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Research Article

Cerebral hemodynamics and oxygenation during brain tumor resection: A comparative study between different types of infusates

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KEYWORDS

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Oxygenation;
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Abstract *Background:* This prospective randomized study was conducted to evaluate the effects of different types of infusates (normal saline, hemaccel and blood) on cerebral hemodynamics and oxygenation during brain tumor resection.
Methods: 60 patients scheduled for the resection of brain tumor were included. They were randomly classified into three groups by closed envelope randomization ($n = 20$) according to type of maintenance fluid, Crystalloid (normal saline), colloid (hemaccel) and blood group. Anesthesia was induced using thiopental sodium 5–7 mg/kg, atracurium to facilitate intubation and isoflurane for maintenance. Hemodynamics and oxygen parameters including Cerebral metabolic rate for oxygen ($CMRO_2$), Cerebral oxygen extraction (CEO_2), Cerebral blood flow equivalent (CBFe) were recorded after induction, 30 min, 1 h, 1.5 h, 2 h and at closure of the dura.
Results: In comparison to the basal value, lactate and glucose displayed significant increase at 1 and 2 h in crystalloid and blood group. $CMRO_2$ in the blood group showed an intra-group

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significant increase when compared to the basal value. Both $CMRO_2$ and CEO_2 displayed a significant increase in the blood group at the second hour in comparison to the colloid group while CEO_2 was significantly dropped in the colloid group from 1 h till the end when compared to the crystalloid group. CBFe displayed significant decrease in crystalloid and blood groups in comparison to the colloid group from 1 h till after closure.

Conclusion: Colloid is an effective maintenance infusate during brain tumor resection as it accompanied with a significant increase in SjO_2 which might be explained with an increase in cerebral delivery of oxygen and a decrease in $CMRO_2$ consumption. Also colloid group is the only group that did not alter the blood lactate level throughout the study period. Lastly, it was observed that flow-metabolism coupling was maintained with colloid group only, where as the coupling was disturbed in the other two groups.

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1. Introduction

Brain tumors represent a major medical problem due to the complex effects either locally on the brain or on different body systems. These effects were produced by alteration of the cerebral blood flow either directly through compression of the adjacent vessels or indirectly via increased intra-cranial pressure and generation of new unhealthy vessels that lack all cerebrovascular properties as barrier mechanisms, carbon dioxide (CO_2) responsiveness and autoregulatory capacities [1].

In neurosurgery, preoperative fasting, induction of general anesthesia, the use of diuretics and bleeding may decrease intravascular volume, blood pressure and/or cerebral perfusion pressure (CPP) as well as compromise perfusion of other organs [2]. The corner stone of intra-operative fluid administration is to maintain adequate oxygen delivery, normal electrolyte concentrations, adequacy of vital organ perfusion and to maintain patients' euglycemic [3]. Fluid replacement in cranial surgery should be limited to glucose free isotonic crystalloid as normal saline or colloid solutions. Controversy still surrounds the choice between crystalloid and colloid solutions [4].

Colloids available in the markets are either polysaccharides or polypeptides; the latter prepared from a chemically modified collagen [5]. Hemaccel is a synthetic polygeline that has been used as a volume replacement. One of the advantages of hemaccel over other colloids like dextran or hetastarch is the respect of blood clotting [6,7]. These generations of gelatins help to fill the gap that exists between crystalloids and blood products [8]. Blood transfusions are usually given to increase oxygen-carrying capacity and intravascular volume. However, increasing oxygen-carrying capacity is the only real indication for blood transfusion [9].

Monitoring of jugular venous oxygen saturation (SjO_2) has been shown to be useful in the intensive care of comatosed head-injured patients and in the intra-operative treatment of patients undergoing neurosurgical procedures [10]. Intra-operative monitoring of cerebral hemodynamics is very difficult. Jugular bulb cannulation and sampling helped a lot in this aspect. Measurements of jugular venous oxygen saturation have been used to assess cerebral oxygenation and metabolism that may alter CBF [11]. Crystalloids, colloids and blood, as infusates, have different compositions, viscosities, acidic activities, oxygen-carrying capacities and electrolyte constituents. All these differences can affect the integrity of the delicate cerebral hemodynamics and metabolism. So, the aim of this study was to evaluate the efficacy and the effects of different types of infusates in patients subjected to brain tumor resection.

2. Patients and methods

This prospective randomized study was conducted after approval by the local ethical committee of Department of Anesthesia and Surgical Intensive Care, Faculty of Medicine, Mansoura University. Randomization was done through closed envelope method. This study was carried out on 60 patients of either sex with an age ranging from 20 to 60 years. These patients admitted to the department of Neurosurgery in Mansoura University Hospital for elective resection of supratentorial brain tumors (47 right sided tumor and 13 left sided tumor). They were randomly classified into 3 equal groups according to the type of the maintenance fluid used. All patients have given a written informed consent prior to enrollment.

Patients with cardiac or respiratory insufficiency, severe hepatic or renal impairment, hypertension, uncontrolled diabetes mellitus, severe polyurea of any cause (e.g. diabetes insepidus), CPAT (cerebello – pontine angle tumor), recent history of intracranial hemorrhage, and patients with moderate and severe increased intra-cranial pressure, all are excluded from this study.

The day before surgery all patients were evaluated fulfilling full medical history, clinical examination, chest X-ray and ECG. Laboratory investigations included complete blood picture and hematocrit, serum creatinine, serum bilirubin, albumin, SGOT, SGPT, prothrombin time and activity, INR and blood glucose.

On the day of surgery and after their arrival to the operating theater two wide bore intravenous cannulae (18 G) were inserted through suitable peripheral veins. I.V. midazolam 0.05 mg/kg and I.V. fentanyl 1.5 μg/kg 10 min before induction were given and an incremental dose of fentanyl was repeated according to the hemodynamic profile. The maximum dose of fentanyl reached up to 200 μg.

Preanesthetic monitoring included pulse, ECG, blood pressure (non-invasive), and peripheral O_2 saturation.

2.1. Induction of anesthesia

Pre-oxygenation with 100% O_2 for 5 min then anesthesia was induced using I.V. thiopental sodium 5–7 mg/kg. With the loss of consciousness, positive pressure ventilation was provided via a face mask at a rate of 12–15 breathes/minute. The trachea was intubated with a suitable cuffed endotracheal tube 2 min after an induction dose of atracurium besylate (0.5 mg/kg) to facilitate intubation, followed by top up doses of 1/5 of the initial dose of atracurium for maintenance of muscle relaxation.

After that, all patients were mechanically ventilated with O_2: air using Dragger (Fabius GS-Germany) ventilator with tidal volume of 8–10 ml/kg and *I*/*E* ratio 1:2 through closed circuit with fresh gas flow around 3 l. End-tidal CO_2 was monitored by main stream capnograph. Minute ventilation was modified to keep $EtCO_2$ around 30 mm Hg.

2.2. Maintenance

Anesthesia was maintained with a mixture of oxygen:air (1:1) and isoflurane (from 0.6 to 1). Fentanyl administration was repeated if needed. Mannitol (20%) was given in a dose of 1 gm/kg starting with the scalp incision in all groups.

2.3. Cannulation

- *Arterial cannula (20 G): it* was inserted into the radial artery of the non-dominant hand (after performance of modified Allen's test) under aseptic conditions for repeated arterial blood gas sampling.
- vv*Central venous catheter (18 G):* A single lumen catheter (Amecath, France) was inserted in the right subclavian vein with strict sterile technique using Sildenger technique. The catheter was then flushed with heparinized normal saline solution and connected to a pressure transducer for central venous pressure monitoring. The position of the catheter was confirmed by anterio-posterior chest X-ray just after insertion by C-arm.
- *Jugular bulb catheter:* The patients were placed flat in supine position with slight extension of the neck. The head was in neutral position or slightly tilted away from the side of insertion. Antiseptic solution was applied to the neck and upper thoracic area. The anatomical landmarks for the internal jugular vein was identified (lateral to a palpable internal carotid artery, medial to the sternomastoid muscle, at the level of cricoid cartilage, where at this site, internal jugular vein is more or less superficial and could be easily accessible. The internal jugular vein (right side in 59 patients and left in one patient where we met difficulty for right sided cannulation) was then cannulated per cutaneously lateral to the artery by retrograde insertion of a 16-gauge catheter(Amecath, France). The catheter was then advanced towards the external auditory meatus using Sildenger technique till the resistance of the base of the skull is reached (at which, about 10–15 cm of the catheter was inserted). The catheter was then withdrawn for about 1–2 mm [13].The position of the catheter was confirmed by antero-posterior and lateral neck X-ray just before skin incision by C-arm.

2.4. Fluid regimen

Patients were randomly allocated (closed envelop method) into three equal groups according to the type of infusate used.

2.4.1. The first group (crystalloid) (n = 20)

It was maintained with crystalloid solution (normal saline 0.9%) from the start, guided by CVP values and urine volume and no blood was given unless there was a severe blood loss (more than 20% of total blood volume) and/or hematocrit value < 30% and in this case the patient was excluded from the study.

2.4.2. The second group (colloid) (n = 20)

It was maintained with colloid solution (Hemaccel solution) from the start (maximum volume was 1000 ml all through the 2 h of the study), guided by CVP and urine volume and no blood was given even with blood loss till our lower hematocrit limit (30%) was reached or with severe blood loss (more than 20% of total blood volume).

2.4.3. The third group (blood) (n = 20)

It was maintained with blood, any blood loss is replaced by blood transfusion from the start of operation, guided by CVP and urine volume.

- From our knowledge, there were no study that uses the blood as a sole infusate for maintenance fluid therapy during brain tumor resection. So the rationale for the use of blood in this group is to assess the blood effect on the rheology of cerebral circulation that might consequently influence cerebral hemodynamics and oxygenation.
- This policy of fluid therapy was maintained for 2 h, then the routinely used regimen was adopted (crystalloid ± blood transfusion guided by blood loss, CVP and urine output).

2.5. Monitoring and sampling

2.5.1. Hemodynamics and oxygen parameters

Heart rate (HR), ECG monitoring, non–invasive arterial blood pressure (NABP), arterial oxygen saturation (SaO_2; using pulse oxymetry), end tidal carbon dioxide ($ETCO_2$) and central venous pressure (CVP).

- The above mentioned parameters were recorded immediately after induction and every 30 min till the end of surgery using Drager (Infinity Kappa, Mexico) monitor with Samsung screen.

2.5.2. Laboratory assessment

Blood gases using blood Gas System (AVL 990, Austria) and the samples taken from radial artery and jugular bulb immediately after induction (after stabilization of $ETCO_2$ between 30 and 35 mm Hg) then at 30, 60, 90 and 120 min after induction and lastly after finishing the surgical procedure.

- Both jugular bulb and arterial blood samples were collected in heparinized syringes and kept in ice till they were analyzed.

Hb and HCT value using Automatic Cell Counter (Sysmex Kx-21, Japan) and blood glucose level: using Cobas Integra 800 (Roche, Germany) were assessed.

Serum lactates (from jugular bulb) were taken immediately after induction, 60 and 120 min.

Lactate Samples: 3 mL blood samples were collected on fluoride, immediately stored at 2–8 °C, transported to the hospital's laboratory and then lactate was measured.

2.5.3. Calculated parameters

(a) Estimated cerebral metabolic rate for oxygen ($eCMRO_2$) was calculated as the product of $PaCO_2$ and arterio-jugular oxygen content difference [14].

$$eCMRO_2 = (a\text{-}jDO_2) \times PaCO_2/100 \quad (1)$$

(b) Cerebral oxygen extraction ratio (CEO_2) was calculated as the difference between arterial and jugular oxygen saturation [11,15].

$$CEO_2 = SpO_2 - SjO_2 \quad (2)$$

(c) Cerebral blood flow equivalent (CBFe) is an index of flow metabolism relationship and it was calculated as a reciprocal of arterio-jugular oxygen content difference [16,17].

$$\text{CBF equivalent} = \frac{1}{a\text{-}jDO_2} \quad (3)$$

(d) Blood losses were calculated through measuring the volume of the blood in suction apparatus, socked surgical towels and gauze.

2.6. Postoperative period

The patient was transferred to a surgical intensive care for at least 24 h with full monitoring, and any complications were recorded (either intra-operative or postoperative).

2.7. Data analysis

The power of this clinical trial was retrospectively calculated using the G Power analysis program version 3.[12] Using post-hoc power analysis with accuracy mode calculations and assuming type-I error protection of 0.05 and medium effect size convention of 0.3, a total sample size of 60 patients produced a power of 0.78.

Statistical Package of Social Science (SPSS), version 10, was used for analysis of data of this study. Distribution of data (normality) was identified using a Kolmogrov–Smirnov test. Normally distributed data (ratio and interval-scale data) were subjected to ANOVA test followed by L.S.D. (as a post-hoc) test to identify the presence or absence of significance, either in inter- or intra-group multiple comparisons. Data (ratio and interval-scale) deviated from normal distribution, as well as ordinal data, were analyzed using Kruskal–Wallis test (multiple comparisons) followed by Mann–Whitney test for single comparison.

Chi-square test was used to identify significant differences between nominal data (e.g. sex as a datum). Any difference or change showing probability (P) less than 0.05 was considered statistically significant.

3. Results

Patients were randomly classified into 3 equal groups; group I (crystalloid group, $n = 20$), group II (colloid group, $n = 20$), and group III (blood group, $n = 20$). Patients in the 3 studied groups showed no significant changes concerning the demographic data (age, sex) as well as duration of surgery (Table 1).

3.1. Hemodynamic parameters

Perioperative HR and MAP did not differ significantly during the whole study period when comparing all groups to each other. However, some intra-group significant differences were noticed in the 3 groups in comparison to the basal values (Table 2). Regarding CVP, there were no significant changes detected between all groups throughout the whole study period. However, in comparison to the basal value in same group, both colloid and blood groups demonstrated a significant elevation in the last two readings of the study (Table 3).

3.2. Hematological changes

Both Hb and HCT were significantly decreased in both crystalloid and colloid groups but significantly increased in blood group in comparison to the corresponding basal values of

Table 1 Patients characteristics and duration of surgery of the studied groups. Values are presented as mean ± SD, (min–max), ratio (M/F).

	Crystalloid (G I) ($n = 20$)	Colloid (G II) ($n = 20$)	Blood (G III) ($n = 20$)
Age (years)	36.6 ± 12.50 (20–55)	42.3 ± 11.07 (20–60)	41.15 ± 7.80 (25–53)
Sex (M/F)	(8/12)	(11/9)	(9–11)
Duration of surgery (h)	3.15 ± 1.46 (2–7)	2.75 ± 0.91 (2–5)	3.15 ± 0.93 (2–5)

Table 2 Perioperative heart rate "HR" (bpm) and mean arterial blood pressure "MAP" (mm Hg) for studied groups. Values are in mean ± SD.

Time	HR (bpm)			MAP (mm Hg)		
	G I (crystalloid)	G II (colloid)	G III (blood)	G I (crystalloid)	G II (colloid)	G III (blood)
Before induction (Basal)	89 ± 12.5	83 ± 8.3	88 ± 11.8	90 ± 11.3	91 ± 8.6	94 ± 8.1
Immed. post-induction	93 ± 13.7	93 ± 10.0*	91 ± 9.9	83 ± 14.1*	86 ± 12.6*	87 ± 12.4*
0.5 h	86 ± 13.9	82 ± 10.9	86 ± 13.6	87 ± 10.2	89 ± 10.8	92 ± 8.7
1 h	84 ± 12.2	84 ± 12.1	85 ± 9.7	84 ± 8.9	84 ± 12.0*	88 ± 8.8*
1.5 h	86 ± 13.6	83 ± 10.4	86 ± 9.9	84 ± 7.3	84 ± 10.6*	88 ± 8.7*
2 h	89 ± 13.2	87 ± 13.2	85 ± 11.7	88 ± 6.8	87 ± 8.8*	89 ± 9.9*
After closure	95 ± 14.3	90 ± 14.4*	87 ± 15.2	94 ± 9.2	97 ± 10.7*	99 ± 8.5*

* $P < 0.05$: significant when compared to the basal value of the same group.

Table 3 Central venous pressure (CVP) of the studied groups. Values are in mean + SD.

Time	CVP (mm Hg)		
	G I (crystalloid)	G II (colloid)	G III (blood)
Immed. post-induction (Basal)	0.1 ± 1.0	−0.1 ± 0.8	−0.2 ± 0.8
0.5 h	0.1 ± 1.1	−0.1 ± 0.7	−0.3 ± 0.4
1 h	0.0 ± 0.9	−0.2 ± 0.8	0.1 ± 0.7
1.5 h	−0.2 ± 0.8	0.1 ± 0.8	0.3 ± 0.8
2 h	0.1 ± 0.9	0.5 ± 0.6*	0.4 ± 0.7*
After closure	0.5 ± 1.1	0.7 ± 0.8*	0.8 ± 0.8*

* $P < 0.05$: significant when compared to the basal value of the same group.

the same group nearly throughout the whole intra-operative period except in blood group for HCT that showed no significant changes in comparison to the basal value. Meanwhile, a significant rise in both Hb and HCT was noticed during the whole study period in the blood group when compared to the other two groups (Table 4).

3.3. Blood lactate and glucose

There were intra-group significant increases of blood lactate in crystalloid as well as in blood group in comparison to the basal value at 1 and 2 h. Blood glucose displayed significant increase in the three studied groups 1 and 2 h in comparison to basal values. (Table 5).

Blood lactate showed a significant increase in the blood group when compared to the colloid group at the second hour intraoperatively. Similarly, blood glucose displayed significant increase in blood group in comparison to the colloid group at 2 h of surgery (Table 5).

3.4. Blood gases variables

SpO_2 displayed no significant alternations in the 3 studied groups at all study periods in comparison to the basal value and in-between the groups. Similarly, SjO_2 showed no significant differences compared to the basal value. However, there were some significant changes detected between the 3 studied groups in SjO_2. In comparison to the crystalloid group, there were significant increases in SjO_2 at all intra-operative periods and at the first 2 readings in both the colloid and blood groups, respectively. However, in comparison to the colloid group, the blood group showed a significant reduction in SjO_2 only at the second hour intraoperatively (Table 6).

Between 1 and 2 h intraoperatively, there was a significant reduction in the value of PaO_2 in blood group if compared with the corresponding readings in the crystalloid and colloid groups. Meanwhile and in comparison to the basal readings, PaO_2 displayed a significant rise starting from 1 h and from 1.5 h till the end of the study in crystalloid and colloid group respectively (Table 7).

As regards PjO_2, it showed a significant drop in blood group between the first and second hours intraoperatively when compared to the basal reading and only at the second hour in comparison to colloid group. However, a significant increase in PjO_2 was noticed in the colloid group at the last two intra-operative readings in comparison to crystalloid group (Table 7). Regarding $PaCO_2$ and $PjCO_2$, it can be clearly seen that values of both variables maintained without any significant changes within the whole monitored periods in comparison to the basal value and in-between the groups (Table 8).

In comparison to the basal readings, CaO_2 displayed significant decrease in the crystalloid and colloid groups whereas it showed significant increase in the blood group nearly at all intra-operative monitored periods. CjO_2 in the crystalloid group displayed significant decrease in comparison to the basal value at all monitored times. In addition, in comparison to the crystalloid and colloid groups, a significant elevation in both CaO_2 and CjO_2 was observed in the blood group nearly throughout the whole study period (Table 9).

3.5. Calculated cerebral values

$CMRO_2$ showed significant increase in the blood group nearly during the whole study period in comparison to the basal value. On comparing the 3 studied groups, both $CMRO_2$ and CEO_2 displayed a significant increase in the blood group at the second hour intraoperatively in comparison to the colloid group while CEO_2 was significantly dropped in the colloid group from 1 h intraoperatively till the end of the study period when compared to crystalloid group (Table 10).

Only in the blood group, CBFe was significantly reduced when compared with the basal value in the same group during the study period. On comparing the 3 studied groups, CBFe

Table 4 Perioperative haemoglobin (gm/dl) and hematocrit (%) for the studied groups. Values are in mean + SD.

Time	Hemoglobin (gm/dl)			Hematocrit (%)		
	G I (crystalloid)	G II (colloid)	G III (blood)	G I (crystalloid)	G II (colloid)	G III (blood)
Before induction (Basal)	12.0 ± 1.6	11.8 ± 1.5	12.8 ± 1.3	39.0 ± 4.4	38.4 ± 4.2	41.8 ± 3.9
Immed. post-induction	12.2 ± 1.5	11.8 ± 1.5	12.8 ± 1.3	39.3 ± 4.1	38.5 ± 4.1	41.9 ± 4.0
0.5 h	11.9 ± 1.5	11.6 ± 1.5*	13.1 ± 1.2*,**,***	38.4 ± 3.6	38.1 ± 3.8	42.5 ± 3.9**,***
1 h	11.6 ± 1.5*	11.4 ± 1.6*	13.4 ± 1.3*,**,***	37.5 ± 3.6*	37.3 ± 4.0*	42.9 ± 4.4**,***
1.5 h	11.3 ± 1.6*	11.2 ± 1.6*	13.5 ± 1.2*,**,***	36.5 ± 3.9*	37.1 ± 4.4*	43.5 ± 3.9**,***
2 h	11.1 ± 1.7*	11.0 ± 1.8*	13.6 ± 1.3*,**,***	35.6 ± 4.5*	36.6 ± 5.5*	44.2 ± 4.1**,***
After closure	11.6 ± 1.5*	11.4 ± 1.4*	13.5 ± 1.4*,**,***	37.3 ± 4.1*	37.2 ± 4.2*	43.9 ± 4.1**,***

* $P < 0.05$: significant when compared to the basal value of the same group.
** $P < 0.05$: significant when compared to group I at the same event.
*** $P < 0.05$: significant when compared to group II at the same event.

Table 5 Perioperative jugular venous blood lactate (mmol/l) and blood glucose (mg/dl) for the studied groups. Values are in mean ± SD.

Time	Blood lactate (mmol/l)			Blood glucose (mg/dl)		
	G I (crystalloid)	G II (colloid)	G III (blood)	G I (crystalloid)	G II (colloid)	G III (blood)
Before induction (Basal for glucose)				93 ± 19	95 ± 24	102 ± 27
Immed. post-induction (Basal for lactate)	0.15 ± 0.05	0.16 ± 0.08	0.17 ± 0.05	91 ± 19	98 ± 30	108 ± 38
0.5 h						
1 h	0.19 ± 0.07 *	0.18 ± 0.07	0. 20 ± 0.05*	112 ± 19*	136 ± 50*	156 ± 59*,**
1.5 h						
2 h	0.22 ± 0.09 *	0.19 ± 0.06	0.26 ± 0.07*,***	129 ± 26*	152 ± 45*	190 ± 69*,**,***
After closure						

* $P < 0.05$: significant when compared to the basal value of the same group.
** $P < 0.05$: significant when compared to group I at the same event.
*** $P < 0.05$: significant when compared to group II at the same event.

Table 6 Measured arterial oxygen saturation "SpO_2" (%) and jugular oxygen saturation "SjO_2" (%) for the studied groups (from ABG). Values are in mean ± SD.

Time	SpO_2 (%)			SjO_2 (%)		
	G I (crystalloid)	G II (colloid)	G III (blood)	G I (crystalloid)	G II (colloid)	G III (blood)
Immed. post-induction (Basal)	98.3 ± 1.16	98.9 ± 0.85	98.4 ± 1.19	68.6 ± 9.96	74.3 ± 8.69	75.1 ± 10.84**
0.5 h	98.2 ± 1.28	98.9 ± 1.07	98.9 ± 1.37	67.1 ± 9.13	73.2 ± 8.57**	74.9 ± 10.36**
1 h	98.4 ± 1.09	98.9 ± 0.98	98.4 ± 1.72	67.1 ± 7.36	73.7 ± 8.42**	70.4 ± 10.86
1.5 h	98.5 ± 1.60	99.0 ± 0.86	98.7 ± 0.85	68.0 ± 8.23	74.3 ± 8.82**	70.8 ± 10.06
2 h	98.7 ± 1.14	99.2 ± 0.83	98.8 ± 0.86	68.2 ± 6.39	75.9 ± 8.05**	69.8 ± 10.24***
After closure	98.7 ± 0.82	99.2 ± 0.86	99.0 ± 0.77	67.3 ± 8.59	74.9 ± 7.54**	70.8 ± 11.15

** $P < 0.05$: significant when compared to group I at the same event.
*** $P < 0.05$: significant when compared to group II at the same event.

Table 7 Measured arterial oxygen tension "PaO_2" (mm Hg) and jugular oxygen tension "PjO_2" (mm Hg) of the studied groups (from ABG). Values are in mean ± SD.

Time	PaO_2 (mm Hg)			PjO_2 (mm Hg)		
	G I (crystalloid)	G II (colloid)	G III (blood)	G I (crystalloid)	G II (colloid)	G III (blood)
Immed. post-induction (Basal)	167.8 ± 58.9	161.5 ± 33.3	159.0 ± 64.1	38.8 ± 7.7	45.9 ± 11.2	46.3 ± 13.9
0.5 h	176.1 ± 56.5	156.4 ± 35.7	152.6 ± 47.3	39.7 ± 8.2	43.8 ± 9.5	44.7 ± 9.4
1 h	189.3 ± 44.6*	169. 3 ± 31.4	145.9 ± 31.6**,***	39.8 ± 7.2	44.4 ± 9.1	41.1 ± 7.8*
1.5 h	207.3 ± 47.4*	185.4 ± 41.6*	154.4 ± 33.8**,***	41.1 ± 10.8	43.9 ± 9.8	41.9 ± 9.1*
2 h	199.9 ± 39.2*	186.1 ± 32.7*	160.6 ± 36.2**,***	39.9 ± 6.5	46.9 ± 8.9**	41.7 ± 8.5 *,***
After closure	210.4 ± 42.6*	210.6 ± 73.5*	189.7 ± 77.9	39.3 ± 7.7	45.9 ± 8.3**	44.7 ± 11.1

* $P < 0.05$: significant when compared to the basal value of the same group.
** $P < 0.05$: significant when compared to group I at the same event.
*** $P < 0.05$: significant when compared to group II at the same event.

demonstrated a significant elevation in the colloid group in comparison to other groups (Table 10).

4. Discussion

In the present study, 3 fluid regimens were compared, crystalloid (0.9% saline), colloid (Hemaccel), and blood during intracranial surgery for excision of cerebral mass lesions. The three infusates were investigated regarding intra-operative cerebral and systemic hemodynamic profile and cerebral oxygenation.

Under general anesthesia, drug effects, surgical stimulus, changes in posture, temperature and blood volume influence autonomic functions [18]. Thus, it would seem probably that changes of HR and MAP differ with different fluid regimens reflecting indirect variable effects of different infusates on the autonomic and cardio-respiratory activities.

Table 8 Measured arterial carbon dioxide tension "$PaCO_2$" (mm Hg) and jugular carbon dioxide tension "$PjCO_2$" (mm Hg) of the studied groups (from ABG). Values are in mean ± SD.

Time	$PaCO_2$ (mm Hg)			$PjCO_2$ (mm Hg)		
	G I (crystalloid)	G II (colloid)	G III (blood)	G I (crystalloid)	G II (colloid)	G III (blood)
Immed. post-induction (Basal)	32.8 ± 3.54	34.4 ± 5.22	33.1 ± 3.83	41.9 ± 11.69	41.8 ± 7.35	39.7 ± 6.01
0.5 h	32.2 ± 3.47	34.1 ± 3.31	32.9 ± 3.73	40.3 ± 11.11	40.1 ± 5.77	38.2 ± 5.04
1 h	31.8 ± 3.39	32.8 ± 3.91	33.0 ± 4.38	39.1 ± 5.04	40.7 ± 5.81	41.8 ± 6.20
1.5 h	31.9 ± 3.33	32.7 ± 4.33	32.5 ± 3.47	40.3 ± 9.64	39.7 ± 5.21	40.4 ± 6.32
2 h	32.6 ± 2.93	34.5 ± 4.18	33.2 ± 5.20	40.4 ± 10.24	41.4 ± 6.41	41.6 ± 7.04
After closure	34.0 ± 4.14	35.8 ± 4.46	35.0 ± 4.97	42.2 ± 9.03	42.1 ± 4.54	42.0 ± 5.68

Table 9 Arterial oxygen content "CaO_2" (ml/dl) and jugular oxygen content "CjO_2" (ml/dl) of the studied groups. Values are in mean ± SD.

Time	CaO_2 (ml/dl)			CjO_2 (ml/dl)		
	G I (crystalloid)	G II (colloid)	G III (blood)	G I (crystalloid)	G II (colloid)	G III (blood)
Immed. post-induction (Basal)	16.5 ± 2.01	16.1 ± 1.91	17.4 ± 1.62***	11.3 ± 1.98	11.6 ± 1.69	12.9 ± 2.04**,***
0.5 h	16.1 ± 1.86*	15.9 ± 2.00*	17.7 ± 1.56*,**,***	10.7 ± 1.23	11.5 ± 1.62	13.2 ± 2.17**,***
1 h	15.8 ± 1.94*	15.6 ± 2.13*	18.0 ± 1.62*,**,***	10.4 ± 1.23*	11.3 ± 1.45	12.7 ± 2.31**,***
1.5 h	15.6 ± 1.94*	15.4 ± 2.22*	18.3 ± 1.53*,**,***	10.5 ± 1.78*	11.1 ± 1.65	12.9 ± 2.24**,***
2 h	15.3 ± 2.19*	15.2 ± 2.50*	18.5 ± 1.62*,**,***	10.3 ± 1.71*	11.3 ± 1.71	12.8 ± 2.34**,***
After closure	16.1 ± 1.92*	15.8 ± 1.92*	18.5 ± 1.73*,**,***	10.5 ± 1.92*	11.6 ± 1.42	12.9 ± 2.35**,***

* $P < 0.05$: significant when compared to the basal value of the same group.
** $P < 0.05$: significant when compared to group I at the same event.
*** $P < 0.05$: significant when compared to group II at the same event.

Immediately after induction of anesthesia, both HR (in colloid group) and MAP (in all groups) showed significant changes (increase in HR but decrease in MAP) from the basal readings. However, in the next intra-operative readings (where the HR and MAP decreased), both hemodynamic variables showed good stability within normal physiological range.

The minimally significant decrease in MAP in the 3 studied groups may be attributed to the relatively decreased systemic vascular resistance (SVR) as a direct effect of isoflurane anesthesia used. This result was supported by Cahalan et al. [19] and Lam and Gelb [20] who proved that isoflurane produced dose-dependent decrease in MAP (by approximately 25% at 1 MAC) when administered to human volunteers due to a decrease in the SVR. This may be also due to the myocardial depression of isoflurane [21].

On the other hand, a significant elevation of the HR and MAP was encountered in the current study in the closure value in the colloid and blood groups, mostly was due to regaining of consciousness after anesthesia leading to a sympathetically mediated neuro-endocrinal excitatory response.

The intravascular administration of Hemaccel in the colloid and blood in blood groups resulted in a significant increase of the CVP, 2 h after induction and immediately after closure, when compared with the baseline values. This may be attributed to the proper fluid resuscitation. That is because colloids and blood remain in the intravascular compartment for long time compared to crystalloids and can augment the intravascular volume as confirmed by Ueyama et al., study [22].

As regard the HCT and Hb, significant decrease in the crystalloid and colloid groups could be explained by the dilutional effect of the fluid used and/or surgical blood loss without immediate blood transfusion at those times. These findings are in agreement with previous findings that in surgical patients, low HCT are usually encountered after advanced surgical blood loss and a sanguineous infusion therapy to maintain normovolaemia as a result of the effects of dilution with crystalloids and colloids [23–25].

Similarly, Tommasino [26] stated that one common accompaniment of fluid administration is a reduction in Hb and HCT. In the face of active blood loss, the use of a sanguineous fluid can cause some degree of anemia.

Meanwhile, the significant rise in Hb and HCT in the blood group could be explained by the immediate compensation of any blood loss with blood transfusion, as planned in the study protocol, which can maintain high Hb and HCT levels inspite of any blood loss. This is supported by the Niraj et al. [27] who stated that intra-operative Hb estimation is considered an effective and simple objective measurement to increase the incidence of appropriate transfusions. It is worth noting that the least recorded value of Hb was 11.1 gm/dl (crystalloid group) and 36.5% for HCT (crystalloid group). These two values are within physiological range and allow very good oxygen delivery for different tissues.

In this study, significant increase in blood lactate was recorded in the crystalloid and blood groups (still within physiological range) when compared to basal values. There was a maximum increase at the second hour in the blood group when compared to colloid group. In the present study blood lactate level was used as an index of anaerobic metabolism, i.e., if it was higher than expected levels this means inadequate oxygen supply to the brain. This might be attributed to the decreased SjO_2, decreased CBF (associated with increased CEO_2) and/or

Table 10 Cerebral metabolic rate for O_2 ($CMRO_2$), cerebral extraction ratio (CEO_2) and Cerebral blood flow equivalent (CBFe) of the studied groups. Values are in mean + SD.

Time	$CMRO_2$ (ml O_2/100 gm/min)			CEO_2 (%)			CBFe (ml blood/ml O_2)		
	G I (crystalloid)	G II (colloid)	G III (blood)	G I (crystalloid)	G II (colloid)	G III (blood)	G I (crystalloid)	G II (colloid)	G III (blood)
Immed. post-induction (Basal)	1.7 ± 0.60	1.5 ± 0.52	1.4 ± 0.67	29.7 ± 10.3	24.6 ± 8.5	23.4 ± 11.2	0.22 ± 0.08	0.27 ± 0.12	0.28 ± 0.11
0.5 h	1.7 ± 0.58	1.5 ± 0.59	1.5 ± 0.67	31.0 ± 9.0	25.7 ± 8.6	25.0 ± 10.8	0.21 ± 0.09	0.27 ± 0.12	0.27 ± 0.13
1 h	1.7 ± 0.49	1.4 ± 0.61	1.7 ± 0.61*	31.4 ± 7.3	25.2 ± 8.7**	27.9 ± 10.6	0.20 ± 0.06***	0.28 ± 0.15	0.21 ± 0.08*,***
1.5 h	1.6 ± 0.50	1.4 ± 0.58	1.7 ± 0.55*	30.8 ± 8.5	24.9 ± 9.4**	27.9 ± 10.1	0.21 ± 0.06***	0.28 ± 0.15	0.21 ± 0.07*,***
2 h	1.6 ± 0.42	1.4 ± 0.59	1.9 ± 0.60*,***	30.5 ± 6.7	23.2 ± 8.1**	28.0 ± 10.3***	0.21 ± 0.07***	0.31 ± 0.14	0.20 ± 0.10*,***
After closure	1.9 ± 0.61	1.6 ± 0.65	1.9 ± 0.64*	31.5 ± 8.7	24.4 ± 7.7**	28.2 ± 11.1	0.20 ± 0.07***	0.27 ± 0.12	0.21 ± 0.09*,***

* $P < 0.05$: significant when compared to the basal value of the same group.
** $P < 0.05$: significant when compared to group I at the same event.
*** $P < 0.05$: significant when compared to group II at the same event.

increased metabolism ($CMRO_2$). Also, it may be due to high level of glucose in these groups that was available for metabolism which exceeded the aerobic metabolic capacity. This is in accordance with previous findings that hyperglycemia can correlate to increased cerebral lactate [28,29]. The use of lactate as an indicator of oxygenation imbalance is in agreement with Ezzat [30], Cruz et al., [31] and Marion [32] who stated that moderate cerebral ischemia associated with lactate production which is used as a reliable indicator of cerebral ischemia in acute brain injury. Another point in our explanation is that elevated lactate in the present study may be due to the surgery itself [33,34].

On the other hand, our results are contradictory to previous studies that did not support inadequate systemic oxygen delivery as a cause of raised lactate levels [35]. Furthermore, one study found that raised lactate levels were associated with reduced levels of oxygen extraction and suggested that peripheral oxygen utilization may be impaired [36].

In comparison to the basal value, the 3 studied groups demonstrated a significant increase in blood glucose values at 1 and 2 h post-induction. Possible causes include surgical stress and the effect of anesthesia with changes in catecholamines and cortisol level which, in turn, tend to reduce insulin secretion or to prevent its glucose-lowering effect leading to hyperglycemia.

This can be supported by Halter and Pflug [37] and Hagen et al. [38] who demonstrated that patients undergoing surgery mount a significant stress response, as measured by the release of catecholamines, corticosteroids (endogenous, or may be also exogenous from IV steroids used), ADH and growth hormone, glucagons and the suppression of insulin release. Most of these hormones are hyperglycemic in action, either through glycolysis or gluconeogenesis.

On the other hand, the intra-operative significant increase in glucose level in the blood group in comparison to the other two groups could be attributed to the presence of dextrose as a preservative in the blood to provide red cell energy.

The increase in SjO_2 in colloid and blood groups in relation to crystalloid group may be due to the increase in oxygen delivery to the brain by colloids infusion or blood transfusion (not with crystalloids).This explanation is in accordance with Pérez et al. [39] who stated that the increase in SjO_2 occurs with an increase in cerebral delivery of oxygen or a decrease in $CMRO_2$ consumption.

On other hand, it could be suggested that reduced values of SjO_2 in the blood group at the second hour of the study in comparison to colloid group results mainly from any factor that decreases cerebral delivery of oxygen, e.g., reduction of the CBF or hyperventilation and/or an increase in the cerebral metabolic activity. Similar findings were demonstrated in other studies where a decrease in the SjO_2 (high a-jDO_2) represents an increase in CEO_2 which may result from systemic hypoxia, low CBF secondary to hypotension or cerebral vasospasm or increased ICP (may be caused by mass lesions, diffuse brain edema) or hyperventilation (hypocapnia) as SjO_2 is highly related to $PaCO_2$ [39,40].

Arterial oxygen tension (PaO_2) rise in crystalloid group proves that pulmonary function is not affected adversely by crystalloid resuscitation [41] or with fewer pulmonary complications and hemodynamic stability [42]. Moreover, lymphatic flow can increase up to 20 times, which explains

why the additional fluid given during crystalloid resuscitation does not normally cause pulmonary edema [43].

As regards PjO_2, our findings (higher with colloid than with crystalloid) may be attributed to improved microcirculation, less tissue swelling and less pulmonary complications with colloid infusion. Our findings correlate with the results of Lang et al. [44] as regards colloidal PO_2 increase, but are contradictory to their results as regards crystalloidal PO_2 (as it increases in our study). They investigated the effects of a colloid-based versus a crystalloid-based intravascular volume replacement regimen on tissue oxygenation in patients undergoing major abdominal surgery. They noticed that colloid resuscitation was associated with an increase in perioperative tissue PO_2, whereas it is decreased in patients who were resuscitated with crystalloid. Improved microcirculation and less endothelial swelling may be responsible for the better PO_2 with colloids.

In our study, SaO_2, jugular and arterial PCO_2 in the three studied groups showed no significant changes and were within accepted physiological ranges throughout the study period. This is indicating good ventilation and oxygenation of all patients with controlled ventilation that maintained the $ETCO_2$ around 30 mm Hg.

A significant elevation in both CaO_2 and CjO_2 was observed in the blood group nearly throughout the whole study period in comparison to crystalloid and colloid groups and in comparison to the basal value in CaO_2. This increased O_2 content may be caused by the blood transfusion which led to increased Hb level observed in the blood group. This explanation can be supported by the fact that blood is transfused to increase oxygen content and improve oxygen delivery, thereby preventing tissue hypoxia. In the absence of clinically reliable direct measurements of adequate tissue oxygenation, Hb concentration is commonly used instead [27].

The decrease in CaO_2 and CjO_2 in crystalloid and colloid groups may be due to a significant decrease in Hb level (dilutional effect). This is because these types of fluids share in volume but not in oxygen carriage.

In this study, the blood group showed a significant steady increase in $CMRO_2$ when compared to the basal value. On the other hand, crystalloid and colloid groups showed more or less stable $CMRO_2$ all through the study period which is a better outcome neurologically. This stability can be attributed to better rheology of the blood (decreased viscosity), more stable blood flow with subsequent more efficient supply of cerebral oxygen and substrates. This explanation depending on viscosity changes can be confirmed by a previous study that proved a significant decrease in blood viscosity using crystalloids and colloids [3].

The blood group, in this study, showed a significant decrease in CBFe all through the study time in comparison to the basal values (disturbed coupling). The colloid group (as well as crystalloid group) showed good stability when compared to the basal values, meanwhile it showed significantly higher values when compared to both the crystalloid and blood groups. An explanation for the increased CBF in the colloid group may be the significantly decreased HCT (with decreased blood viscosity) by Hemaccel infusion. This is can be supported by other studies where a decrease in HCT (e.g. in anemia), cerebral vascular resistance is reduced and CBF increases, i.e., a decrease in HCT improves CBF. This is attributed to decreasing blood viscosity [45,46]. This is because organ blood flow (maintained by fluid resuscitation) is determined by the perfusion pressure, vascular resistance and blood viscosity [47] which, in turn, can influence CBF. As HCT is the single most important determinant of blood viscosity, changes in HCT lead to substantial changes in CBF [45]. A further support of our findings is that volume replacement with Hemaccel markedly reduced HCT and viscosity [3].

Potential explanation for this decrease in CBF in blood group from the basal value could be related to an increase in the viscosity and HCT of blood as a result of blood transfusion without any fluid infusion. This was confirmed by Brian et al., [48] who stated that elevated HCT (as in patients with polycythemia) can reduce CBF as a result of increased blood viscosity.

This current study had certain limitations that include relatively small number of patients, limitation of the study time to 2 h, different surgeons. We could not fix the surgeons and so the duration of the surgery and the severity of bleeding varied from one surgeon to another which might have its effect on hemodynamics and oxygenation variables. Other limitations include, inability to measure ICP, inability to blind the study, limited groups of patients, and no fluids combination group.

Continuous monitoring and measurement of cerebral parameters are very important as much as those of systemic parameters. According to the monitored variables with the positive and negative findings of the studied infusates, we can shift from one regimen of infusate to another. Future studies in this field should continue trying to exclude limitations and drawbacks of this study through near perfect research design.

5. Conclusion

Inspite of the continuous practice that used crystalloid as a main infusate during neurosurgery, colloids (hemaccel in our study) has a hopeful future to be use as an effective maintenance infusate during brain tumor resection as it accompanied with a significant increase in SjO_2 which might be due to an increase in the oxygen delivery to the brain and a decrease in $CMRO_2$ consumption. Also colloid group is the only group that did not alter the blood lactate level through out the study period. Lastly, it was observed that flow-metabolism coupling was maintained with the colloid group only.

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