Vitamin C in Burn Resuscitation

Julie A. Rizzo, MD[a,b,*], Matthew P. Rowan, PhD[a], Ian R. Driscoll, MD[a,b], Kevin K. Chung, MD[a,b], Bruce C. Friedman, MD[c]

KEYWORDS

• Reactive oxygen species • Free radical • Ascorbic acid • Vitamin C • Burn

KEY POINTS

- Damage from reactive oxygen species significantly contributes to the increased resuscitative requirements after burn injury.
- Vitamin C is an inexpensive, readily available antioxidant.
- Preclinical and clinical studies demonstrate vitamin C can be an effective adjunct in burn resuscitation by decreasing overall fluid requirements and edema.
- Vitamin C appears to be well tolerated, but further investigation is needed to identify unanticipated effects from high-dose administration to burn patients.

INTRODUCTION

Proper fluid management in the immediate phase after significant burn injury is important for optimizing outcomes. The goal of burn resuscitation is to ensure adequate end-organ perfusion at the lowest physiologic cost. The pathophysiology of the massive fluid shifts that occur after burn injury and the underlying microvascular changes have been studied previously in an attempt to identify targets to reduce overall fluid requirements.[1–3] Increased capillary permeability results in the escape of fluid and protein from the intravascular into the interstitial space and is greatest in the first 8 hours after burn injury.[4] Compared with other forms of traumatic injury, the increased

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[a] United States Army Institute of Surgical Research, 3698 Chambers Pass, JBSA Fort Sam Houston, TX 78234, USA; [b] Department of Surgery, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814, USA; [c] JM Still Burn Center at Doctor's Hospital, 3651 Wheeler Road, Augusta, GA 30909, USA

* Corresponding author.

E-mail address: Julie.a.rizzo.mil@mail.mil

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resuscitative requirements after burn injury are largely due to intravascular volume losses from capillary leakage. Excess fluid can accumulate in any tissue bed, resulting in resuscitation-related morbidity. These morbidities include pulmonary edema, compartment syndromes (muscle compartments, abdomen, and the orbits), and even cerebral edema.

Various inflammatory mediators have been shown to contribute to increased vascular permeability after burn injury, but mediator-targeted therapies have largely been unable to significantly mitigate capillary leak and thus decrease the resuscitation volumes needed. Reactive oxygen species (ROS) have also been reported to make a significant contribution to the increased vascular permeability, and antioxidant therapy has been investigated as a potential therapy to decrease ROS-induced damage. However, the pathophysiology of ROS-mediated damage and its effect on vascular permeability is complex and requires further investigation.

PATHOPHYSIOLOGY: INCREASED CAPILLARY PERMEABILITY

Increased capillary permeability after burn injury is due to several mechanisms. Immediately after a burn, mast cells release histamine that increases the activity of xanthine oxidase, which is one of many pathways that contribute to the increased production of ROS observed after burn injury.[2] ROS are formed endogenously during the metabolism of oxygen and can be produced through a variety of different enzymatic pathways, including NADPH oxidase, xanthine oxidase, and endothelial nitric oxide synthase, and in the electron transport chain.[5] ROS have vital physiologic roles in cell signaling, immune defense, and vascular tone, among others, but can also damage proteins, lipids, and nucleic acids at higher concentrations and have been implicated in many disease processes, such as cancer, insulin resistance, and atherosclerosis.[6] ROS-induced endothelial damage to lipids and proteins of cell membranes has been shown to contribute to the increased capillary leakage associated with burn injury.[7–10]

ANTIOXIDANT THERAPY

Therapies targeted at blocking the action of xanthine oxidase to reduce the formation of ROS have shown improved survival in preclinical burn models only when inhibitors are administered before burn injury,[11] which suggests that redundant formation pathways and enzyme activity create a complex barrier for effective targeting of ROS production. Therefore, a better strategy for preventing or minimizing increases in capillary permeability following burn injury might be to attenuate ROS-induced damage by removing ROS from circulation with a scavenger.[2,12] Therapies scavenging ROS as an adjunct in burn resuscitation could minimize capillary leak, and in turn, reduce the resuscitative requirements of large burns and minimize edema.

Because excess ROS is damaging to lipids, proteins, and nucleic acids, multiple endogenous systems exist to reduce ROS levels and include enzymes such as superoxide dismutase, catalase, peroxiredoxin, and thioredoxins.[12] For example, superoxide dismutase is part of an antioxidant system shown to decrease lipid peroxidation, a process that propagates chain reaction production of ROS.[13] However, the excessive ROS levels produced following a burn injury overwhelm endogenous systems, and exogenous ROS scavengers are needed to reduce ROS levels. Antioxidants are a class of effective ROS scavengers that act as reducing agents and become oxidized to neutralize ROS. Examples of nonenzymatic antioxidants include vitamins (such as C and E), minerals (such as selenium), and glutathione.[14] Several antioxidant therapies have been evaluated for their efficacy at reducing the capillary permeability after