

*Original Article*

## Effect of fluid temperature in intravenous fluid resuscitation of hemorrhagic shock

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### Abstract

**BACKGROUND:** Treatment of hemorrhagic shock is the major problem in emergency surgery. Fluid therapy is one of the first steps but, the conflict has been over the temperature used for the fluid injected to the patient. The aim of this study was to determine the effect of fluid temperature in intravenous fluid resuscitation of hemorrhagic shock.

**METHODS:** In this experimental study, 3 groups of 10 rabbits underwent hemorrhagic shock class III (mean arterial pressure = 40 mmHg) by catheter on femoral artery. Within 25 minutes, ringer lactate solutes with controlled temperatures of 15°C, 25°C and 37°C were injected through femoral venous line. They were followed for 72 hours.

**RESULTS:** In the lowest, middle and the highest fluid temperature group, mortality rate was 90%, 10% and 40%, respectively. Statistically significant difference was seen between the 15°C and 25°C resuscitation groups ( $P < 0.001$ ).

**CONCLUSIONS:** Our findings showed possible benefit of room temperature as the optimal fluid temperature for fluid resuscitation in hemorrhagic shock.

**KEY WORDS:** Hemorrhagic shock, hypothermia, fluid therapy, rabbit, temperature.

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Treatment of hemorrhagic shock is a major issue in surgery especially in emergency cases. Clinically, following the loss of fluid, patients with hemorrhagic shock often become hypothermic, which has been associated with an increased mortality<sup>1</sup>. Hypothermia is defined as a decrease in core temperature  $< 36^{\circ}\text{C}$ <sup>1</sup> and can cause detrimental systemic effects in the nervous system, heart and kidney and also in acid base balance, coagulation and immune functions<sup>2,3</sup>. Therefore, an intervention is needed, within a short period of time to reduce these effects. For hypothermia treatment, several methods of re-warming of the patients have been evaluated. Among these

are humidification and warming of the inspired air, warming blankets and body cavity irrigation and extracorporeal rewarming; the latter being the most effective method<sup>2,4-6</sup>. The origin of hypothermia can be endogenous, controlled, or accidental<sup>7</sup>. Controlled and systemic mild hypothermia has been shown to improve survival in animal models of hemorrhagic shock<sup>8-13</sup>. In fact, fluid therapy in combination with external cooling of body has shown to produce the highest rate of survival in animals with hemorrhagic shock<sup>14-16</sup>. Deliberately, mild hypothermia ( $32.2$  to  $35^{\circ}\text{C}$ ) has been suggested to provide cerebral protection although its effects on neurologic outcome are

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debatable. Hypothermia has also been shown to alter contractility and relaxation of blood vessels in the brain and other vascular beds<sup>17,18</sup>. Wu et al have shown that inhibition of lipid peroxidation and systemic inflammatory reactions are influenced by mild hypothermia<sup>16</sup> while the less metabolic needs of myocardium have been known to be responsible for the treatment of hemorrhagic shock<sup>19</sup>. The possible benefits of complete thermal resuscitation and the restoration of patient's core temperature are a matter of speculation. In the present study, we examined whether in normothermic cases, hypothermic fluid therapy can have a positive effect on survival. Thus, we designed experiments to assess the effects of different fluid temperatures on fluid therapy in animal model.

## Methods

Three random groups of 10 wild type male rabbits weighing 1.25-1.75 kg were included in the present study. The rabbits had free access to food and water before the experiment. They were anesthetized using intraperitoneal ketamine (250 mg/kg). No artificial respiration was used. Afterwards, a temperature probe (4 F, Physiotemp Instrument, Inc, Clifton, NJ) was inserted into the peritoneum via an abdominal incision for monitoring of the rabbit's body temperature. One ml of a lidocaine solution (5%) was injected subcutaneously in the proximal left foot and a 22 G catheter was inserted into the left femoral vein for blood withdrawal and fluid infusion. Additionally, right femoral artery was catheterized for monitoring the blood pressure. Catheters were kept patent by intermittently flushing with 0.9% saline containing 2 U/ml heparin. No heparin was given systemically. After a 5-minute time period needed for the relaxation of the arterial primary spasm, hemorrhagic shock was introduced by blood withdrawal over a 15-minute time period via the femoral venous catheter until the mean arterial pressure descended to 35-45 mmHg. A 30-minute stabilization period was allowed during which the blood drainage was continued if the arterial pressure in-

creased. Then, the rabbits were ready for resuscitation. During the shock operation, for prevention of heat loss due to low room temperature, rabbits were kept in a controlled temperature cage in 37-39°C and the body temperatures of the rabbits were constantly monitored. The animals were randomly allocated to one of the three groups. One group received lactated ringer's solution having a controlled 14-16°C temperature (15°C). The temperature of the solution for the second group was 24-26°C (25°C group) and for the third group it was 36-38°C (37°C group). These solutions were infused via the venous catheter for 25 minutes until the mean arterial pressure reached 89-91 mmHg. Body temperature was monitored during this period and the end time. After recovering from anesthesia, the rabbits were transferred to a regular cage with the room temperature of 25°C and an unlimited supply of food and water for 72 hours. During the follow up, no further control of the body temperature was attempted. The rabbits were monitored twice a day for any mortality. Differences in the amount of fluid needed for resuscitation compared with ANOVA statistical test and mortality rates among these groups were compared using Fisher exact test. P value less than 0.05 was considered significant.

## Results

The body temperature of each rabbit before the induction of the hemorrhagic shock was  $38 \pm 0.5^\circ\text{C}$ . Mean arterial pressure (MAP) was  $90 \pm 5$  mmHg before any experimental manipulations. A total of  $42 \pm 5$  ml blood was drained during the bleeding time. Three rabbits were not able to tolerate the shock and died during stabilization period, which were replaced. During resuscitation, the amount of fluid needed for restoration of normal pressure was  $124 \pm 15$  ml,  $131 \pm 15$  ml and  $130 \pm 12$  ml in 15°C, 25°C and 37°C fluid resuscitation groups, respectively. There was no statistically significant difference between the injected fluid volumes. However, the body temperature was respectively  $35 \pm 0.5^\circ\text{C}$ ,  $36.5 \pm 0.3^\circ\text{C}$  and  $38 \pm 0.2^\circ\text{C}$  in 15°C, 25°C and 37°C fluid resuscitation groups

after fluid resuscitation. In the 15°C fluid resuscitation group only one rabbit survived after 72 hours. On the other hand in the 25°C resuscitation group only one rabbit died and 9 survived after 72 hours while in the 37°C fluid resuscitation group 4 died during this time period. Statistically significant difference was seen between the 15°C and 25°C resuscitation groups ( $P < 0.001$ ). Regarding mortality properties, there was no significant difference between the 15°C and 37°C resuscitation groups and 37°C and 25°C resuscitation groups.

## Discussion

Our results in animal model showed that in treatment of hemorrhagic shock, the ideal temperature for resuscitative fluid is 25°C as it showed less mortality compared to fluid temperatures of 15°C and 37°C. Induced hypothermia in elective surgery and in experimental studies with hemorrhagic shock has been shown to have beneficial effects<sup>1</sup>. Since cold resuscitation fluids lower body temperature, it can be suggested that the beneficial effects of these fluids are due to systemic hypothermia, consistent with what has been done before. The only difference is that in previous studies, the experiments performed on animal models showed a decreased mortality rate when the body temperature was lowered to 34°C<sup>8,16,20,21</sup>. Even some beneficial effects were seen at 30°C<sup>11,22,23</sup>. On the other hand, in the present study we demonstrated that the reduction of rabbit's body temperature to 36.5°C but not 35°C has positive effects. The method of producing hypothermia in previous studies has been external cooling of the body while in our study cold resuscitation fluids were utilized, and this may explain the observed differences in the obtained results between the two methods. Indeed, the effects of hypothermia in elevation of

blood concentrations of norepinephrine<sup>24</sup>, angiotensin II<sup>25</sup> and corticosterone<sup>26</sup>, and enhancing the cardiac contractile performance, and increasing the coronary perfusion<sup>27</sup>, peripheral vasoconstriction and also blood pressure<sup>20,24</sup>, are expected and proven but the different results may be due to variance in the degree of these effects by the two methods. Given the effects of optimum hypothermia in reduction of hemorrhagic shock related mortality, it is obvious that infusion of cold fluids is more practical than external cooling of the body. Since the room temperature is around 25°C, the use of a 25°C temperature for resuscitation fluid eliminates the need for its warming and thus wasting time. Winker et al found that in surgical patients with a core temperature of 36.1°C, blood loss was increased compared with that in patients having an intraoperative temperature of 36.6°C<sup>28</sup>. As mentioned before, the best survival rate was seen in the study group with central body temperature of 36.5°C. Then, we may conclude that if fluid resuscitation alone (without induction of hypothermia) in hemorrhagic shock subjects lead to low body temperature (core body temperature  $< 36^\circ\text{C}$ ), it will result in the best survival rates. But more experimental studies and obviously controlled clinical trials are necessary to prove this hypothesis specially, when we saw the difference between 37°C and 25°C resuscitation groups in survival rate was not significant. On the other hand, it should be kept in mind that reduction of the body temperature has its own limitations such as cardiovascular complications. Thus, under any protocol used, lowering of the body temperature should be constantly monitored. This means that lowered body temperature can reduce mortality rate in hemorrhagic shock if the body temperature is monitored and controlled.

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