and hemodynamic Parameters at various stages of study in group I (mean ± SD)

Parameter	Baseline (Preop)	At maximum Blood loss	After transfusion
Hemoglobin (gm/dl)	12.61±1.16	9. 93±1.45*	11.35±1.40*
Hematocrit (%)	38.41±3.81	29.94±4.39*	34.47±4.37*
Heart Rate (bpm)	87.88±10.94	91.53±10.37**	88.71±13.08**
Mean Arterial pressure (mmHg)	94.47±10.64	91.76±10.92**	91.53±10.87**

* Significant change from baseline values (p< 0.05)
** Non Significant change from baseline values (p> 0.05)

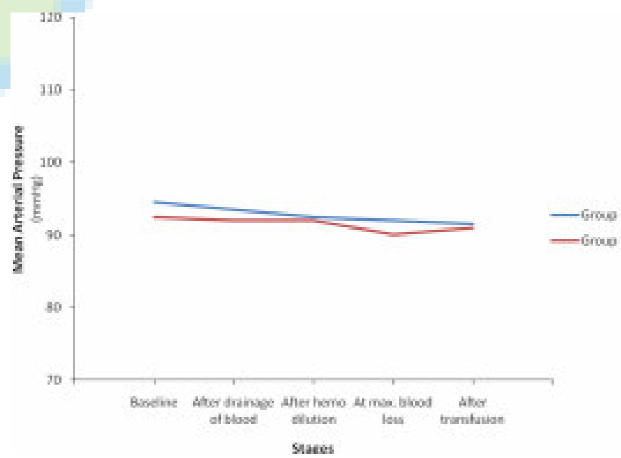

Figure 2
Changes in Mean Arterial Pressure in the two Groups

Table 3
Hematological and hemodynamic Parameters at various stages of study in group II (mean + SD)

Parameter	Baseline (Preop)	After blood Drainage	After Hemodilution	At Maximum Blood Loss	After Transfusion
Hemoglobin (gm/dl)	13.35 ± 1.40	10.44 ± 0.97*	9.38 ± 0.94*	9.11 ± 1.47*	10. 67 ± 1.26*
Hematocrit (%)	39.57 ± 4.26	30.95 ± 2.68*	27.80 ± 2.15*	26.85 ± 4.33*	31.80 ± 3.66*
Heart Rate (bpm)	88.71 ± 13.08	92.65 ± 15.29**	91. 75 ± 17.70**	92. 10 ± 20.27**	87.88 ± 10.94**
MAP (mmHg)	92.50 ± 6.29	91.75 ± 17.70**	92.10 ± 20.27**	89.71 ± 13.08**	90.76 ± 10.92**

* Significant change from baseline values (p< 0.05)
** Non Significant change from baseline values (p> 0.05)

various stages of surgery ($p<0.05$). Although mean hemoglobin levels at maximum blood loss and after transfusion of blood in group II were lower than in group I, yet the variation between the groups at different stages was statistically insignificant ($p>0.05$). In group II, during blood drainage and hemodilution, the hematocrit decreased significantly from an initial average hematocrit value of 39.57% to a mean of 26.85±4.33% at maximum blood loss, which when compared with group I at the same stage was statistically significant ($p<0.05$). On all other occasions, the variation in mean hematocrit value between the two groups was statistically insignificant.

The hemodynamic parameters at various stages of study were well maintained in both the groups. The heart rate and mean arterial pressure did not differ significantly between the two groups (Fig.1&2). CVP was also maintained within normal range indicating normovolemia in both the groups.

DISCUSSION

In neurosurgery, a major problem during excision of intracranial meningioma is the extensiveness of the surgical procedure associated with significant amount of blood loss due to high vascular nature of the tumor. Moreover the hemostasis is usually very difficult to achieve especially in deep-seated meningioma, often requiring blood transfusion. However it is also now realized that transfusion of homologous blood carries with it a potential risk for the recipient such as hemolytic reactions, transmission of infections, metabolic disturbances, coagulation disorders, and immune-suppression.[2,3,4]

The need to limit homologous blood and blood component transfusion has been emphasized in many studies and audits relating to transfusion practices.[8] Several blood conservation strategies have been advocated with the aim of reducing homologous blood transfusion. Use of ANH and autologous blood transfusion as a practice to reduce the use of homologous blood was recommended by National Institute of Health (NIH) Consensus Conference.[9] ANH and autologous blood transfusion has decreased not only the need for intraoperative homologous blood transfusion but also the hazards associated with it. Autologous blood collected on the operation table prior to surgery and stored at room temperature has viable platelets and clotting factors in addition to other constituents of blood.[10]

Acute normovolemic hemodilution has been employed from limited to extreme degree of dilution. Hemodilution up to 27 to 30% hematocrit value is called moderate hemodilution and it is the acceptable value for elective surgery of ASA grade I patients even without hemodilution.[11] It reduces blood viscosity and hence improves blood flow in the macro as well as microcirculation, improves tissue perfusion and oxygen supply.[12] This could be beneficial especially in patients undergoing intracranial surgery.

In the present study, ANH was performed to a target hematocrit of 30% using 6% HES. The removal of autologous blood units and hemodilution was accompanied with hemodynamic stability and without any evidence of electrocardiographic changes. We did not observe any significant changes in heart rate although decrease in heart rate during hemodilution has been reported.[13] An increase in heart rate during hemodilution usually indicates hypovolemia, too low Hct or insufficient oxygen transport.[12] Statistically significant fall in blood pressure during hemodilution has been observed by Kafer et al.[14]

In our study, we used 6% Hydroxyethyl starch as the replacement fluid. Hydroxyethyl starch solution is physiologically compatible and contains spherical, branched chains of glucose molecules similar to glycogen. Average molecular weight of hydroyethyl starch is 200000 dalton. There is still a debate on whether crystalloids or colloids should be used as diluents to maintain normovolemia during autologous blood collection. Large volumes of crystalloids cause interstitial edema and dilute the coagulation factors. Colloids have the advantage of superior intravascular retention, smaller volume requirement and less pulmonary complications.[7] Hursh et al reported an increased incidence of transoperative hypotension and pulmonary morbidity in patients diluted with Ringer's lactate as compared to those hemodiluted with Dextran 40.[9] Watzer et al have demonstrated safety with the use of hydroxyethyl starch as diluents during ANH.[15]

The efficacy of ANH for reducing the use of homologous blood has remained a controversial issue. Olsfanger et al reported that in patients undergoing total knee replacement, ANH was an effective blood conservation strategy.[16] Monk et al also demonstrated that ANH was a safe, effective and inexpensive method of blood conservation.[17] In contrast, Nash et al showed that in a group of patients undergoing ANH, 20% required homologous blood, a similar number to an untreated control group.[18] In our study too, 5 patients (25%) needed homologous blood in ANH group, compared to control group where all (100%) needed homologous blood transfusions.

The results of our study indicate that Acute Normovolemic Hemodilution with Autotransfusion is a safe and feasible technique to reduce intraoperative blood loss and the need for homologous blood transfusion in patients undergoing excision of intracranial meningioma. However the use of controlled hypotension in combination with ANH may further improve the results of this technique.

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