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Vitamin C in Severe Burns: What Does the VICTORY Trial Really Tell Us?

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The recently published VICTORY trial reported that intravenous vitamin C administration in patients with severe burn injury was associated with increased mortality and greater organ dysfunction compared with placebo [1].

These findings will undoubtedly be interpreted by many as evidence that intravenous vitamin C is ineffective-or even harmful-in critically ill burn patients.

However, a closer examination of the study suggests that such conclusions may be premature.

What Did the Study Actually Test?

The VICTORY investigators administered vitamin C at 50 mg/kg every 6 hours for 96 hours.

For an 80-kg patient, this corresponds to approximately 16 grams per day.

While higher than nutritional supplementation, this protocol differs considerably from the pharmacologic intravenous vitamin C (HDIVC) approaches commonly used in orthomolecular medicine, where individual infusions frequently range from 25-100 grams or more and are often individualized according to patient status and therapeutic goals [2, 3].

Therefore, the VICTORY trial should not be viewed as a definitive test of all forms of intravenous vitamin C therapy.

Rather, it tested a specific ICU protocol in a highly specialized patient population.

Pharmacologic Vitamin C Is Not the Same as Nutritional Vitamin C

One of the most important distinctions in vitamin C research is the difference between nutritional and pharmacologic dosing.

Padayatty and colleagues demonstrated that intravenous administration can achieve plasma vitamin C concentrations many times higher than those achievable through oral administration [2].

At these pharmacologic concentrations, vitamin C may exert biologic effects distinct from its traditional nutritional role, including effects on oxidative stress, endothelial function, inflammatory signaling, immune function, and cellular redox balance.

Vitamin C also has well-established roles in collagen synthesis, wound healing, endothelial integrity, catecholamine synthesis, and antioxidant defense-functions that are especially relevant in serious burn injury.

This raises an important question:

Did the VICTORY protocol achieve and maintain the pharmacologic plasma concentrations required to fully test the mechanisms proposed by advocates of HDIVC?

The trial does not definitively answer this question.

Burn Injury Is a Systems-Level Disorder

Severe burn injury is among the most complex physiologic challenges encountered in medicine.

Patients experience:

- massive oxidative stress
- capillary leak
- endothelial injury
- mitochondrial dysfunction
- immune dysregulation
- hypermetabolism
- infection risk
- sepsis
- multi-organ dysfunction

Burn recovery also depends on coordinated nutritional and antioxidant networks. Albumin, protein status, zinc, selenium, sulfur-containing amino acids, vitamin D, and other nutrients may influence oxidative stress, collagen synthesis, immune function, and tissue repair. Critically ill burn patients often

experience capillary leak, wound exudation, metabolic stress, and low albumin levels, raising the possibility that baseline nutritional and redox status could modify responses to vitamin C.

From a systems-medicine perspective, severe burns represent a profound disruption of multiple biologic systems simultaneously.

Expecting a single nutrient intervention to reverse such widespread physiologic injury may be unrealistic.

A negative outcome from vitamin C monotherapy should not automatically be interpreted as evidence against broader metabolic and nutritional approaches.

This broader nutrient-network view is consistent with a recent NHANES-based analysis reporting that higher intake of several nutrients-including vitamin C, vitamin D, magnesium, folate, vitamin B6, and vitamin K-was associated with lower hs-CRP levels in U.S. adults [4].

Timing Matters

The intervention was administered during the first 96 hours following injury.

Yet many of the complications responsible for burn mortality-including infection, sepsis, and progressive organ dysfunction-often develop days to weeks after the initial injury.

The accompanying JAMA editorial raised questions regarding whether a short-course intervention early after injury would be expected to influence outcomes that may develop much later in the disease course [5].

This raises an important question:

Was the trial testing vitamin C, or was it testing the ability of a brief intervention to alter a prolonged and highly complex disease process?

Third-degree burns do not heal in 96 hours. Collagen synthesis, immune recovery, wound remodeling, and tissue repair continue well beyond the first four days.

Historical Context

The burn literature regarding vitamin C is not new.

More than 25 years ago, Tanaka and colleagues reported that high-dose vitamin C administered during burn resuscitation reduced fluid requirements and edema formation in patients with severe

burns [6].

Subsequent studies reported improvements in endothelial function, oxidative stress markers, and clinical outcomes associated with antioxidant therapy in critically ill and burn patients [7, 8].

Long before modern burn-resuscitation protocols were developed, Fred R. Klenner, MD, reported clinical observations suggesting that vitamin C requirements may increase dramatically during severe physiologic stress, including burns, infections, and trauma [8]. Although these observations were not conducted according to modern randomized-trial methodology, they helped stimulate decades of investigation into the role of vitamin C in critical illness [9].

These earlier observations helped establish the biologic rationale for vitamin C use in burn medicine.

The VICTORY findings therefore stand in contrast to portions of the previous literature and deserve careful examination rather than immediate acceptance as definitive.

The Context of Previous Critical-Care Vitamin C Trials

The VICTORY protocol closely resembles the dosing strategy used in the LOVIT sepsis trial, which also reported unfavorable outcomes [10].

Both studies differ from many earlier reports suggesting benefit from intravenous vitamin C in selected settings.

The reasons for these discrepancies remain unclear.

Potential explanations include:

- differences in patient selection
- timing of administration
- disease stage
- dose and duration
- concurrent therapies
- critical-care management practices

Further investigation is warranted before broad conclusions are drawn.

What Can We Conclude?

The VICTORY trial is an important study and its findings should be taken seriously.

However, it does not establish that all intravenous vitamin C therapy is ineffective or harmful.

Rather, it demonstrates that one specific vitamin C protocol-50 mg/kg every 6 hours for 96 hours-did not improve outcomes in patients with severe burn injury and was associated with worse results in this particular setting.

The broader question remains unanswered:

Can optimization of vitamin C status improve physiologic resilience, recovery, and clinical outcomes under appropriate circumstances?

The VICTORY trial does not definitively answer that question.

As with many negative studies, the most important lesson may not be that vitamin C does not work, but rather that patient selection, timing, dose, duration, and clinical context matter.

The challenge moving forward is not simply to ask whether vitamin C works, but to determine when, where, for whom, and under what conditions it may provide benefit.

From an Integrative Orthomolecular Systems Medicine (IOM) perspective, the VICTORY trial highlights a broader principle: severe burn injury is not a single-pathway disorder but a complex systems-level disturbance involving oxidative stress, inflammation, immune dysfunction, endothelial injury, mitochondrial impairment, metabolic disruption, protein loss, and nutrient depletion. In this context, vitamin C should not necessarily be viewed as an isolated intervention, but as one component of a larger biologic network supporting antioxidant defense, collagen synthesis, vascular integrity, immune regulation, and tissue repair. Future research may therefore benefit from evaluating vitamin C within broader systems-based strategies designed to improve physiologic resilience, recovery, and clinical outcomes.

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