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Original Article (Pages: 7201-7209)

The Effect of Inhalation Anesthesia with Hyperventilation and Total Intravenous Anesthesia on Intracranial Pressure Control in Pediatrics with Craniosynostosis Surgery: A Randomized Clinical Trial

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Abstract

Background: Intracranial pressure (ICP) control is one of the anesthesiologist challenges in craniosynostosis repair surgery, especially in multiple sutures involvement. The aim of this study was comparing the effect of two anesthesia methods including inhalation with hyperventilation and total intravenous anesthesia (TIVA) on ICP control and surgeon satisfaction in pediatrics with craniosynostosis surgery.

Materials and Methods: In this randomized clinical trial study, 40 pediatric patients with American society of anesthesiologists (ASA) I-II, 6 months to 2 years old were included. All of the patients were scheduled for craniosynostosis repair at Mofid Children Hospital, Tehran, Iran, in May 2016 to January 2017. The patients were randomly divided into two groups. In hyperventilation group, patients received isoflurane for maintenance of anesthesia and hyperventilation ($Paco_2$=25-30 mmHg) established during surgery. The total intravenous anesthesia (TIVA) group received propofol infusion for anesthesia maintenance and $Paco_2$ was maintained 35 mmHg. Intra cranial pressure (ICP) was assessed by surgeon using a 4-point scale. Hemodynamic (mean arterial pressure and heart rate) changes and blood loss were compared between hyperventilation and TIVA groups.

Results: The mean age of patients in hyperventilation group was 10.9±3.25 months and in TIVA group was 8.7 ± 2063 months (p=0.11). Fourteen (70%) patients in hyperventilation group and 6 (30%) patients in TIVA group were male (p=0.74). A significant difference was seen in ICP control and surgical condition between hyperventilation and TIVA groups (p=0.032). ICP was controlled better in hyperventilation group. There was no difference in hemodynamic parameters and blood loss between hyperventilation and TIVA groups (p>0.05).

Conclusion: This study showed inhalation anesthesia with hyperventilation was more effective than TIVA on ICP control in craniosynostosis surgery.

Key Words: Craniosynostosis, Intracranial pressure, Hyperventilation, Total intravenous anesthesia.

*Please cite this article as: Mahdavi A, Malekianzadeh B, Sadeghi A. The Effect of Inhalation Anesthesia with Hyperventilation and total Intravenous Anesthesia on Intracranial Pressure Control in Pediatrics with Craniosynostosis Surgery: A Randomized Clinical Trial. Int J Pediatr 2018; 6(2): 7201-209. DOI: **10.22038/ijp.2018.28956.2529**

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Received date: Dec 15, 2017 ; Accepted date: Jan 12, 2018

1- INTRODUCTION

Craniosynostosis is a congenital anomaly in which one or more cranial sutures fuse prematurely leading to focal or global growth delay of the skull (1, 2). 1/2000 to 1/2500 live births may have craniosynostosis, with more incidences in male (1). Craniosynostosis is usually evident at birth or during the first 2 years of life when rapid brain growth takes place (3). It may be isolated or syndromic. In complex or syndromic type multiple sutures are involved (1, 2, 4). Over 50% of cases involve sagittal suture (3, 5). Patients with syndromic type may experience functional abnormalities due to raise of Intracranial pressure (ICP), hydrocephalus and amblyopia (1). Increased intracranial pressure occurs when brain growth continues against a non-expanding calvarium (6). As a result of raised ICP, lethargy, nausea, vomiting and papilledema may be presented (7, 8). Surgical procedures should be performed early to prevent potential complications associated with increased ICP (8).

Anesthesia management should be tailored to the presence of any concomitant congenital anomalies and potential intracranial hypertension. Once the trachea is intubated, controlled ventilation should be set to maintain normocarbia unless hypocarbia is desired to minimize preexisting intracranial hypertension (3). Children with chronically elevated ICP may be relatively asymptomatic. However, acute elevation in ICP has serious consequences which affects surgical and anesthesia techniques (9). Few specific treatment options for intracranial hypertension in craniosynostosis have been studied in clinical trials. Though, most of recommendations are based on clinical experiences. Normal values of ICP are less than 10-15 mmHg for adults and older children, 3-7 mmHg for young children, and 1.5-6 mmHg for term infants (3, 10, 11). ICP values greater than 20-25 mmHg requires treatment (3, 11, 12). Cerebral perfusion pressure (CPP) depends on the level of mean systemic arterial pressure (MAP), and ICP (CPP=MAP-ICP) (10). Elevation of the head is a simple way to decrease ICP during surgery (3). Another method to lower ICP is hyperventilation and keeping Paco2 around 25 mmHg which is rapid and very effective (10). Hyperventilation constricts the vessels and reduces cerebral blood flow (CBF) (12). This technique is recommended for a short period, progressively losing effectiveness after 6 hours of continuous use (3). Moreover, osmotherapy and use of mannitol, hypertonic saline, acetazolamide, diuretics and steroid drugs are used for ICP control in various situations, whereas use of these drugs have been associated with reduction of intravascular volume in craniosynostosis patients (11, 13).

The ideal anesthesia technique for neurosurgical procedures must ensure the hemodynamic stability in order to preserve cerebral autoregulation, and reduce cerebral metabolic rate (CMR) (14, 15). Two anesthesia approaches are commonly used in neurosurgery: total intravenous anesthesia (TIVA) and inhalation anesthesia (16). TIVA is currently used more frequently in neurosurgery and is preferred method because of the fast onset of action (15). But it has several drawbacks and limitation to use in neurosurgery patients (17). TIVA is more costly, unavailability of adequate and safe intravenous drugs and instruments, difficulty in determining anesthetic plane and lack of education and training to perform than inhalation anesthesia (14). Zuleta-Alarcon et al., showed that inhaled anesthetics are good alternatives to TIVA especially in patients with normal ICP and in hospitals with limited facilities and equipment (15). Also, in Petersen et al. study, ICP was much higher in patients receiving TIVA compared to patients

treated with Cytarabine (IA) (18). Furthermore, Inhalation anesthesia with hyperventilation has previously been shown to provide neuroprotection, reduce excitotoxicity and increased physiological stability (14, 17). At a dose of 1 minimum alveolar concentration (MAC) of inhalation anesthetics, CBF increases but CMR values remain low (14). However TIVA is regarded as the technique of choice for neurosurgery, but few studies performed to compare outcome of anesthesia methods indicated a better ICP control in inhalation anesthesia than TIVA (19). Therefore, further study is needed to compare the effect of inhalation anesthesia with hyperventilation and TIVA on ICP control. This study aimed to determine the effect of inhalation anesthesia with hyperventilation and total intravenous anesthesia on intracranial pressure control in pediatrics with craniosynostosis surgery.

2- MATERIALS AND METHODS

2-1. Study design and population

In this randomized clinical trial (TCTR20180129002), 40 pediatric patients with multiple sutures craniosynostosis repair surgery who referred to Mofid Hospital, Tehran, Iran, in May 2016 to January 2017 were recruited.

2-2. Methods

According to similar studies (7), the sample size calculation was based on the assuming a standard deviation of 2.25 points, an alpha of 0.05, and a beta of 0.20 (power of 0.80) (20). This analysis indicated that a sample size of at least 20 patients per group was required. All patients were randomly assigned into group of hyperventilation or TIVA groups.

2-3. Measuring tools: Laboratory measurements

The same team of surgeons and anesthesiologist were responsible for all the cases in our study. Preoperative consultations were comprehensively provided to all patients. The neurologic evaluations were performed to determine increased intracranial pressure (ICP) by the surgeons, which were recorded based on a 4-point scale. Score 1: tense brain, 2: bulge brain, 3: acceptable, and 4: ideal (21). The surgeon was not informed about patient's group. Intraoperative blood loss were assessed and recorded in both groups according to standard measurements : blood volume in suction, surgical field, bloody sterile gauzes (each immersed gauze considered as 15 ml bleeding) (21). Arterial blood gas (ABG) samples were used to measure partial pressure of carbon dioxide in arterial blood ($Paco_2$).

2-4. Intervention

Induction was performed with thiopental 5mg/kg, fentanyl 2 µg/kg and atracurium 0.5 mg/kg in both groups and patients were intubated with spiral uncuffed endotracheal tubes (ETT). In addition to standard monitoring [Blood pressure (BP), Pulse rate (PR), Electrocardiography (ECG), end tidal carbon dioxide (ETCO2)], invasive monitoring including arterial line and central venous catheter was established. All of patients were in 15 degree head up position. Maintenance of anesthesia was provided by Isoflurane 1 MAC in hyperventilation group and Propofol 150 ug/kg/min and remifentanil 0.1ug/kg/min in TIVA group. MAP and heart rate (HR) were recorded every 5 minutes. In hyperventilation group, 15 minutes before starting craniotomy, hyperventilation with the aim of keeping partial pressure of end tidal carbon dioxide (PETCO2) around 25-30 and Paco2 30-35 mmHg was established. In TIVA group, normocapnia ($PETCO_2$=35 mmHg) was maintained.

2-5. Ethical consideration

The study was reviewed and approved by the university review board and hospital

ethics committee. Informed consent was obtained in accordance with the principles outlined in the Declaration of Helsinki from all parent preoperatively and they were assured that unwillingness to participate in the study would not affect the normal course of treatment.

2-6. Inclusion and exclusion criteria

Inclusion criteria were pediatric patients with American society of anesthesiologists (ASA) I-II, age 6 months to 2 years old undergoing multiple sutures cranioplasty. Patients with concurrent cardiac, renal, hematologic or pulmonary disease and body mass index (BMI) > 30 were excluded.

2-7. Data Analyses

Data were statistically analyzed by SPSS software version 22. The quantitative variables were expressed as mean ± standard deviation (SD); t-test was used to compare the quantitative variables including age, heart rate, MAP and blood loss and also, Chi-square test was used for comparison of ICP condition between hyperventilation and TIVA groups. P-value less than 0.05 were considered as statistically significant.

3- RESULTS

The aim of the study was to compare the effect of inhalation anesthesia with hyperventilation and TIVA on ICP control in pediatric patients with craniosynostosis surgery. Totally, 40 patients entered the study. The mean age of patients in hyperventilation group was 10.9±3.25 months and in TIVA group was 8.7 ± 2063 months (p=0.11). Fourteen (70%) patients in hyperventilation group and 6 (30%) patients in TIVA group were male (p=0.74). There were no differences in age and gender between two groups (**Table.1**).

According to the surgeons' evaluation, ICP conditions in hyperventilation group during surgery were ideal 45%, acceptable 30%, bulge 15%, and tense 10%; while, in TIVA group, ICP conditions were reported as ideal 10%, acceptable 35%, bulge 45% and tense 10%. There was a significant difference in surgeon assessments between two groups (p=0.034). Blood loss was estimated 171 ± 49.77 mL in hyperventilation group and 155 ± 47.90 mL in TIVA group. There was no difference between groups regarding blood loss (p=0.473) (**Table.2**).

Mean arterial pressure during surgery in hyperventilation group was 97.1 mm Hg and in TIVA group was 99.9 mm Hg. (P=0.81). Mean pulse rates in both groups showed no significant difference (p=0.127) (**Table 3, 4 and Figures 1, 2**).

Table-1: Age and gender of patients in both groups.

Group	Hyperventilation (n=20)	TIVA (N=20)	P-value
Age, year	10.90±3.25	8.70±2.63	0.113
Gender			
Female	6(30.0%)	14(70.0%)	0.074
Male	14(70.0%)	6(30.0%)	0.074

TIVA: Total intravenous anesthesia.

Table-2: ICP conditions and amount of bleeding in hypertension and TIVA groups.

Group	Hyperventilation (n=20)	TIVA (N=20)	P-value
ICP control			0.032
1 (tense)	2(10.0%)	2(10.0%)	
2 (bulge)	3(15.0%)	9(45.0%)	
3 (acceptable)	6(30.0%)	7(35.0%)	
4 (ideal)	9(45.0%)	2(10.0%)	
Bleeding	171.00±49.77	155.00±47.90	0.473

ICP: Intracranial pressure; TIVA: Total intravenous anesthesia.

Table-3: MAP measurements at before and during surgery in hyperventilation and TIVA groups.

MAP	Hyperventilation (n=20)	TIVA (N=20)	P-value
During surgery (min)			
0	71.50±7.81	67.20±5.03	0.160
10	73.50±12.69	65.70±7.29	0.109
20	69.20±9.26	62.30±5.54	0.058
30	69.70±16.34	63.70±8.65	0.323
40	65.30±12.64	61.10±8.53	0.395
50	66.60±10.78	60.80±5.01	0.140
60	65.20±10.01	62.20±7.93	0.467
70	64.70±8.08	61.40±7.34	0.352
80	64.70±6.38	60.90±7.65	0.243
90	58.00±11.73	64.50±7.96	0.164
100	58.30±7.42	63.40±9.32	0.193
110	60.70±9.43	63.30±8.14	0.518
120	61.80±9.84	59.70±7.60	0.600
130	61.30±9.44	57.00±7.07	0.264
140	62.20±8.80	62.20±5.63	>0.999
150	63.40±8.59	64.20±5.41	0.732
Total			0.817

MAP: Mean arterial pressure; TIVA: Total intravenous anesthesia.

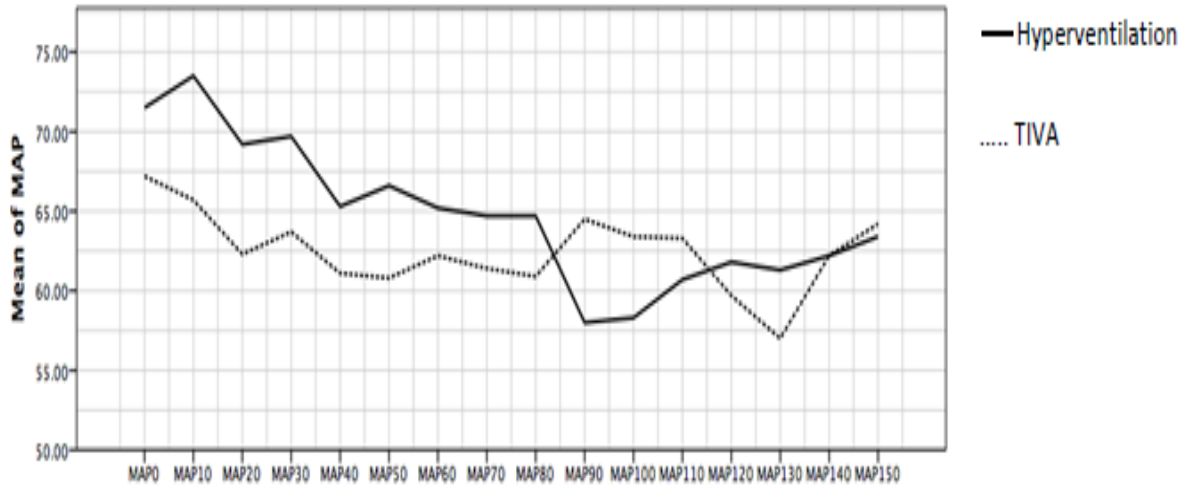

Fig.1: The mean arterial pressure in hyperventilation and TIVA groups.

Table-4: The heart rate measurements at before and during surgery in hyperventilation and TIVA groups.

Heart rate	Hyperventilation (n=20)	TIVA (n=20)	P-value
During surgery (min)			
0	136.90±16.45	133.10±9.61	0.536
10	137.90±15.16	137.30±16.40	0.933
20	134.80±16.85	135.70±12.13	0.893
30	137.50±17.51	144.00±9.35	0.318
40	131.20±15.17	140.30±17.75	0.234
50	128.90±12.28	140.90±15.90	0.075
60	131.80±9.37	136.30±15.85	0.225
70	127.40±15.71	134.20±13.33	0.311
80	123.80±12.97	129.10±12.11	0.357
90	122.30±10.89	128.90±14.87	0.272
100	121.60±10.55	123.20±9.83	0.730
110	120.80±8.50	126.00±11.70	0.270
120	121.70±7.29	122.70±10.49	0.849
130	120.40±9.83	122.20±10.61	0.699
140	123.90±10.09	126.80±9.15	0.509
150	122.20±10.70	125.70±9.45	0.448
Total			0.127

TIVA: Total intravenous anesthesia.

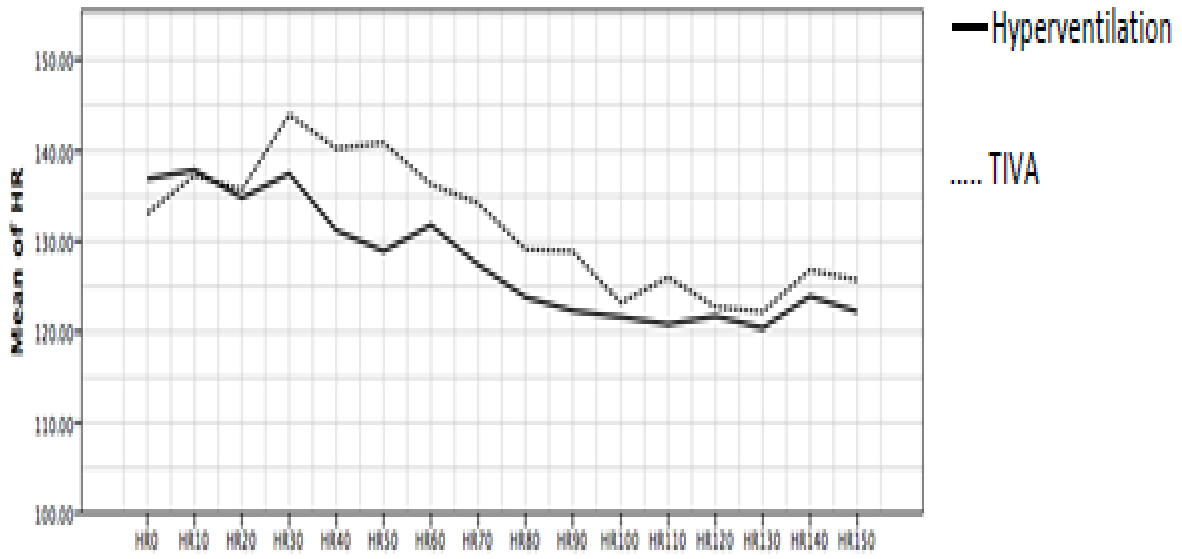

Fig.2: The heart rate measurements in hyperventilation and TIVA groups.

4- DISCUSSION

In this study, the effect of two anesthesia maintenance methods on intracranial pressure during craniosynostosis repair surgery was evaluated. Results showed that anesthesia maintenance with Isoflurane and hyperventilation is more effective than TIVA with propofol on ICP control in patients with craniosynostosis. We could not find similar study in literature. In fact,

there are few articles evaluating ICP in craniosynostosis surgeries. Most studies have compared inhalation anesthesia and TIVA in craniotomies and traumatic brain injuries. In most of these studies, TIVA have been more effective in ICP control (12, 15, 17). Propofol decreases CMR, cerebral blood flow(CBF), and ICP (18, 22). In anesthesia with propofol, brain auto regulation and CBF response to carbon dioxide (CO_2) are preserved (10). All of the halogenated inhalational agents (Isoflurane, Desflurane, and sevoflurane) are dose dependent cerebral vasodilators (23). In less than 1 MAC, cerebral blood flow decreases moderately and in greater than 1 MAC, CBF and ICP increases. CBF response to CO2 is maintained during inhalation anesthesia (3, 15). According to previous studies, hyperventilation $Paco_2$=25-30 mmHg can improve surgical condition during craniotomy (12).

However, the ideal anesthesia regimen for craniotomy is still controversial. Chui et al., in a meta-analysis surveyed 14 studies with 1,600 patients and concluded that in TIVA method ICP was 5 mmHg lower and CPP was 16 mmHg greater than inhalational anesthesia, but there was no difference in surgical condition, recovery profile, postoperative complications and neurologic outcomes (23). Fischer et al., studied the influence of TIVA and inhalational anesthesia with nitrous oxide (N_2O) and volatile anesthetics under normoventilation and hyperventilation on blood flow velocity (BFV). They showed a reduction in BFV and a decrease in CBF during TIVA. Also, they concluded that TIVA had more advantages for patients with reduced intracranial compliance (24). These findings are in contrast to our results. Our study showed that surgical condition was better and surgeon satisfaction was greater with inhalational anesthesia combined with hyperventilation rather than TIVA and normocapnia. Inhalational anesthesia is a cost benefit and titratable method. On the other hand, due to side effects of hyperosmotic drugs, some anesthesiologists are not interested in using these drugs except in emergency situations. Although Mannitol decreases ICP rapidly, it may be associated with hypovolemia, hyperosmolarity, electrolyte imbalance and need for laboratory monitoring (25, 26). Moreover, rebound intracranial hypertension, hypernatremia and hyperosmolarity are complications of hypertonic saline administration (27). So a safe, effective and cost benefit anesthesia can reduce hyperosmolar drugs usage during surgery. In our study, if elevated ICP occurred in TIVA group during surgery, we hyperventilated the patients and ICP decreased rapidly. It seems to be due to preservation of brain autoregulation with propofol. A weakness of this study was the method of ICP evaluations, which were reported by the surgeons, based on a 4-point scale. However, to access an accurate analysis of ICP, an invasive measurements is required which most of the surgeon avoid it. Low sample size was another study limitation. We suggest greater sample size studies in future.

5- CONCLUSION

This study showed that ICP in inhalation anesthesia with hyperventilation was lower than TIVA in pediatric craniosynostosis surgery. Further studies are needed to confirm the effect of inhalation anesthesia with hyperventilation on ICP control

6- CONFLICT OF INTEREST: None.

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