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Original Article

Effects of fluid resuscitation on cerebral tissue oxygenation changes in a piglet model of hemorrhagic shock

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Abstract

Background: Acute blood loss linked to severe hypovolemia and hemorrhagic shock is a critical condition in pediatric intensive care. This study was to investigate the role of various fluid resuscitation approaches to cerebral tissue oxygenation using a piglet model of hemorrhagic shock.
Methods: Thirty piglets received blood removal to induce hemorrhagic shock, and then were randomly assigned to a control group (no treatment), a control-normal saline (NS) group (treated with bolus normal saline 10 mL/kg only), or one of three treatment groups treated with 15 mL/kg/dose fluid every 30 min with either whole blood (WB), lactated Ringer's solution (LR), or NS in addition to an initial bolus of saline. The piglets' physiological profiles, arterial blood gases, and regional cerebral oxygen saturation ($rScO_2$) levels were recorded, fractional tissue oxygen extraction was calculated, and blood hemoglobin levels were measured.
Results: The results showed that no matter whether treated with only one dose of bolus NS (control-NS group) or with extra WB, LR, or NS, all the treated animals had a significantly higher survival rate, mean arterial blood pressure (MAP), arterial oxygen tension, arterial oxygen saturation, and $rScO_2$ than the control group ($p < 0.05$). Animals treated with WB all survived the full experimental period, and their hemoglobin levels, MAP, and $rScO_2$ were the highest comparing to all other groups ($p < 0.05$).
Conclusion: Effective resuscitation using a high concentration of inspired oxygen and adequate fluid infusion, either as a single-dose bolus of NS or combining this with a subsequent transfusion of WB, LR, or NS, helped to stabilize the cardiovascular condition of the tested young subjects and improved cerebral tissue oxygenation over the emergent first four hours. Furthermore, WB was the best fluid choice when used in addition to the bolus NS challenge for maintaining better brain tissue oxygenation when treating hemorrhagic shock.

Keywords: cerebral tissue oxygenation; hemorrhagic shock; near-infrared spectroscopy; piglet; resuscitation

1. Introduction

Acute blood loss linked to severe hypovolemia and hemorrhagic shock is a critical condition in pediatric intensive care. Many conditions can induce hemorrhagic shock or a shock-like state in newly born infants, including trauma, internal bleeding, coagulopathy, surgery or massive maternal bleeding.[1,2] In hemorrhagic shock, the blood loss has exceeded the body's ability to compensate and the body is unable to provide adequate tissue perfusion and oxygenation. The failure of the compensatory mechanisms that causes hemorrhagic shock leads to devastating changes and high mortality. The neurological sequelae, such as impaired cognition, development delay and cerebral palsy, also cannot be neglected as consequences when an infant survives hemorrhagic shock.

Stopping bleeding and providing adequate fluid resuscitation are the major keys to treating hemorrhagic shock. The

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primary goals are restoration of tissue perfusion and oxygenation, while shortening the time interval during which global and regional ischemia occurs; this minimizes brain injury and prevents neurological sequelae. However, there are few clinical and experimental investigations that have focused on hemorrhagic shock in infants and children.[3,4] In addition, brain tissue oxygenation changes during fluid resuscitation have not been well investigated. Conventionally, oxygen delivery and consumption are calculated from the hemoglobin concentration, the oxygen saturation, and the cardiac output. Unfortunately these parameters are indicative of the whole-body oxygen debt and not oxygenation at a local level; measuring the latter requires the placement of an invasive monitoring device, or intermittent blood sampling.

Near-infrared spectroscopy (NIRS) provides a continuous, non-invasive method to measure regional changes in tissue oxygenation.[5–7] It relies on the relative transparency of biological tissues to near-infrared light where oxyhemoglobin, deoxyhemoglobin, and cytochrome aa_3 have different absorption spectra. As a result, because the hemoglobin monitored by NIRS is located in the tissue circulation (venules, capillaries, and arterioles) and cytochrome aa_3 is present in the neurons, when there is an appropriate distance between the near-infrared emitter and detector, the absorption of oxygenated and deoxygenated hemoglobin in the local tissue can be measured noninvasively.

Previous studies using NIRS in newborn piglets at high risk of hypoxic-ischemic brain damage have observed episodes of decreased cerebral hemoglobin oxygenation.[8,9] NIRS has also been used to study infant and adult changes in cerebral oxygen utilization during periods of sepsis, transient hypoxia, mental work, surgery, cardiopulmonary bypass surgery, extracorporeal membrane oxygenation and intensive resuscitation.[10–13] However, regional cerebral oxygen saturation ($rScO_2$) changes during volume expansion therapy in hemorrhagic shock events have not been well investigated.

We hypothesized that fluid resuscitation with different volume expanders, when used to treat hemorrhagic shock, may influence changes in brain tissue oxygenation. Therefore, we designed this study to investigate the role of different types of fluid resuscitation on cerebral tissue oxygenation employing NIRS monitoring using a piglet model of hemorrhagic shock.

2. Methods

All animals were managed in accordance with the principle of laboratory animal care of the National Institutes of Health. In addition, all procedures were approved by the Institutional Animal Care and Use Committee of Taipei Veterans General Hospital.

2.1. Animal preparation and physiological monitoring

Newborn piglets, less than two weeks of age, were anesthetized with intramuscularly administered atropine (0.1 mg/dose) and ketamine (25 mg/kg/dose) prior to the surgical procedures. All animals were placed in supine position and given a subcutaneous injection of lidocaine hydrochloride (2%) for local anesthesia. After placing a 3.5-mm inside-diameter uncuffed endotracheal tube (Murphy, Unomedical Sdn. Bhd., Kedah, Malaysia) via a tracheotomy, controlled mechanical ventilation was established using a volume-controlled ventilator (Model 683, Harvard, South Natick, MA, USA). The tidal volume was set at 10 mL/kg, the ventilator rate at 30 breaths/min, the inspiratory to expiratory time (I:E) ratio at 1:1 and the positive end-expiratory pressure at 5 cmH_2O. Finally, the fractional concentration of inspired oxygen was set at 0.21 initially. After the induction of anesthesia, a solution of 0.33% sodium chloride in 5% dextrose was infused continuously at a rate of 5 mL/kg/h. Animals were then paralyzed with intravenous pancuronium bromide (0.2 mg/kg), sedated with midazolam (0.5 mg/kg), and maintained with a continuous infusion of ketamine (5 mg/kg/h), midazolam (0.5 mg/kg/h), and pancuronium bromide (0.2 mg/kg/h). A 3.5-Fr umbilical vessel catheter (Argyle, Sherwood Medical Corp., Chicopee, MA, USA) was placed into the right femoral artery for the continuous monitoring of arterial blood pressure and for arterial blood sampling. Another 3.5-Fr umbilical catheter was inserted into the left jugular vein for administration of fluids, anesthesia and central venous blood sampling. Body temperature was maintained at 38–39°C throughout the experiments via a servo-controlled heating blanket.

Throughout the experiment, electrocardiography, arterial blood pressure, peripheral oxygen saturation and body temperature were continuously monitored (Agilent M1205A, Philips Medical Systems, Andover, MA, USA).

2.2. Near-infrared spectroscopy

A pair of fiberoptic optodes was attached to the scalp of the animal using a probe holder after induction of anesthesia. The optodes were connected to the NIRS device (NIRO-200; Hamamatsu Photonics K.K., Hamamatsu City, Japan). The emitter and receiver were fixed to the probe holder to ensure an interoptode distance of 4 cm. The unit uses safe, faint light (wavelength approximately 700–950 nm) that passes through the brain tissue to measure $rScO_2$. The readings were continuously monitored until the end of each experiment.

2.3. Experimental protocol

After surgical preparation, the experimental animals underwent a 20-minute equilibrium, followed by an artificial hemorrhage that induced hemorrhagic shock [mean arterial blood pressure (MAP) <45 mmHg]. This was done by withdrawing four aliquots of whole blood out from the arterial line during the first 20 min (10 mL/kg/aliquot at the 4^{th}, 8^{th} and 12^{th} min and 5 mL/kg or 10 mL/kg at the 16^{th} min). After induction of hemorrhagic shock, the animals received treatment with inhaled 100% oxygen, and then were immediately randomized into one of the following experimental groups. These were as follows: (1) control group (n = 6): animals did not receive any extra fluid resuscitation; (2) control-normal saline (NS) group (n = 6): animals received one dose of

standard bolus fluid challenge consisting of 10 mL/kg of normal saline (0.9% sodium chloride) over 5 min; (3) whole blood (WB) group: the animals received a bolus of NS (10 mL/kg) over 5 min in a similar manner to the control-NS group, and this was then followed by an intravenous infusion of 15 mL/kg of WB over 20 min. Additional infusion (15 mL/kg/dose) of WB would be given every 30 min if MAP did not rise higher than 45 mmHg until the end of the experiment; (4) Lactated Ringer's (LR) group (n = 6): the animals received the same protocol as the WB group, but with the infusion fluid replaced by LR solution; (5) NS group (n = 6): the animals received the same protocol as the WB group but with the infusion fluid replaced by NS.

During the study period, sodium bicarbonate (1–2 mEq/kg/dose) was given to any animal displaying metabolic acidosis, namely a base excess larger than −8 mmol/L and a pH less than 7.20. Epinephrine (0.01 mg/kg/dose) was given to any animal displaying bradycardia, namely having a heart rate of less than 100 beats/min. Cardiac massage was performed if the heart rate dropped to less than 60 beats/min and this lasted until the heart rate was equal to or higher than 60 beats/min or at most for 30 min.

After baseline measurement, the physiological profiles, $rScO_2$, and arterial blood gas levels were recorded every 4 min during the first 20-min blood-drawing period, and then at 40 min, 60 min, 120 min, 180 min and 240 min after the beginning of the experiments. An additional 1 mL blood was drawn in order to measure hemoglobin levels at baseline, 20 min, 60 min, 120 min and 240 min. At the end of the experiments (240 min), animals were sacrificed with a high dose of 15% potassium chloride while they were under deep anesthesia.

Fractional cerebral tissue oxygen extraction (FTOE) was calculated from $rScO_2$ and SaO_2 values.[10] A ratio of (SaO_2-$rScO_2$)/SaO_2 was calculated to represent the balance between oxygen delivery and oxygen consumption. An increase in FTOE reflects an increase in oxygen extraction by the brain tissue, and a decrease in FTOE suggests that there is less utilization of oxygen by brain tissue, in relation to the supply of oxygen.[10]

2.4. Statistical analysis

All data are expressed as mean ± standard error of the mean (SEM). Statistical analysis was performed using SigmaStat® 3.1 (Systat Software, Inc., Point Richmond, CA, USA). The basic characteristics, hemorrhagic amounts and infusion amounts among the study groups were compared by one-way analysis of variance (ANOVA) or Kruskal-Wallis one-way ANOVA on ranks as appropriate, which was followed by the *post hoc* Student-Newman–Keuls' test for pairwise multiple comparisons. The physiological data between the baseline and after blood loss of the same group were compared by paired *t* test. The continuous data in terms of cardiopulmonary profiles and cerebral tissue oxygenation at different time points for the five study groups were compared by two-way repeated measures ANOVA, which was followed by the *post hoc* Student-Newman–Keuls' test for pairwise multiple comparisons. The survival curves of the study groups were compared by the Gehan–Breslow test followed by the Holm–Sidak method for pairwise multiple comparisons. Significance was accepted at the $p < 0.05$ level.

3. Results

Mean body weight, age and the blood loss volume needed to induce hemorrhagic shock did not vary significantly among the five study groups (Table 1). At baseline, all cardiovascular profiles, $rScO_2$ and FTOE levels did not vary among the groups (Table 2). Immediately after induction of hemorrhagic shock, MAP, hemoglobin and $rScO_2$ decreased significantly in all animals ($p < 0.05$), but heart rate and FTOE levels increased significantly ($p < 0.05$), shown in Table 2. There was no significant difference in the gas exchange across the study groups from baseline to after blood loss status.

The total fluid transfusion volume was significantly higher in the LR group ($p < 0.05$), and there was no significant difference between WB and NS groups ($p > 0.05$) (Table 1). During the course of the experiments, all animals in the control group died earlier than the end of the expected experimental time period after induction of hemorrhagic shock (Fig. 1), and the survival rate was significantly lower than in the other four groups ($p < 0.05$). The median survival time for the control group was 45 min (range 20–125 min) after induction of hemorrhagic shock. In addition, the survival rate in the animals receiving only one dose of 10 mL/kg NS (control-NS group) was not significantly different from those of the other three treatment groups (WB, LR, and NS) that received additional 15–60 mL/kg (mean: 38 ± 6 mL/kg) of the various different volume expanders (Table 1 and Fig. 1).

Table 1
Basic characteristics, blood loss volume and infusion volume of the animals across the various study groups

Groups	Control (*n* = 6)	Control-NS (*n* = 6)	WB (*n* = 6)	LR (*n* = 6)	NS (*n* = 6)
Age (days)	10 ± 3	9 ± 2	9 ± 3	9 ± 3	9 ± 2
Body weight (kg)	1.9 ± 0.2	2.0 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	2.0 ± 0.2
Blood loss (mL/kg)	35 ± 3	38 ± 2	40 ± 2	37 ± 3	40 ± 0
Infusion volume					
Initial saline (mL/kg)	0 ± 0	10 ± 0[a]	10 ± 0[a]	10 ± 0[a]	10 ± 0[a]
Fluid transfusion (mL/kg)	0 ± 0	0 ± 0	28 ± 7[ab]	53 ± 3[abc]	33 ± 3[abd]

NS = normal saline; LR = lactated Ringer's solution; WB = whole blood
[a] $p < 0.05$ *vs.* Control group; [b] $p < 0.05$ *vs.* Control-NS group; [c] $p < 0.05$ *vs.* WB group; [d] $p < 0.05$ *vs.* LR group.

Table 2
Cardiovascular profiles and regional brain tissue oxygenation of animals compared between baseline and after induction of hemorrhagic shock across the study groups

Groups	Control ($n = 6$)	Control-NS ($n = 6$)	WB ($n = 6$)	LR ($n = 6$)	NS ($n = 6$)
Baseline					
MAP (mmHg)	93 ± 6	94 ± 4	86 ± 5	85 ± 2	92 ± 7
Heart rate (beats/min)	200 ± 18	181 ± 17	190 ± 9	200 ± 18	173 ± 21
Hemoglobin (g/dL)	8.8 ± 0.4	7.5 ± 0.4	9.4 ± 0.4	9.4 ± 0.4	8.7 ± 0.4
$rScO_2$ (%)	59 ± 1	53 ± 3	59 ± 2	57 ± 2	59 ± 1
FTOE	0.38 ± 0.01	0.42 ± 0.03	0.38 ± 0.02	0.39 ± 0.02	0.35 ± 0.02
After blood loss					
MAP (mmHg)	35 ± 2^a	41 ± 4^a	35 ± 3^a	40 ± 5^a	35 ± 3^a
Heart rate (beats/min)	286 ± 10^a	224 ± 22^a	272 ± 12^a	282 ± 8^a	255 ± 25^a
Hemoglobin (g/dL)	6.3 ± 0.5^a	5.9 ± 0.1^a	6.8 ± 0.3^a	7.6 ± 0.4^a	6.6 ± 0.3^a
$rScO_2$ (%)	46 ± 1^a	48 ± 1^a	46 ± 2^a	47 ± 3^a	47 ± 1^a
FTOE	0.53 ± 0.02^a	0.50 ± 0.01^a	0.53 ± 0.02^a	0.51 ± 0.03^a	0.52 ± 0.01^a

FTOE = fractional tissue oxygen extraction; LR = lactated Ringer's solution; MAP = mean arterial blood pressure; NIRS = $rScO_2$, regional cerebral tissue oxygenation; NS = normal saline; WB = whole blood
$^a p < 0.05$ *vs.* baseline value of the same group.

The WB group was the only group where all members survived the full experimental period.

The hemoglobin concentrations and MAP were both significantly higher in the WB group compared to all other groups over the experimental period ($p < 0.05$) (Fig. 2). Without any fluid resuscitation, the control group animals presented with a progressively deteriorating MAP and heart rate until death. However, the MAP of all the other treatment groups, including the control-NS group, rose by 10–20 mmHg in response to the initial 10 mL/kg NS challenge (Fig. 2). On treating the WB, LR, and NS group with the follow-up fluid infusion therapies, only the WB group showed a rising pattern of MAP during the follow-up time (Fig. 2). Although animals from the LR group received the highest fluid infusion volume (Table 1), their MAP did not show any further improvement after the initial saline challenge. Furthermore, the LR group had the lowest MAP and highest HR among the four treatment groups (Fig. 2). The animals from the Control-NS group (total saline infusion volume = 10 mL/kg) were able to successfully maintain their MAP, and showed no significant difference

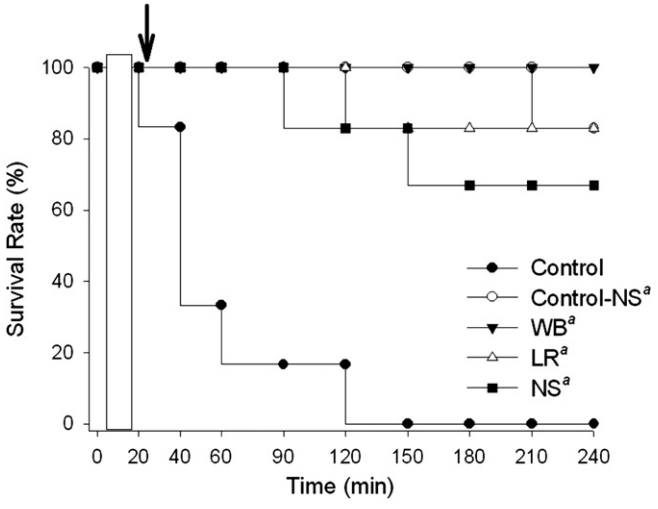

Fig. 1. Survival curves for the experimental animals in the five groups. White bar: period of blood loss; black arrow: infusion of 10 mL/kg normal saline except for the control group. NS = normal saline; LR = lactated Ringer's solution; WB = whole blood. $^a p < 0.05$ *vs.* control group.

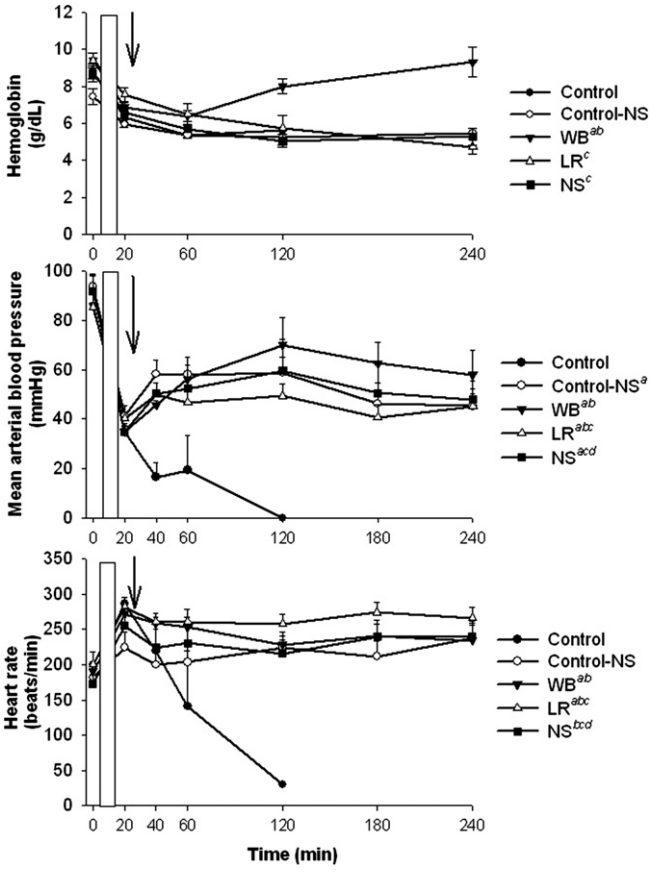

Fig. 2. Changes in heart rate, blood pressure, and hemoglobin during the experimental period. White bar: period of blood loss; black arrow: infusion of 10 mL/kg normal saline except control group. LR = lactated Ringer's solution; NS = normal saline; WB = whole blood. $^a p < 0.05$ *vs.* control group; $^b p < 0.05$ *vs.* control-NS group; $^c p < 0.05$ *vs.* WB group; $^d p < 0.05$ *vs.* LR group by two-way repeated measures ANOVA.

when compared to the NS group (total saline infusion volume = 43 ± 3 mL/kg) (Table 1 and Fig. 2). None of the experimental animals were able to increase their MAP back to that at the original baseline within the experimental period.

After the induction of hemorrhagic shock and the use of 100% oxygen, the PaO_2 rose in all groups, but the animals in the control group could not maintain oxygenation in their blood or their brain tissue for more than 20 min. Thus, the serial values for PaO_2, SaO_2, and $rScO_2$ of the control group were all significantly lower than those for the other groups ($p < 0.05$), as shown in Fig. 3. Comparing the $rScO_2$ levels across the four treatment groups, those of the WB group were highest ($p < 0.05$). However, their $rScO_2$ levels were not able to reach baseline. When the animals' cerebral FTOE levels were examined, it was briefly highest in the control group compared to all other groups over the first 40 min after induction of hemorrhagic shock ($p < 0.05$) (Fig. 3). However, there was no significant difference between LR and NS groups for $rScO_2$ and cerebral FTOE.

4. Discussion

Our study demonstrated that effective fluid resuscitation in addition to 100% oxygen supplementation was able to maintain cardiovascular function and brain tissue oxygenation during the emergent first four hours, even when only one dose of bolus NS challenge was given. WB transfusion was most effective at maintaining blood pressure and brain tissue oxygenation comparing to LR and NS in this piglet model with hemorrhagic shock.

Hypovolemia is the most common cause of circulatory failure in infants and children,[3,4] and fluid resuscitation is the major key to restoring intravascular volume. When the tissue perfusion cannot be restored rapidly, critical tissue hypoxia and ischemia may develop, and this leads to multiple organ failure. Different fluid infusion therapies have been discussed to treat hemorrhagic shock and restore intravascular volume, including modified hemoglobin solution, LR solution, 3% hypertonic saline, colloid treatment, other crystalloid treatment, and others.[14,15] The design of this present study was based on the most commonly used clinical management protocols used during neonatal and pediatric resuscitation for hemorrhagic shock. Therefore, only the most common volume expanders, namely NS, WB, and LR, were tested in our experiments. The potential effects of other volume expanders will need further investigation to elucidate their benefits in terms of brain tissue oxygenation.

There are several physiological variables used by physicians to detect and treat shock-induced tissue hypoxia.[16–18] Some endpoints of resuscitation, such as heart rate, mental status, and blood pressure, are nonspecific, subjective, or both. Other endpoints, such as mixed venous oxygen saturation, arterial lactate, and arterial base deficit, are accurate and objective but are limited in the scope of their applicability because they need invasive monitoring and/or intermittent blood sampling from a central venous catheter, or often even a pulmonary artery catheter. Each of these invasive monitoring modalities adds risk to critically ill patients. A key disadvantage of using these global values is that they provide only a general picture of the patient's oxygenation and do not

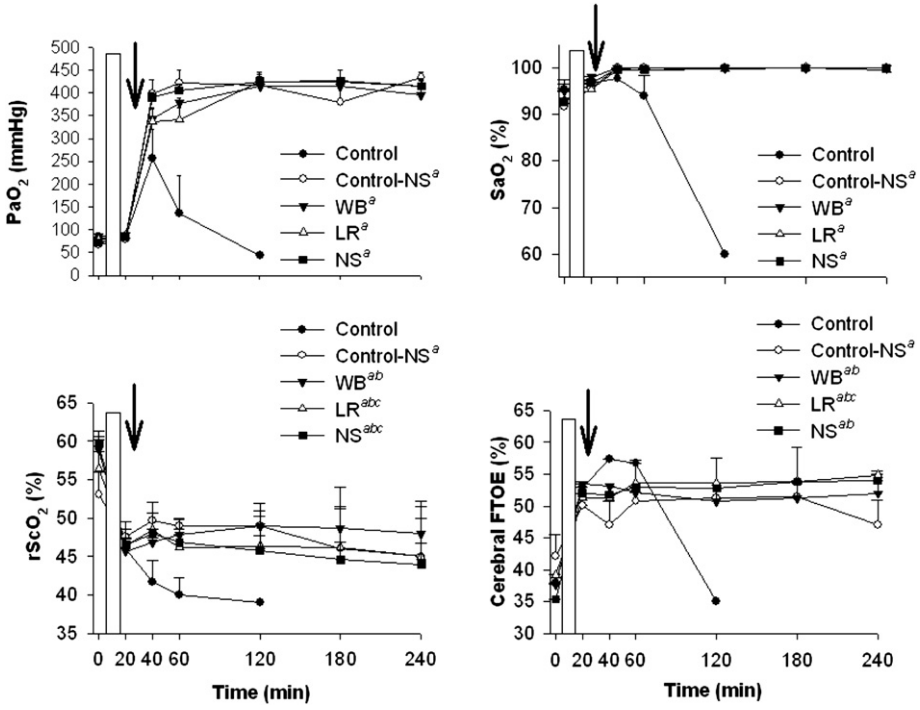

Fig. 3. Changes in blood and brain tissue oxygenation during experimental period. White bar: period of blood loss; black arrow: infusion of 10 mL/kg normal saline except control group. FTOE = fractional tissue oxygen extraction; LR = lactated Ringer's solution; NS = normal saline; $rScO_2$ = regional cerebral tissue oxygenation; SaO_2 = arterial oxygen saturation; WB = whole blood. $^{a}p < 0.05$ *vs.* control group; $^{b}p < 0.05$ *vs.* control-NS group; $^{c}p < 0.05$ vs. WB group; $^{d}p < 0.05$ *vs.* LR group by two-way repeated measures ANOVA.

examine the variations in oxygen debt seen at the regional tissue level. Pulse oximetry, although noninvasive, is not that easy to read when the patient's condition is unstable, especially when the blood pressure is low or undetectable during hemorrhagic shock; this is because its signal depends on small artery pulsation. Furthermore, this parameter indicates systemic circulation rather than regional tissue oxygenation.[19] When compared with the above, noninvasive NIRS monitoring is able to provide a continuous estimation of regional tissue oxygenation and thus may be a better choice when assessing brain tissue oxygenation in critical patients. Our experiments also demonstrate that it can be used conveniently for the real-time monitoring of a subject's $rScO_2$ throughout a long experiment without any interruption.

There have been only a few investigations that have evaluated the feasibility of NIRS as a monitoring approach for neonatal and pediatric patients,[20,21] and this is also true for animal models undergoing hemorrhagic shock.[22–27] Investigations of the relationship between jugular bulb oxygen saturation and regional cerebral oxygenation under conditions of hypoxia were measured by NIRS and found to have good correlation.[20,21] Previous hemorrhagic shock studies examining the ability of NIRS to determine adequacy of tissue oxygenation have mostly focused on peripheral muscles, the stomach, the liver, the kidneys, or the legs.[22–24] However, in these studies, the investigators have found that regional tissue oxygen saturation is correlated with measurements of systemic oxygen delivery in a linear fashion.[22] Furthermore, it has also been found that total body oxygen delivery is correlated with cytochrome aa_3 and tissue oxygen saturation during the hemorrhagic phase, and that post-resuscitative NIRS values were low within the gastric and muscular beds, despite normal systemic measures of oxygen delivery.[23] Thus, resuscitation would seem to not uniformly restore cellular oxygenation to all tissue beds. Predicting organ dysfunction during traumatic shock resuscitation using NIRS monitoring tissue oxygenation has also been reported.[25] Thus, using NIRS to detect $rScO_2$ would seem to be a convenient and reliable technique for monitoring and predicting neurological outcome in hemorrhagic shock cases. Low tissue oxygen saturation is thought to be associated with a worse outcome in critically ill infants, so intervention needs to be started as early as possible in selected high-risk patients, which will result in it being more likely that the intervention will have a demonstrably favorable impact on early survival.[28–30] The present study has shown the effects on $rScO_2$ and FTOE of using different fluids to perform resuscitation over the first four hours after hemorrhagic shock. However, long-term effects were not included in our experiments. A more meticulous study design that evaluates the subjects' long-term neurological outcome is necessary in the future.

One limitation of our investigation is a failure to measure cerebral perfusion and the added inotropic agents in the studied animals. Meybohm et al reported on the effects of rapidly restoring cerebral perfusion pressure in piglets undergoing hemorrhagic shock and showed that brain tissue oxygenation and the tissue oxygen index could not be improved without blood transfusion.[26] Using our animal model, our findings are in agreement and demonstrate that WB is the best fluid for raising $rScO_2$ when used with 100% oxygen supplementation. Therefore, blood transfusion to increase total hemoglobin level to restore oxygen carrying capacity is important to brain tissue oxygenation. However, other volume expanders will still have some role in restoring $rScO_2$. Based on the present results, there is no reason why they should not be used in an emergency when WB is not available during the first hours of treatment. Another limitation of our study is that the maintained MAP (between 50–70 mmHg) of the treatment groups did not reach the baseline blood pressure (approximately 85–95 mmHg) of the study animals, and, similarly, the $rScO_2$ of the treated animals also did not reach the baseline value of the animals. Therefore, the treatments used here are still suboptimal. A more aggressive design using oxygen, fluid resuscitation and inotropic agents to maintain optimal condition may be very useful when evaluating brain tissue oxygenation in clinical cases with acute hemorrhagic shock.

In conclusion, hemorrhagic shock events decrease brain tissue oxygenation and influence oxygen extraction, and such an event results in high mortality in young subjects when there is no effective fluid resuscitation. Inspired oxygen supplementation and effective fluid resuscitation with either one-dose bolus of NS, or this combined with a subsequent transfusion of WB, LR or additional NS would seem to help to stabilize cardiovascular condition and improve cerebral tissue oxygenation during an emergency period. In these circumstances, WB is the best fluid for maintaining an ideal $rScO_2$ when treating hemorrhagic shock.

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