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Editorial

Vitamin C: A Possible Role in Hemorrhagic Shock?

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Hemorrhagic shock is a state of alteration of the body's homeostasis. It is the reduction of blood volume necessary for adequate organ perfusion as a result of acute excessive blood loss. This leads to tissue and cellular dysfunction [1].

Depending on controlled or uncontrolled hemorrhagic shock, the ideal treatment may differ, but parenteral vitamin C has not been used as an integral part, despite there being some evidence of its use as an aid in such circumstances [2]. Currently, there has been some literature regarding the use of the Vitamin C, Thiamine and hydrocortisone in the septic shock [3,4]. Are we at the point that the use of vitamin C in the hemorrhagic shock can be entertained?

In the United States of America, trauma is the third leading cause of death among ages 1 - 44 years. The cause is multifactorial, depending on the situation. Penetrating injuries like gunshot or stab wounds accounts for 49% of deaths, while blunt injuries like falls and motor vehicle accidents may account for 60% of deaths. Hemorrhage accounts for 30 - 40% of traumatic deaths and there is a greater association between penetration wounds and hemorrhage [5].

Hemorrhagic shock treatment, besides stoppage of exsanguination, is treated by packed red blood cell unit transfusions and blood products, which has led to increased length of stay, multiple organ failure, and mortality [2,6-8].

After PRBC, crystalloid solutions such as Ringer's Lactate are used as the most frequent solution for fluid resuscitation in hemorrhagic shock. However, aggressive therapy with it may increase neutrophil's oxidative burst and interleukin-1 [IL-1], interleukin-6 [Il-6], and tumor necrosis factor-alfa [TNF-a] activation [1,6].

Unlike crystalloid, colloid solutions tend to remain in the intravascular compartment longer, requiring a smaller resuscitation fluid volume. Examples of these are albumin, hydroxyl-ethyl starch, and dextran [9]. These solutions, however, have been shown to reduce ionized calcium, immunoglobulins, renal insufficiency and negatively influence the extracellular compartment, unlike crystalloids [10].

Oxygen-carrying blood substitutes try to counter storage, blood type compatibility, and disease transmission problems associated with plain blood transfusion. There are options for fluorocarbon-based synthetic oxygen carriers which are easy to produce, have a long shelf life, and have a low risk of infections or immune reactions. The stroma-free cross-linked human or non-human hemoglobin products have high oxygen carrying capacity, good oncotic effect, and prolonged shelf life. They are not free of side effect and they do increase the risk of renal toxicity, hypertension, and immune reactions. Further clinical trials are necessary before the routine use of these substitutes be established [1].

Spoerke., *et al*. used lyophilized plasma, a known alternative to fresh frozen plasma for volume recovery therapy and vitamin C was added and there was a decrease in pro-inflammatory IL-6. Lyophilized plasma requiring reconstitution with an acidic compound and vitamin C was also empirically used [2]. In order to see if this was attributed to the use of lyophilized plasma versus fresh frozen plasma or the added vitamin C, another group of researchers used lyophilized plasma with vitamin C, citric acid, and hydrochloric acid. Vitamin C greatly reduced IL-6 at 2 hours when compared to citric acid [CA] and hydrochloric acid [HCl], and when compared to HCL at 4 hours after administration [7].

Ischemia-reperfusion injury in shock is a real concern. A study sought to find out the efficacy in post-transfusion bleeding. A hemorrhagic shock model in rats was used with among 3 groups. A control group was given 1ml of normal saline intraarterially, one of the two experimental groups received a dose of 1 mg/100g bodyweight vitamin C dissolved in 1ml normal saline intraarterially, and the second experimental group received a dose of 5mg/100g bodyweight vitamin C in a similar fashion. After 15 minutes of induced hemorrhagic shock, the removed blood was re transfused, and bleeding within the gastric cavity ceased after 30 minutes. Evaluation of intravascular blood in the gastric wall was evaluated via gastric excision. Both vitamin C groups had smaller ischemic areas after re-transfusion and both had smaller amounts of exsanguinations, however, the smaller, 1mg/100g dose group showed the least blood loss after re transfusion [11].

In a study, a group investigated the effect of vitamin C over *in vivo* heme oxygenase-1 expression [12,13]. They hypothesized administration of vitamin C prior to a hemorrhagic shock model would modify injury of the intestine in rats. After intraperitoneal injection of 100mg/kg vitamin C dissolved in normal saline, the study group was compared to a control [normal saline only]. Heme oxygenase-1 induction began 2 hours after vitamin C administration and increased in the following 24 hours. The damage observed, such as "epithelial edema, villi necrosis, and hemorrhaging", was noticeably diminished by the prior administration of vitamin C. Vitamin C effect on down-regulating TNF-a and IL-6 and protected effect against apoptosis by raising the Bcl-2/Bax ratio was seen [8].

In another study by the same group, the heme oxygenase-1 induction was tried again. In this study, vitamin C was used as hemorrhagic conditioning and post-hemorrhagic shock treatment. Vitamin C use in pre-treatment served as "organ preconditioning", whereas posterior administration would increase heme oxygenase-1 mRNA, level, and activity. Twelve hours after the onset, both pre and post treatment groups showed reduced vital organ markers such as alanine aminotransferase [ALT], aspartate aminotransferase [AST], blood urea nitrogen [BUN], creatinine, lactate dehydrogenase [LDH], and lactate compared to the control group [14].

In this editorial, we tried to pose the questions for the role and future of Vitamin C use in hemorrhagic shock. Earlier studies among rats have shown that using vitamin C, as a pre-conditioning agent could ameliorate hemorrhage caused by interventions. Post-hemorrhagic treatment would help by protecting vital organs from reactive oxygen species [ROS], neutrophil induced damage and apoptosis. Promising results would lead to lower mortality, less probability of ICU admission, and shorter length of overall hospital stay. The verdict is not out yet, though a thought-provoking idea has been introduced. Future studies are suggested.

Conflict of Interest

There is no declared competing conflict of interest between authors.

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Volume 2 Issue 9 December 2018