THE BENEFICIAL VALUES OF TRANSOESOPHAGEAL DOPPLER IN INTRAOPERATIVE FLUID GUIDANCE VERSUS STANDARD CLINICAL MONITORING PARAMETERS IN INFANTS UNDERGOING KASAI OPERATION

Eman Sayed Ibrahim*, Taha Aid Yassein**
and Wesam Saber Morad***

Abstract

Background: Fluid overload in infants can result from inappropriate volume expansion (VE). The aim of this work was to evaluate the beneficial values of Transoesophageal Doppler TED in intraoperative fluid guidance versus standard clinical monitoring parameters in infants undergoing Kasai operation.

Methods: Forty infants scheduled for Kasai procedure were randomly allocated into two groups (Doppler and clinical group). In Doppler group decided to provide VE (10-30 ml/kg of Hydroxyethyl starches HES) when the index stroke volume decreased by ≥15% from the baseline value, in clinical group, hemodynamic variables triggering colloid administration mean arterial blood pressure (MAP) less than 20% below baseline or central venous pressure (CVP) <5 cmH_2O in both groups: Ringer's acetate was infused at constant rate (6 m l/kg/h). Standard and TED-derived data were recorded before and after VE. Follow up the postoperative outcome and hospital stay.

Results: There were significantly lower mean volume of HES (42.85 ± 3.93 versus 84 ± 14.29 ml) and percent of infants required it (30% versus 90%) associated with earlier tolerance to oral feeding (2 ± 0.66 versus 3.4 ± 0.51), shorter hospital stay (5.30 ± 0.47 versus 6.7 ± 0.92 days) and lower rate of chest infection (15% versus 30%) in Doppler group than clinical group. There was no difference between the two studied groups regarding heart rate, MAP.

Conclusions: TED guided intraoperative fluid intake in infants undergoing Kasai operation optimize fluid consumption and improve outcome associated with shorter hospital stay.

Keywords: Infants, Kasai operation, Transoesophageal Doppler, volume expansion.

* MD, Lecturer of anesthesia (National Liver Institute)-Menoufia University.
** MD, lecturer of hepatobilliary surgery (National Liver Institute) Menoufia university.
*** MD, lecturer of public health (National Liver Institute) Menoufia university.
Corresponding author: Eman Sayed Ibrahim MD, Lecturer of anesthesia (National Liver Institute)-Menoufia University. Phone: 01282271464 - 0123548537. E-mail: emansayed825@gmail.com. Address: 18 Hassan Abdel Latif, Maleka, Fesal, Giza, Egypt.

Introduction

Extrahepatic biliary atresia (EHBA) is an inflammatory, progressive, fibrosclerosing cholangiopathy of infancy, affecting both the extrahepatic and intrahepatic bile ducts to a variable extent that results in destruction and obstruction of the biliary tract[1]. Without medical and surgical intervention, disease progression leads to hepatic fibrosis, cirrhosis with portal hypertension, liver failure, and death within 2 to 3 years. It classically presents in 1 in 8,000 to 1 in 18,000 live births, during the neonatal period, with cholestatic jaundice, acholic stools, and hepatomegaly, in an otherwise apparently healthy infant[2]. Current treatment of EHBA is surgical hepatoportoenterostomy (Kasai procedure) for the relief of biliary obstruction in these infants[3].

Perioperative fluid optimization is essential in Kasai procedures for reducing morbidity. Hypovolemia is associated in particular with improper organ perfusion and increased length of hospital stay, while excessive fluid administration produces the clinical picture of pulmonary peripheral and gut edema with associated morbidity and mortality[4].The assessment of perioperative hypovolemia and the trigger for volume expansion (VE) in pediatric anesthesia are based on the interpretation of multiple variables and clinical endpoints such as arterial pressure, heart rate (HR), pulse pressure, urine output, type of surgery, surgical events (e.g. bleeding), and laboratory findings (e.g. hematocrit, lactate). Fluid requirements when based only according to these variables can be inappropriate[5]. Minimally invasive tools that could predict patient responsiveness to VE would be extremely useful. Transoesophageal Doppler (TED) has been shown to effectively measure CO in newborns and children and therefore, could allow for better assessment of the efficacy of VE[6].

We therefore designed a prospective, randomized, controlled trial to evaluate the effectiveness of TED on intraoperative fluid optimization versus standard clinical monitoring parameters in infants undergoing Kasai operation.

Methods

After receiving approval from Ethical Committee and informed consent from patient's parents, this prospective cohort study enrolled 40 infants who were randomly assigned into two groups using a random number generator in sealed envelopes of 20 each: the Doppler group and the clinical group. Infants aged ≤3 months, weighing <10 kg, without myocardial dysfunction, American Society of Anaesthesiologists (ASA) grade I/II, who required general anesthesia and tracheal intubation for hepatoportoenterostomy for biliary atresia (BA) were included in the study. Exclusion criteria were ASA class >II, preoperative hemodynamic instability or catecholamine infusion, known congenital heart disease with hemodynamic consequences and esophageal malformation, any patient with history of bleeding tendency, and no written informed consent. All infants received an oral intake of 15 ml/kg of 10% glucose 2 h before surgery. Patients were optimized before operation and deemed hemodynamically stable and clinically euvolemic before the induction of anesthesia. After denitrogenation, general anesthesia was induced by inhalation of 100% oxygen and 8% sevoflurane until the patient lost consciousness and then the sevoflurane concentration was decreased to 4%. An IV cannula was inserted and fentanyl (1 μg/kg) and atracurium (0.5 mg/kg) were administered to facilitate tracheal intubation. Anesthesia was then maintained with 50% oxygen, air and sevoflurane (1 MAC end-tidal concentration). Mechanical ventilation was performed in all patients using a semi closed system adjusted to keep SaO_2>95% and end tidal CO_2 between 25 mmHg and 35 mmHg (GE Datex Ohmeda S/5 Anesthetic Delivery Unit System). Arterial pressure was measured using a standard non-invasive cuff applied to the upper limb. Nasopharyngeal temperature was monitored and maintained in a normal range with a forced-air warmer (Bair Hugger Temperature Management Unit, Arizant, USA). Following induction of anesthesia, data of patients in the Doppler group (age, weight, and height) were registered in the Doppler monitor. A 4 MHz, flexible TED probe specific for single-patient pediatric use (KDP n-Kinder Doppler Probe®) was greased with a lubricating gel and passed orally into the mid esophagus until aortic blood flow signals were best identified. The optimal position of the probe was suggested by an audible, maximal pitch and a sharply defined velocity waveform with minimal spectral dispersion. The monitoring system used (Cardio QPTM, Deltex Medical TM, Chichester, UK) which shows all the needed hemodynamic variables both in numerical and graphical forms... The probe was rotated to display the best aortic blood flow signal before each measurement. Cardiac index (CI), index stroke volume (ISV), corrected flow time (CFT) (length of time of systolic blood flow adjusted for HR, that is, divided by the square root of the heart cycle time), peak velocity (PV) (maximal velocity during systole), of the descending aorta velocity waveform were recorded. TED measurements pre- and post-VE were completed and averaged In the clinical group (A 4- to 5.5-Fr central venous catheter AMECATH single lumen central venous catheter) was placed through the right internal jugular vein by ultrasound guided method (Sonosite-Nano Max ultrasound system-USA).

In Doppler group. Boluses of colloid were administered, guided by an algorithm depending on the Doppler estimations of ISV, when the ISV decreased by ≥15% from the baseline value.VE consisted of an infusion of 10-30 ml/ kg of colloid (Voluven hydroxyethyl starch 130/0.4 6%). Over a period of 20-40 min, repeated by other boluses only if ISV is not increased by ≥15% this algorithm was similar to that used by Roux et al.[7], In clinical group, hemodynamic variables triggering colloid administration based on clinical appreciation and standard monitoring data that involves either a decrease in mean arterial blood pressure less than 20% below baseline or CVP<5 mmHg.VE was the same of that used in TED group. In both groups, Ringer's acetate solution was infused intraoperative at approximately constant rate (6 m l/ kg/h) via an infusion pump (Fresenius Kabi, Germany) to cover fluid deficit and basal fluid requirements. Four sets of data were recorded and each set included: heart rate (HR), mean arterial pressure (MAP), end tidal CO_2 ($ETCO_2$), ISV, CFT, PV and cardiac output (CO). The measurements were obtained at 10 min after induction of anesthesia when hemodynamicaly stable with controlled ventilation established, (To) before VE (T1), T2: after VE (T2) and at the end of surgery (T3).

The primary out-come was to evaluate the beneficial values of TED in intraoperative fluid guidance versus standard clinical monitoring parameters in infants undergoing Kasai operation regarding volume of colloid administered. Secondary outcomes included evaluation of complications such as vomiting, post-operative pulmonary complications, return of bowel function and the length of intensive care and hospital stay.

20 patients in arm 1 (Doppler group) and 20 patients in arm 2 (clinical group) were recruited based on the following assumptions: with the power of 80 %, $\alpha = 0.05$ and the ratio of cases to controls = 1:1. The required sample size was determined using (power and sample size calculation) software.

The sample size was determined as regard patients attending our institute meeting the inclusion and exclusion criteria which are 40/year. Normally distributed data were analyzed using *t*-test, and categorical data were analyzed using the Chi-square test. Continuous data are presented as mean and standard deviation, whereas categorical data are presented as number of patients and percentage. Data were analyzed using IBM SPSS statistics 20.0 software. $P < 0.05$ was considered statistically significant.

Results

Data is presented at baseline, before and after VE (Table 1). There were no differences in the demographic data between Doppler and clinical groups (Table 1). The percentage of patients who required volume expansion was significantly lower in the Doppler group (Table 1). Furthermore, the volume of HES needed was also significantly smaller I the Doppler group (Table 1). There was no statistically significant difference between both groups regarding Ringer's acetate requirements (Table 1). There were no differences between the two studied groups regarding heart rate, mean blood pressure (MAP) (Table 2). The TED group demonstrated significant hemodynamic changes in post fluid boluses, increase of ISV and cardiac output associated with an increase in CFT and PV (Table 4). There was statistically significant decreased in mean heart rate post vs. pre- VE (123 ± 6.548 versus 136.8 ± 10.04 beat /min; $p < 0.05$) and (112.2 ± 5.20 versus 132 ± 8.67 beat /min; $p < 0.05$) in

Table 1

Patient characteristic data, and characteristics of VE differences between groups.

Variables	Clinical group (n=20)	Doppler group (n=20)	P-value
Age (days)	73.40 ±18.06	74.40 ± 19.06	0.87
Weight (gm.)	4.77 ± 0.71	5 ±0.62	0.28
Height (cm)	65.70±65.70	65.20±5.28	0.97
Sex :male/ female	13/7	12/8	0.74
ASA I/II	18/2	17/3	0.63
Operative time (min)	202±54	186±44	0.31
Volume expansion			
Colloids (%pts)	18 (90%)	6 (30%)	0.00#
Volume (ml)	84±14.29	42.85±3.93	< 0.01*
Total RA (ml)	290±39.44	274±39.44	0.20*

TED – Transoesophageal Doppler; ASA – American society of anaesthesia

RA- Ringer acetate

Table 2

Hemodynamic data for both groups.

Variable	Clinical (n=20)	Doppler (n=20)	P-value
HR (beat/min)			
T0	125.4±10.57	123.2±8.67	0.48
T1	136.8±10.04	132±8.67	0.11
T2	123±6.54	122.2±5.20	0.67
T3	123.5 ±8.07	122.5 ±12.14	0.76
MAP (mmHg)			
T0	54.2±3.42	55.5±4.22	0.29
T1	43.4±2.72	44.6±4.50	0.31
T2	58.1±2.64	61.2±4.04	0.05
T3	56.5±2.95	56.8±5.37	0.82

Values are presented as mean (SD); HR – Heart rate; MBP – Mean blood pressure; TED – Transoesophageal Doppler; T0 – 10 min after induction of anesthesia; T1– before fluid bolus ; T2 – After fluid bolus ; T3– At end of operation .

the clinical and Doppler group respectively, associated with statistically significant increase in MAP post VE compared to before it (58.10 ± 2.64365 versus 43.40 ± 2.71 mm Hg; p <0.01) and (61.20 ± 4.049 versus 44.60 ± 4.50 mm Hg; p <0.01) in the control and TED group respectively. These changes associated with stable CVP with no statistically significant changes after fluid bolus in it Table 3. There was no mortality reported during the study period in any case involved in the study. There were earlier tolerance to oral feeding (2 ± 0.66 versus 3.4 ± 0.51 days), shorter hospital stay (5.30 ± 0.47 versus 6.7 ± 0.92 days) and lower rate of chest infection (15% versus 30%) and oral intolerance (10% versus 40%) in Doppler group than clinical group (Table 5). Eight patients in the clinical group needed antiemetic in comparison to two patients in the Doppler guided group. All patients were extubated immediately postoperative in the operating room and admitted to the intermediate care unit for the first 24 h.

Discussion

The results of this study demonstrate that TED was able to predict responsiveness to fluid

Table 3
Central venous pressure changes for the clinical group.

Variable	To	T1	T2	T3
CVP(cmH_2o)	4.10 ±0.99	4.10± 0.87	3.80±0.63	3.87±0.44

Values are presented as mean (SD);CVP- Central venous pressure T0 – 10 min after induction of anesthesia; T1– before fluid bolus(VE) ; T2 – After fluid bolus(VE) ; T3– At end of operation . Data compared by paired t test

Table 5
Postoperative outcome.

Variable	**Doppler group** (n=20)	**Clinical group** (n=20)	P-value
Chest infection n (%)	3(15%)	6 (30%)	0.26
Oral intolerance	2(10%)	8(40%)	0.03
Hospital stays (days)	5.30 ± 0.47	6.7 ± 0.92	< 0.01
Day of oral feeding (days)	2± 0.66	3.4 ± 0.51	< 0.01

and optimize intraoperative fluid consumption, as indicated by significant lower mean volume of colloid (HES) received and percent of infants requiring volume expanders.. In a study by Lee, et al.[8], FTC and PPV (Pulse Pressure Variation) of Doppler were found to be better than CVP and LVEDAI (left ventricular end end-diastolic area index) in predicting fluid responsiveness and that changes in the stroke volume index caused by fluid loading correlated significantly with the FTC values. Estimation of intravascular volume status in critically ill infants and neonates is a particular challenge as traditional indices, such as blood pressure and heart rate, may not reflect mild to moderate blood loss and because, in the majority of cases, invasive monitoring is not used[9]. In our study, fluid boluses based on standard clinical monitoring data was shown to be inappropriate in the patients as CVP was stable after fluid boluses in spite of significant changes in heart rate and MAP. MAP and HR did not reliably reflect CO in anesthetized pediatric patients[10,11]. Kumar et al and Marik et al found that CVP is not able to indicate changes in intravascular volume and fluid responsiveness accurately[12,13]. Value of CVP is influenced by the diastolic compliance of the right ventricle, intra-abdominal pressure, positive end expiratory pressure, and forced expiration. Indeed, CVP does not predict fluid responsiveness and only poorly reflects preload in adults, children, and pediatric animal models[14]. The hypotensive effect of sevoflurane is well described and is especially significant in the youngest pediatric patients[15].This effect, mostly attributable to a decrease in systemic vascular resistance, may explain the arterial hypotension among our patients before fluid bolus. The increase in MAP observed in control patient's post-fluid bolus, without an improvement in CVP may be explained by other factors such as the subsequent reduction in sevoflurane during the period of arterial hypotension. Our study was able to demonstrate the ability of minimally invasive TED to reduce fluid therapy when compared to standard clinical monitor parameter guided fluid management associated with earlier tolerance to oral feeding, shorter hospital stay

Table 4
TED variables for the Doppler group.

Variable	To	T1	T2	T3
COP(ml/min)	1.19±0.21	0.76±0.05*	1.16±0.16#	1.09±0.16
CFT(m/sec)	333.74±31.88	311.3±11.73*	350.4±11.08#	338.2±6.72**
ISV(ml/beat/m2)	30.13±2.31	25.52±2.22*	32.88±1.83#	33.2±2.24
PV (cm/sec)	111.3±8.18	84.44±5.08*	109.80±7.32#	100.50±3.62*

Values expressed as mean (SD); COP(Cardiac output); ISV (index Stroke volume); CFT (Corrected flow time); PV (Peak velocity); T0 –10 min after induction of anesthesia; T1– before fluid bolus(VE) ; T2 – After fluid bolus(VE) ; T3– At end of operation.* $P < 0.05$ vs. To # $P < 0.05$ vs. T1 ** $P < 0.05$ vs. T2 and lower rate of chest infection and oral intolerance. Recent randomized trials and meta-analyses have confirmed that intraoperative fluid optimization using TED improve outcome[8,16] Absi et al[17] reported that the application of esophageal Doppler guided fluid management has produced a similar improvement in outcome for patients undergoing cardiac surgery. Roche et al[18] studied Goal-directed fluid management with trans-esophageal Doppler and found a significant reduction in hospital stay. In the current study, chest infection and post-operative vomiting and intolerance to oral feeding were significantly less reported in the Doppler guided fluid group. This was also supported by Mythen and Webb study, which demonstrated that the esophageal Doppler guided plasma volume optimization significantly reduced the incidence of gastric mucosal hypoperfusion leading to a significant reduction in complication rates and length of hospital stay following cardiac surgery[19]. Increase extravascular lung water from excessive intravascular volume may predispose patients to pneumonia and respiratory failure. It can lead to edema of the gut, which may inhibit gastrointestinal motility and prolong postoperative ileus and intolerance for enteric alimentation. The potential for bacterial translocation and development of sepsis and multiorgan failure is also increased. Increase cutaneous edema may decrease tissue oxygenation, which can lead to delayed wound healing[20]. Previous literatures suggest that perioperative goal-directed therapy (GDT) based on flow-related hemodynamic parameters improve patient outcome[21,22]. Clinical studies have mostly shown outcome benefits only within postoperative nausea and vomiting, ileus, morbidity, and hospital stay[23,24]. However, only limited pathophysiological data are available to explain this benefit. Lopes et al.[25], in their work revealed that there is reduced morbidity and hospital stay by GDT and this also associated with a reduced interleukin-6 response. Other studies on perioperative changes of the vascular barrier suggest that the endothelial gly-cocalyx plays a key role[26,27].

The limited number of cases enrolled in our study was related to the limited number of cases of biliary atresia selected for kasai surgery in our national liver institute. The use of TED for intraoperative fluid guidance in infants undergoing Kasai operation need to be studied in further planned research work.

In conclusion: TED guided intraoperative fluid management in infants undergoing Kasai operation optimizes fluid consumption and improve outcome associated with shorter hospital stay.

References

1. Kahn E: Biliary atresia revisited. *Pediatr Dev Pathol;* 7: 109-124, 2004.
2. Perlmutter DH and Shepherd RW: Extrahepatic biliary atresia: a disease or a phenotype? *Hepatology*; 35:1297-1304, 2002.
3. Kasai M: Treatment of biliary atresia with special reference to hepatic porto-enterostomy and its modifications. *Prog Pediatr Surg*; 6:5-52, 1974.
4. Brandstrup B, Tonnesen H, Beier-Holgersen R, Hjortso E, Ording H, Lindorff-Larsen K, Rasmussen MS, Lanng C, Wallin L, Iversen LH, Gramkow CS, Okholm M, Blemmer T, Svendsen PE, Rottensten HH, Thage B, Riis J, Jeppesen IS, Teilum D, Christensen AM, Graungaard B and Pott F: Effects of intravenous fluid restriction on postoperative complications comparison of two perioperative fluid regimens. *Ann Surg*; 238:641-8, 2003.
5. Tibby SM, Hatherill M, Marsh MJ, Murdoch IA: Clinicians' abilities to estimate cardiac index in ventilated children and infants. *Arch Dis Child;* 77:516-8, 1997. Archives of Disease in Childhoodadc.bmj.com
6. Tibby SM, Hatherill M, Murdoch IA: Use of transesophageal Doppler ultrasonography in ventilated pediatric patients: derivation of cardiac output. *Crit Care Med;* 28:2045-50, 2000.
7. Raux O, Spencer A, Fesseau R, Mercier G, Rochette A, Bringuier S, lakhal K, Capdevila X and Dadure C: Intraoperative use of transoesophageal Doppler to predict response to volume expansion in infants and neonates. *Br J Anaesth*; 108(1):100-7, 2012.
8. Lee JH, Kim JT, Yoon SZ, Lim YJ, Jeon Y, Bahk JH and Kim CS: Evaluation of corrected Flow time in oesophageal Doppler as a predictor of fluid responsiveness. *Br J Anaesth*; 99:343-8, 2007.
9. Richardson JR, Ferguson J, Hiscox J and Rawles J: Noninvasive assessment of cardiac output in children. *J Accid Emerg Med*; 15(5):304-307, 1998.
10. Osthaus WA, Huber D, Beck C, Roehler A, Marx G, Hecker H and Sümpelmann R: Correlation of oxygen delivery with central venous oxygen saturation, mean arterial pressure and heart rate in piglets. *Paediatr Anaesth*; 16(9):944-7, 2006.
11. Kluckow M and Evans N: Relationship between blood pressure and cardiac output in preterm infants requiring mechanical ventilation. *J Pediatr*; 129(4):506-12, 1996.
12. Kumar A, Anel R, Bunnell E, Habet K, Zanotti S, Marshall S, Neumann A, Ali A, Cheang M, Kavinsky C and Parrillo JE: Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. *Crit Care Med*; 32(3):691-9, 2004.
13. Marik PE, Baram M and Vahid B: Does central venous pressure predict fluid responsiveness? A systematic review of the literature. *Chest;* 134(1):172-8, 2008.
14. Choi DY, Kwak HJ, Park HY, Kim YB, Choi CH and Lee JY: Respiratory variation in aortic blood flow velocity as a predictor of fluid responsiveness in children after repair of ventricular septal defect. *Pediatr Cardiol*; 31(8):1166-1170, 2010.
15. Lerman J, Sikich N, Kleinman S and Yentis S: The pharmacology of sevoflurane in infants and children. *Anesthesiology*; 80:814-24, 1994.
16. Wakeling HG, McFall MR, Jenkins CS, Woods WG, Miles WF, Barclay GR and Fleming SC: Intraoperative oesophageal Doppler guided fluid management shortens postoperative hospital stay after major bowel surgery. *Br J Anaesth*; 95:634-42, 2005.
17. Absi MA, Lutterman J and Wetzel GT: Noninvasive cardiac output monitoring in the pediatric cardiac intensive care unit. *Current Opinion in Cardiology*; 25:77-79, 2010.
18. Roche AM, Miller TE and Gan TJ: Goal-directed fluid management with trans-oesophageal Doppler. *Best Practice & Research Clinical Anaesthesiology*; 23:327-334, 2009.
19. Mythen MG and Webb AR: Perioperative plasma volume expansion reduces the incidence of gut mucosal hypoperfusion during cardiac surgery. *Arch Surg*; 130:4239, 1995.
20. Holte K, Sharrock E and Kehlet H: Pathophysiology and clinical implication of perioperative fluid excess. *Br J Anaesth*; 89:622-32, 2002.
21. Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM and Bennet ED: Early goal-directed therapy after major surgery reduces complications and hospital stay.A randomized, controlled trial. *Crit Care*; 9:687-93, 2005.
22. Bundgaard-Nielsen M, Holte K, Secher NH and Kehlet H: Monitoring of perioperative fluid administration by Individualized goal-directed therapy. *Acta Anaesthesiol Scand*; 132:1817-24, 2007.
23. Abbas SM and Hill AG: Systematic review of the literature for the use of oesophageal Doppler monitor for fluid replacement in major abdominal surgery. *Anaesthesia*; 63:44-51, 2008.
24. Buettner M, Schummer W, Huettemann E, Schenke S, vanHout N and Sakka SG: Influence of systolic-pressure-variation-guided intraoperative fluid management on organ function and oxygen transport. *Br J Anaesth;* 101:194-9, 2008.
25. Lopes MR, Oliveira MA, Pereira VO, Lemos IP, Auler Jr and Michar F: Goal-directed fluid management based on pulse Pressure variation monitoring during high-risk surgery: a pilot randomized controlled trial. *Crit Care*; 11:100-9, 2007.
26. Noblett SE, Snowden CP, Shenton BK, Horgan AF: Randomized clinical trial assessing the effect of Doppler Optimized fluid management on outcome after elective colorectal resection. *Br J Surg*; 93:1069-76, 2006.
27. Jacob M, Bruegger D, Rehm M, Welsch U, Conzen P and Becker BF: Contrasting effects of colloid and crystalloid resuscitation fluids on cardiac vascular permeability. *Anesthesiology*; 104:1223-31, 2006.