

Original article

Subject: Dermatology

High prevalence of ascorbate deficiency in patients with *Pemphigus vulgaris*.

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ABSTRACT

Background

Proper intake of ascorbate is essential for human health since we cannot produce it. Ascorbate requirements increase in chronic diseases and during stress. *Pemphigus vulgaris* (PV), an autoimmune blistering disease, is characterized by symptoms that clinically resemble scurvy, although ascorbate levels have not been determined in these patients.

Aim

To determine ascorbate levels in patients with *Pemphigus vulgaris* and to correlate with clinical severity.

Methods

We measured the serum levels of ascorbate in patients with PV in newly diagnosed and/or during relapse. We considered ascorbate insufficiency at levels between 2-4 mg/L and deficiency at levels <2 mg/L. Disease severity (PDAI) was determined. Healthy subjects matched by age and gender with cases were selected.

Results

Ascorbate levels were markedly decreased compared to that observed in the control group. Ascorbate levels were negatively correlated with disease severity.

Conclusions

In our study, we remarked that ascorbate levels were markedly reduced in patients with PV, compared with healthy subjects.

Key Messages:

Ascorbate is essential for the human health.

Ascorbate deficiency can be seen in chronic diseases.

PV is a disease where low levels of ascorbate can be observed.

The severity of PV correlates with low levels of ascorbate.

Introduction

Ascorbate or vitamin C is an essential nutrient for collagen synthesis, immune function, and for corticosteroids and catecholamine synthesis.[1,2] Deficiency (<2 mg/L) and insufficiency (2-4 mg/L) of serum ascorbate, occurs when ascorbate reserves

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are drained, leading to clinical scurvy (fatigue, hyperkeratosis, psychological distress, hemorrhages, gingivitis and immune disorders).[3] Ascorbate deficiency in autoimmune diseases has not been completely described, however, it has been found to be important for normal immune functioning. We have observed that patients with *Pemphigus vulgaris* (PV) develop severe mucositis with frequent gingival bleeding, and most have significant periodontal disease;[4] additionally, these patients have hypoalbuminemia, which is also observed in patients with low ascorbate levels.[5] Therefore, we decided to evaluate serum levels of ascorbate in these patients.

Methods

Newly diagnosed or relapse PV patients not taking corticosteroids or vitamin supplements or vitamin C at least 2 months before the study and signed informed consent were included. A 5ml venous blood sample was obtained for serum ascorbate levels. The sample was collected in EDTA tubes. In 2 hr of collection, the sample was centrifuged at 1500 revolutions/minute and plasma was deproteinized. The supernatant was stored in cryotubes at $<-15^{\circ}\text{C}$. The analysis was performed with the chromatographic method with normal range of 4-14mg/L.[6] The same procedure was performed in the control group, matched by age and gender. The patients and controls having history of smoking, alcoholism and/or diseases which alters serum vitamin C concentration such as cancer were excluded.

Statistical analysis

The results were reported in medians, interquartile ranges. Comparison between medians in both groups was performed with Mann Whitney test. Pearson's correlation test was used to determine association between numerical variables. P values were considered significant with values $<.05$. Statistical analysis was performed using SPSS version 23 (Chicago, III).

Results

We investigated the serum levels of ascorbate in patients with PV and healthy subjects. Table 1 summarizes the characteristics of the sample of 40 patients with PV and controls. Ascorbate levels were found markedly decreased (1.27 mg/L, IQR 0.33-5.45). In the control group, decreased levels of ascorbate (3.35 mg/L, IQR 1.5-8.22, $P=.001$) were also observed (Fig 1).

Table 1. Characteristics of the patients with PV and controls.

Variable	Cases (n= 40)	Controls (n= 40)	P value
Age (years) \pm SD	48.7 \pm 12.2	47.6 \pm 15.3	NS
Gender, M/F (%)	26/14 (65/35)	26/14 (65/35)	NS
Ascorbate serum level, mg/L (IQR)	1.27 (0.33-5.45)	3.35 (1.5-8.22)	.001
Ascorbate insufficiency (<4mg/L)	35 (87.5)	6 (15)	.001
Ascorbate deficiency (<2mg/L)	30 (75)	2 (5)	.001
Disease severity (PDAI)	32.3 \pm 25.43	----	----
Serum albumin (g/L)	1.22 (0.27-3.15)	3.05 (1.8-4.3)	.001

SD= Standard deviation; M/F= Male/Female; IQR= Interquartile range.

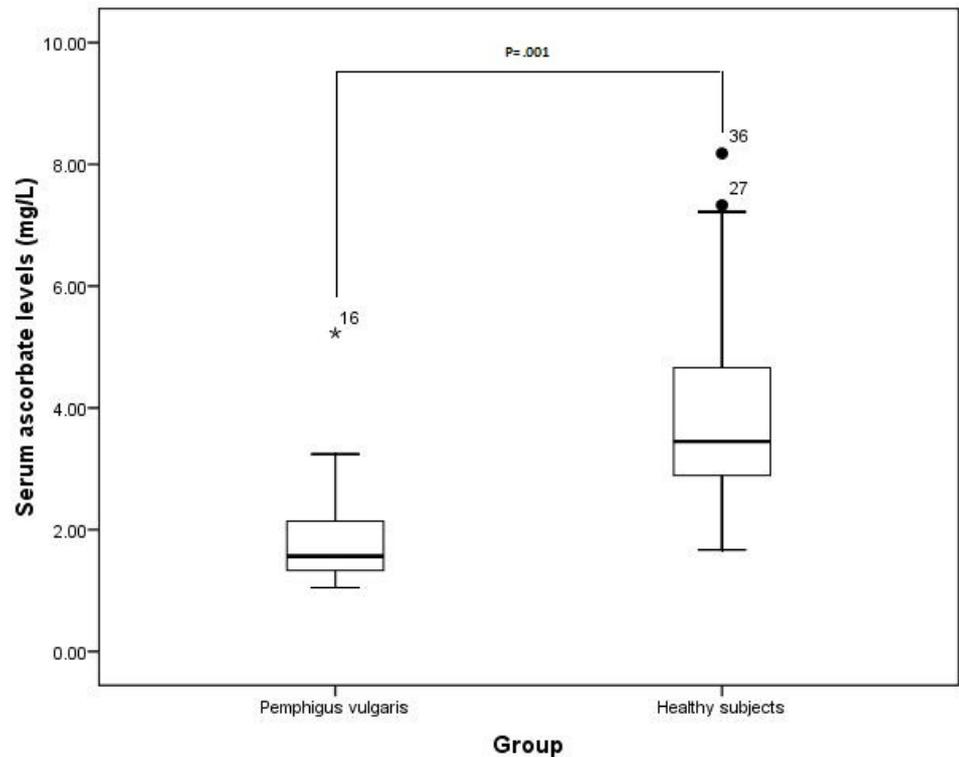


Figure 1: Ascorbate levels on patients with pemphigus vulgaris and healthy subjects.

Ascorbate levels correlated with serum albumin levels, both in patients with PV, as in healthy subjects. A low negative correlation was observed, although significant between levels of ascorbate and disease severity, however, the most important difference was observed correlating the levels of albumin and ascorbate levels ($R=-0.37$; $P=.03$ versus $R=0.476$, $P=.01$, respectively).

Discussion

Ascorbate is one of the important and essential vitamins for human health. It is required for many physiological processes in humans. Ascorbate cannot be produced in some species included *Homo sapiens*, and thus it is necessary to obtain it from the diet or concentrated supplements. Biological effects of ascorbate include anti-oxidant, anti-atherogenic and anti-carcinogenic effects.[1,2] The risk of patients with chronic disease to develop ascorbate deficiency has been recognized for several decades, this may be due increased utilization.[6] In our study we remarked that in patients with PV, ascorbate levels were markedly reduced when compared with controls. Yousefi *et al.*,[7] observed that the levels of ascorbate in patients with PV were similar to the controls, although with a much lower sample than in our study, which could lead to partial conclusions, in our study we found a clear difference in ascorbate levels between patients with PV and control.

It is an important fact that PV has pathologically low serum levels of ascorbate. It is not only the biochemical stresses of the autoimmune disease which may low the ascorbate levels, but also the abnormal activity of white blood cells which scavenge and remove ascorbate from blood. The white blood cells, mainly B-cells, selectively absorb up to 40 times ascorbate from the blood serum than red cells, decreasing its levels and made it unavailable to the tissues.[2,8]

Our study has some limitations; no mucocutaneous signs of scurvy deficiency were evaluated; however, the skin lesions of PV could mask the clinical data from scurvy, while mucosal lesions of scurvy as gums edema and gingival bleeding are often seen in patients with PV.[9] Anemia is described in over 75% of patients with scurvy,[10] often because of blood loss from tissues, with folate and iron deficiency, gastrointestinal bleeding and intravascular hemolysis; PV patients also develop anemia because of blood loss through the skin and gastrointestinal tract as well as for nutritional deficiencies related to pain due to severe mucositis that difficulty the proper feeding.

On the basis of our findings, the increased prevalence of oxidative stress in PV patients, the antioxidant and immunoregulatory effect of vitamin C, more studies of this topic are needed, and thus determine if vitamin C supplement can prevent PV onset/relapse and improve outcome.

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None declared

Declaration

The author declares that this contribution is original and is not published elsewhere in part or in whole, elsewhere.

Conflict of Interest

The authors declare that no conflict of interest exists.

Author Contributions

Both authors contributes equally to be part of the credits of the study.

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