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Original Article

The application of early goal directed therapy in patients during burn shock stage

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Abstract: Early goal directed therapy (EGDT) provided at the earliest stages of burn shock, has significant benefits for ordinary burn patients, however, its effect on patients with more than 80% of total surface area burned (TBSA) still remains unclear. In this study, 34 extensively burned patients with (87.3±5.6)% of total surface area burned were collected from January 2008 to January 2014. All burn patients here had similar monitoring or treatment modalities. Of these 34 burn patients, 13 patients were treated with EGDT under pulse indicator continuous cardiac output (PICCO) monitoring, and 21 patients were treated with conventional fluid management. Information obtained in the course of treatment included mean arterial pressure (MAP), central venous oxygen saturation ($ScvO_2$), oxygenation index (PaO_2/FiO_2), blood lactic acid and urine volume, infusion volume ($mL{\cdot}1\%\ TBSA^{-1}{\cdot}Kg^{-1}$), complications of over-resuscitation (hydrothorax or pulmonary edema), case rate of burn sepsis and fatality. Our results demonstrated that there existed significant difference between the two groups in parameters below: 1. Higher $ScvO_2$ (%) after EGDT (EGDT: 78.1±8.6, CG: 65.5±11.2; t=-3.446, P<0.05), 2. Higher PaO_2/FiO_2 after EGDT (EGDT: 381.4±56.6, CG: 328.9±48.6; t=2-875, P<0.05), 3. Lower mean infusion volume after EGDT ($mL{\cdot}1\%\ TBSA^{-1}{\cdot}Kg^{-1}$) (EGDT: 3.29±0.26, CG: 3.71±0.31; t=5.292, P<0.05), 4. Lower complications of over-resuscitation after EGDT (EGDT: 2/13, CG: 15/21; P<0.05); However, no statistical significance existed in parameters below: 1. MAP (EGDT: 76.2±13.1, CG: 74.3±15.6; t=-0.36, P>0.05), 2. Urine volume (EGDT: 0.83±0.12, CG: 0.85±0.17; t=0.370, P>0.05), 3. Case of burn sepsis (EGDT: 13/13, CG: 20/21; P=1), 4. Case fatality (EGDT: 1/13, CG: 3/21; P=1). The finding results showed that patients with more than 80% of total surface area burned during burn shock phase could get better outcome from EGDT.

Keywords: Early goal directed therapy (EGDT), serious burn, shock phase, fluid resuscitation

Introduction

The skin plays a crucial protection barrier against water loss and exterior harmful factors, its disruption of integrity can probably cause patients' severe disability or even death [1]. Skin burn injury is a considerably common trauma, which may induce several rare complications, such as adrenal hemorrhage with subsequent insufficiency [2]. In these patients with extensive skin burn, the internal organs are some of the most vulnerable distant organs, such as lungs [3]. At present, fluid resuscitation is not only the most important task during the first 24 to 48 hours post-burn, but also the earliest systemic treatment towards serious burns. Even though advanced technologies, which are minimally invasive, allow beat-to-beat cardiac output monitoring and permit assessment of fluid responsiveness, have become available in critically ill patients, we have to admit that patients of suffering extremely large burn size (TBSA%≥80) were rather difficult to cure, and most were tended to have a high mortality rate.

Currently, there exist resuscitation regimens based solely on intravenous crystalloids, however, the universal applicability of resuscitation regimens has been questioned by several investigators. The first one is to use certain solution to perform enteral resuscitation, such as oral resuscitation solution of the World Health Organization (WTO) or an equivalent therapy [4, 5]. The second one is to use fresh frozen plasma or 5% albumin as the mainstay of resuscitation starting on admission, rather than at the 24-h point or as a salvage therapy [4, 6]. An aggressive third approach to the application of colloid is also embodied in the Western Pennsylvania formula, which makes use of fresh frozen plasma as the main resuscitation fluid during the first 24 hours [7].

Conventional fluid management depending on pressure-based indices of ventricular filling has been used to guide resuscitation. However, lack of standardization makes it difficult to modulate the fluid volume precisely. Empirical treatment for adjusting fluid volume could only base on urine volume, blood pressure, heart rate, peripheral blood supply of patients.

Over the past decade, many performed researches showed that cardiac filling pressures are unworkable to guide fluid resuscitation, or to estimate fluid responsiveness, because of the extremely low possibility of acquiring clinical determination of the intravascular volume in critically ill patients [8-10]. In recent years, with the development of medical treatment technology, early goal directed therapy (EGDT) plays a more and more important role in fluid management during shock phase. As we know, burn shock is resulted from insufficient effective circulating blood volume, consequently, it is vital to improve blood circulation for patients. Nowadays, EGDT can effectively improve blood circulation for burn patients with pulse indicator continuous cardiac output (PICCO) guidance. PICCO device has been extensively used to measure hemodynamic parameters, including central venous pressure (CVP), systemic vascular resistance index (SVRI), cardiac output (CO) index, dedicated end-diastolic volume index (GEDI), extravascular lung water index (EVLWI), and intrathoracic blood volume index before and after EGDT. What is more important, the information obtained from PICCO alters the management practices of severe burn patients, and provides necessary assistance in the determination of immediate and subsequent therapies.

Our study was designed to retrospectively appraise whether PICCO provides additional useful information beyond that obtained by conventional empirical evaluation. Therefore, this article compared the efficacy of the conventional fluid resuscitation with EGDT, with the aim of exploring more effective anti-shock treatment in shock phase.

Materials and methods

General treatments

This study is a retrospective case series, including 34 seriously burned patients (97≥%TBSA≥80, the average TBSA% burn of 87.3±5.6) collected from January 2008 to January 2014. They all had similar monitoring or treatment modalities at this burn center. Based on a randomized trial (Random Number Table), selected patients were classified into two groups (no significant differences in age, TBSA and treatment modalities between these two groups), an EGDT group and a conventional group (CG). The EGDT group consisted of 13 patients aged from 17 to 62 years old (a mean age of 31.7 years), and the CG group consisted of 21 patients aged from 18 to 71 years old (a mean age of 33.0 years). This study was conducted in agreement with the declaration of Helsinki, and approved by the ethical committee of Fujian Medical University Union Hospital.

In this study, patients who had one of the followings had been excluded: high blood pressure, diabetes, and incomplete fluid records during the first 48 h.

Pulse indicator continuous cardiac output (PICCO)

An indwelling catheter was inserted into the patients' femoral artery for PICCO monitoring, and a central venous catheter was placed in the internal jugular vein. Cold isotonic saline (4-8°C) was injected through the central venous catheter within 4 seconds, and replaced when global end-diastolic volume index (GEDI) and CVP reached certain points, in this way, the PICCO catheter could detect temperature variation of blood within the arteries. In this operation, the goal of resuscitation is to maintain GEDI between 650 and 800 $ml \cdot m^{-2}$. The consumption of dobutamine was regulated to keep stroke volume index (SVI) between 40 and 60 $ml \cdot m^{-2}$ and left ventricular systolic force index between 1200 and 2000 $mmHg \cdot s^{-1}$. In the meantime, the consumption of dopamine was also adjusted to remain systemic vascular resistance index (SVRI) between 1200 and 1800 $dyn \cdot s \cdot cm^{-5} \cdot m^2$ and MAP≥65 mmHg.

Table 1. Comparison of the observed indicators and relevant parameters in EGDT and CG groups

Variables	EGDT (n=13)	CG (n=21)	t-value	*p*-value
MAP (mmHg)	76.2±13.1	74.3±15.6	-0.366	>0.05
$ScvO_2$ (%)	78.1±8.6	65.5±11.2	-3.466	<0.05
PaO_2/FiO_2	381.4±56.6	328.9±48.6	2.857	<0.05
Levels of lactic acid (mmo·L^{-1})	2.0±0.6	3.9±1.2	5.292	<0.05
Mean fluid volume (mL·1% $TBSA^{-1}$·Kg^{-1})	3.29±0.26	3.71±0.31	4.654	<0.05
Urine output (mL·Kg^{-1}·h^{-1})	0.83±0.12	0.85±0.17	0.370	>0.05

EGDT means "early goal directed therapy group"; CG means "conventional group"; MAP means "mean arterial pressure"; $ScvO_2$ means "Central venous oxygen saturation"; PaO_2 means "arterial pressure of oxygen"; FiO_2 means "Fraction of inspiration O_2". Data are shown as mean ± SD.

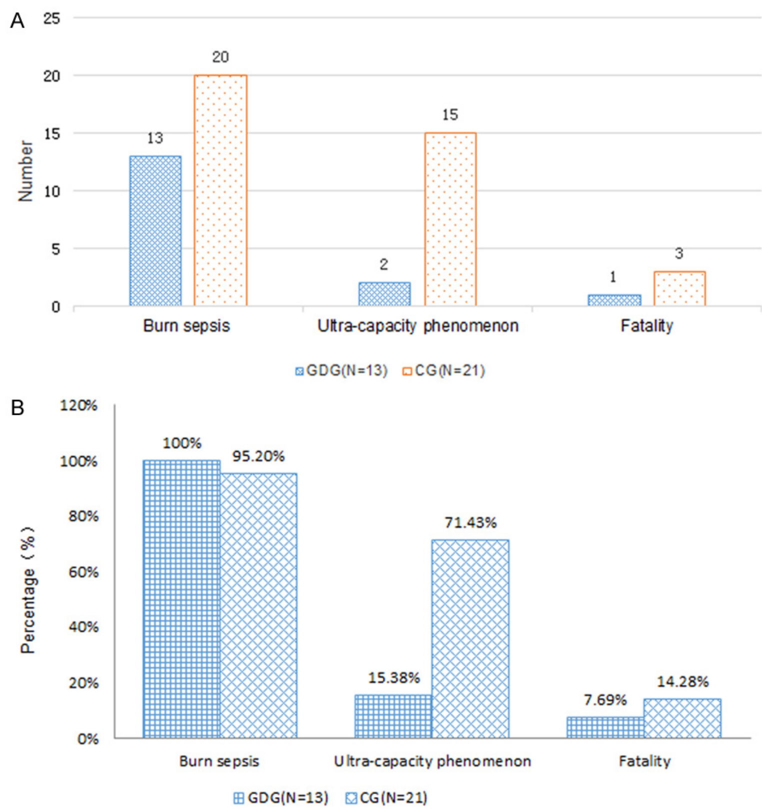

Figure 1. Comparison of the numbers (A) and percentage (B) of ultra-capacity phenomenon, burn sepsis and fatality. EGDT means "Early Goal Directed Therapy", and CG means "Conventional Group".

Criteria of resuscitation

After initial assessment, patients with TBSA%≥ 80 were admitted to hospital within 6 hours. Patients treated with EGDT were asked to be treated immediately with fluid resuscitation of crystalloid-colloid (ratio 1:1), until their physiological characters reached the resuscitation criteria under PICCO guidance in 6 hours. In EGDT group, CVP was maintained between 8 and 12 cm H_2O, mean arterial pressure (MAP) was kept ≥65 mmHg, urine volume was remained ≥1 mL·Kg^{-1}·h^{-1}, and extravascular lung water index (EVLWI) was maintained between 3.0 and 7.0 mL·Kg^{-1}, and some special cases as below were strongly advised to take appropriate doses of norepinephrine booster drug. Firstly, arterial blood pressure and tissue perfusion of patients failed to recover to normal levels, or presented severely low pressure after sufficient resuscitation. Secondly, SVRI reduced to 1000 dyn·s·cm^{-5}·m^2 or lower after sufficient resuscitation. While in control group (CG), patients from were conducted fluid management by traditional formula (First Affiliated Hospital of PLA General Hospital).

Index for further observation

The needed volume of crystalloid-colloid (mL·1% $TBSA^{-1}$·Kg^{-1}), the cases of limb peripheral cyanosis, multiple organ dysfunction syndrome (MODS), ultra-capacity, and fatality were all observed and recorded in 48 hours. Additionally, hemodynamic parameters, including CVP, CO index, SVRI, GEDI, intrathoracic blood volume index, and EVLWI were also recorded before and after EGDT.

Statistical analysis

Statistical analyses were performed with SPSS13.0 software. The measurement data are presented as the means ± the standard deviations, and processed with Student's t test for independent sample, thus the count data was analyzed with Chi-square test. Statistical significance was set when $P<0.05$.

Results

Demographic data

A total of 34 patients met inclusion criteria, 21 selected EGDT patients had a mean age of 31.7 and an average TBSA of (88.7±3.6)%, the other 13 selected CG patients had a mean age of 33.0 and an average TBSA of (86.1±6.2)%.

Effect of EGDT and conventional fluid management on systemic oxygenation

Systemic oxygenation including $ScvO_2$ (%), PaO_2/FiO_2, levels of lactic acid, and urine output were monitored in this study (**Table 1**).

EGDT group had significantly higher level of $ScvO_2$ and PaO_2/FiO_2, and significantly lower level of lactic acid than conventional fluid management after treatment ($P<0.05$). However, no significant difference was found in urine output after EGDT ($P>0.05$) between the two groups.

Besides the contrast of systemic oxygenation made between the two groups, MAP and mean fluid volume were also monitored after treatments. In EGDT, MAP was 76.2±13.1 mmHg, and mean fluid volume was 3.29±0.26 mL·1% $TBSA^{-1}·Kg^{-1}$, while in CG, MAP was 74.3±15.6 mmHg, mean fluid volume was 3.71±0.31 mL·1% $TBSA^{-1}·Kg^{-1}$. No significant difference was seen in MAP ($P>0.05$), but mean fluid volume from EGDT was significantly lower than from CG.

Mortality

As the small sample size, there were too few cases of burn sepsis and fatality for a valid statistical interpretation (**Figure 1A** and **1B**).

As shown in **Table 1**, EGDT had lower ratio of ultra-capacity phenomenon and fatality.

Discussion

Burn injury is a considerably common trauma, and for burn patients, the vital initial component in the management is sufficient fluid resuscitation. Patients, however, who suffered from extremely large burn size (TBSA%≥80) were difficult to cure and tended to have a high mortality rate, because the hypoxidosis of tissues and visceral organs, and many symptoms may induce hypoxidosis, such as extravasation of plasma, damage of vascular endothelial basement membrane continuity and integrity, and increase of systemic capillary permeability after severe burn. Urgent priority for treating severe burn patients was to restore effective blood volume at the shock stage quickly, and thus improve the condition of micro-circulating to ensure enough oxygen delivery. Therefore, fluid resuscitation has been one of the most common measures against burn injury during the first 24 to 48 hours post-burn. Fluid resuscitation and edema management are the two primary tasks during the first 24 to 48 hours post-burn, which of both were fundamental measures for anti-shock. As for burns, burn shock is resulted from the lack of effective circulating blood volume. In extensive burns, intravenous (i. v.) fluid therapy is required to avoid the life-threatening consequences of hypovolaemic shock, and to this aim, a number of resuscitation formulas have been advocated (http://www.ameriburn.org/.), some are currently in use on account of the general consensus of their effectiveness, such as Parkland or the Muir and Barclay formula. Due to the intensive medicine development, the experience of anti-septic shock was increasingly being accepted, such as theory of goal-directed therapy for the past few years [11], however, the problem was that EGDT might cause fluid volume overload that resulted in several significant complications, for instance, tissue edema or oxygen utilization disorders, and finally affect the prognosis [12]. Therefore, while conducting EDGT, PICCO device was generally used to measure hemodynamic parameters, including CVP, SVRI, CO, GEDI, EVLWI, and intrathoracic blood volume index. No doubt that monitoring of hemodynamic and volumetric parameters together in severe burns is of great importance, which would be able to provide accurate assessments of constant and hemodynamic statuses. SVRI, one of the hemodynamic parameters recorded during the observation period, is a sensitive indicator for judging hemodynamic type, and presented a descend trend continuously early in the perioperative burn period [13]. When SVRI changed significantly, stroke volume variation (SVV) was recorded. There exist significant correlations between SVV and SVRI at 16 hours and 24 hours post-burn [14]. In this retrospective, continuous PICCO measurements were performed to monitor SVRI of 13 EGDT patients, of these, two cases returned to normal levels after EGDT with PICCO guidance, though they suffered from hypotension and tachycardia first. In this guidance process, vasoactive drug was used when SVRI<700 dyn·s·cm^{-5}/m^2. However, what we should notice here is that current study is limited to individual cases, unable to draw statistically significant conclusions, therefore, further research needs to be carried out.

There also existed significant difference in $ScvO_2$ (%), PaO_2/FiO_2, mean infusion volume and levels of lactic acid besides in SVRI. It was reported that $ScvO_2$ widely accepted as a marker could accurately reflect the balance between global oxygen consumption and oxygen supply, and a cutoff of 70% for $ScvO_2$ has been regarded as an endpoint of early resuscitation [11]. Whereas, negative results from performed EGDT studies in the past a few years have questioned the goal of early resuscitation, whether $ScvO_2$ would be equal to or greater than 70% requires further research [15, 16]. In this study, patients with higher $ScvO_2$ had lower fatality and complications of over-resuscitation in critically ill patients, which was converse to some recent studies of high $ScvO_2$ being related to poor outcome [17-19]. Therefore, we speculated the interpretation of high $ScvO_2$ should be careful in clinical practice. There exist many factors that might contribute to the high $ScvO_2$, the confounders of high $ScvO_2$ need to be better controlled in future studies [20]. The ratio of PaO_2/FiO_2, which depends on both the FiO_2 level and the arterial oxygen saturation level [21], has already been applied to quantify the degree of abnormal gas exchange in pulmonary. In this study, Student's t test was used to assess the statistical difference between hemodynamic parameters from EGDT and CG patients, it revealed that EGDT improved the local tissue oxygenation of critically ill patients. And also, Student's t test showed patients with higher PaO_2/FiO_2 ($P<0.05$) had lower fatality and complications of over-resuscitation. The advantage of the PaO_2/FiO_2 ratio is clear for its ease to use, but the disadvantage is that it behaves differently from varying altitudes [22] and FiO_2 values [21, 22]. Consequently, it is unreliable to diagnose burn patients with PaO_2/FiO_2 ratio from different attitudes. We know significantly increased level of lactic acid is one of the most obvious hallmarks of tissue hypoxia and insufficient blood perfusion. Compared to oxygen dynamics and blood pH, lactic acid is a more appropriate clinical marker of blood volume fluctuations and disease severity, since it directly reflects the level of oxygen metabolism [23, 24]. In this study, EGDT significantly reduced lactic acid level in comparison to conventional fluid management. We appreciated the advantage of EGDT to conventional fluid management.

However, the parameters of MAP (mmHg) and urine output (mL·Kg^{-1}·h^{-1}) showed no significant difference. Urine output, normally used to monitor the patient's progress and adjust the resuscitation fluid, was the essential guidance to adequate resuscitation. This study showed slight difference in urine output between EGDT and conventional fluid management. MAP target plays a pivotal role in preventing complications, and it should be no more than 60 mmHg in limited fluid resuscitation [25, 26], whereas, when MAP increased from 65 mmHg to the usual levels, these septic shock patients with previous hypertension would probably improve microcirculatory function, although the cause and effect remained unknown [27]. In this study, MAP in EGDT patients was a little higher than CG patients, and the long-term effects of different MAP targets need to be evaluated in further studies.

In our study, fluid resuscitation was performed as a systemic treatment process under EGDT guidance and conventional fluid management. When guided by traditional resuscitation formulae, different perfusion rate and volume were set in the first 8 hours, second 8 hours, first 24 hours, and second 24 hours post-burn [28]. This approach seemed to quantify the perfusion rate, but its time distribution was so extensive that the body was unable to make timely adjustments to pathophysiological changes. What is different with conventional resuscitation, the goal directed guidance for resuscitation is able to perform a fine tuning against perfusion volume, with the aim of making the body keep in a relatively stable state to protect vital organs. To sum up, it implies that EGDT should be used more frequently with patients suffering severe burn injury.

However, some limitations and points are still needed to improve: (1) the small sample size made it unable to perform statistical analysis upon the odds of burn sepsis and fatality, therefore, larger size of patients is eager for further investigation; (2) the potential inaccuracy of retrospective records existed in this study. However, the effect was minimized via reviewing the medical record from the time of injury rigorously in this study.

As we know, it is certainly difficult to distinguish cause and effect between non-experimental and retrospective studies [29]. Although causality can only be predicated on the assumption, differing fluid management practices from the temporal relationship of events and reasons is still the primary task. Our studies had a preliminary indication that EGDT could improve local tissue perfusion for severe burn patients, by contrast, conventional fluid management may not directly reflect local tissue perfusion during the resuscitation.

Conclusions

Patients with more than 80% of TBSA during burn shock phase could get better outcome from EGDT.

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Disclosure of conflict of interest

None.

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