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Editorial Board Member of *World Journal of Diabetes*, Fernando Cordido, MD, PhD, Professor, Department of Medicine, University A Coruña, Coruña 15006, Spain

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World Journal of Diabetes
Baishideng Publishing Group Inc
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Pleasanton, CA 94588, USA
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Role of vitamin C in diabetic ketoacidosis: Is it ready for prime time?

Sebastian Casillas, Alan Pomerantz, Salim Surani, Joseph Varon

Sebastian Casillas, Alan Pomerantz, Dorrington Medical Associates, PA, Houston, TX 77030, United States

Salim Surani, Division of Pulmonary, Critical Care and Sleep Medicine, Texas A and M University, Health Science Center, Corpus Christi, TX 78414, United States

Joseph Varon, Acute and Continuing Care, The University of Texas Health Science Center at Houston, Houston, TX 77030, United States

Joseph Varon, Department of Medicine, the University of Texas, Medical Branch at Galveston, Houston, TX 77030, United States

Joseph Varon, Critical Care Services, United Memorial Medical Center/United General Hospital, Houston, TX 77030, United States

ORCID number: Sebastian Casillas (0000-0002-7465-1768); Alan Pomerantz (0000-0001-6609-1417); Salim Surani (0000-0001-7105-4266); Joseph Varon (0000-0002-7622-9974).

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Corresponding author to: Joseph Varon, FACP, FCCP, MD, Professor, Acute and Continuing Care, The University of Texas Health Science Center at Houston, 2219 Dorrington Street, Houston, TX 77030, United States. joseph.varon@uth.tmc.edu
Telephone: +1-713-6691670

Fax: +1-713-6691671

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Abstract

Diabetic ketoacidosis (DKA) is life-threatening acute metabolic complication of diabetes mellitus (DM) that is characterized by acidosis, ketosis, and hyperglycemia, currently affecting mostly patients under 30 years of age with diabetes mellitus type 1. In both, DM and DKA, a pro-inflammatory state exists. This clinical entity occurs as a result of hyperglycemia-induced disturbances, resulting in an increased oxidative metabolism. For the latter reason, the use of vitamin C seems promising in DKA due to its antioxidant role in reducing the superoxide radicals that are consequence of the oxidative stress. This can decrease the pro-inflammatory state and avoids complications. Vitamin C, or also known as ascorbic acid, has been widely used in several illnesses, such as common cold, tissue healing, fertility, atherosclerosis, cancer prevention, immunity restoration, neuro-degenerative disease and also has been suggested to decrease the risk of DM, and this reason is giving place to believe that vitamin C can have an important role in treating diabetic complications such as DKA. In order to counteract these oxidative disturbances in DKA patients, we analyzed the current data regarding vitamin C and evaluate its role in any type treatment of this complication in the near future.

Key words: Vitamin C; Diabetes complications; Ascorbic acid; Diabetic ketoacidosis; Diabetes mellitus

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Core tip: The use of vitamin C in diabetic ketoacidosis (DKA) has remained controversial due to insufficient clinical data. The lack of concrete evidence, and no randomized controlled trials available on the use of vitamin C for DKA has caused significant controversies and debate. Some preliminary data, however, has shown a decrease in lipid peroxidation and limitation of endothelial damage. There is a significant need for a large randomized clinical trial to evaluate the role of vitamin C in patients with diabetes mellitus and specifically in those with DKA.

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INTRODUCTION

Diabetes mellitus (DM) continues to present a global challenge, with a large number of individuals being diagnosed daily around the world. It is estimated that the number of patients with DM in the world will be 366 million, or approximately 4.4% of the population by the year 2030^[1]. A life-threatening complication of DM is diabetic ketoacidosis (DKA), which is an acute metabolic complication marked by acidosis, ketosis, and hyperglycemia. It results from lack of insulin, or insulin resistance along with increased levels of cortisol, glucagon, catecholamine and growth hormone. In addition, this clinical entity may be precipitated by an inadequate insulin administration, infection or other comorbidities (such as acute myocardial infarction, hyperthyroidism, stress)^[2].

In the United States, most patients with DKA (54%-76%) are less than 30 years of age and have type 1 DM, with a mortality rate of less than 1% in hospitalized patients^[3]. In these critically ill patients, an increase in the oxidative metabolism is commonly seen^[4].

Ascorbic acid, most commonly known as vitamin C, is a water-soluble antioxidant, which has a role in scavenging superoxide radicals, and has been reported to inhibit low-density lipoprotein oxidation and stabilize the endothelium^[4,5]. Vitamin C is essential for the normal physiological function of the body by playing a role in the synthesis and metabolism of tyrosine, tryptophan and folic acid, in addition to hydroxylation of proline, glycine and catecholamine. This vitamin also helps in lowering the cholesterol level by conversion of cholesterol into bile acid^[6,7]. Vitamin C has also been widely used in the treatment of common cold, tissue healing, fertility, atherosclerosis, cancer prevention, immunity restoration, and neurodegenerative disease and

has been suggested to decrease the risk of developing DM^[7]. Furthermore, vitamin C is known to participate in the regeneration of antioxidants molecules such as tocopherol, glutathione, carotenes and urate^[8].

DISCUSSION

Diabetes is characterized by a pro-inflammatory state, which leads to oxidative stress that results in the production of free radicals^[9]. This has been studied in the context of DKA. For example, Lee *et al*^[4] studied the degree of oxidative stress by determining the levels of fatty acids in six patients before, during and after DKA, as well as, the levels of vitamin A, C and E during these periods. In this study, lipid peroxidation was noted 24 to 72 h after correction of DKA; In addition, the levels of vitamin C and E were also decreased 24 to 72 h post correction of DKA. These authors suggested that vitamin C and E may play and important role in the presence of oxidative stress in DKA^[4].

Recently, vitamin C has been shown to be beneficial in-patient with septic shock, opening a new era of interest in the role of vitamin C on many other diseases. There are several studies that have clearly documented vitamin C deficiency among patients who are critically ill with sepsis and septic shock^[10-12]. To our knowledge, no randomized clinical trial analyzing the role of vitamin C in DM complications, such as DKA, is being done. Prior studies have shown that vitamin C ingestion interferes with testing devices that monitor glucose and ketones, giving false-positive results^[13].

Cerioti *et al*^[14] showed that vitamin C exhibited falsely elevated readings for glucose and beta-hydroxybutyrate in hospitalized patients. Moreover, the use of vitamin C in diabetic patients has remained questionable due to a prior study performed by Beckman *et al*^[15] showing that oral intake of vitamin C achieved a low concentration of plasma level, being unlikely to scavenge extracellular superoxide anion.

CONCLUSION

The use of vitamin C in DKA has remained controversial due to insufficient data collected in recent years. For the latter reason, it has not been applied in the clinical field. We believe that based on the data mentioned above vitamin C supplementation may have a role in patients with DKA. A large randomized controlled clinical trial aimed to identify if vitamin C supplementation in patients with DKA modifies their outcome is needed.

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