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The current condition of the paper is fully ok and need no further edit for the publications. The editor is really pleased to see this kind of paper and the research applications. In order to proceed for publication, kindly send the Application process charge of the publication within 7 days and submit the completed copyright Agreement paper into your Author Dashboard or through the mail, you can submit it as soon as your payment is done.

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ORAL GLUTATHIONE MONOTHERAPY IN MILD to MODERATE ACNE VULGARIS

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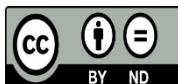


Keywords:

acne vulgaris, oxidative stress, antioxidant, glutathione.

ABSTRACT

Acne vulgaris (AV) is one of the most common chronic skin diseases with unknown but has four main pathogenesis factors. In recent years, researchers have begun to look at the role of oxidative stress in the pathophysiology of acne. Several studies have shown an increase in oxidative stress in the skin and systemic conditions found in acne patients. Glutathione is known as the "mother of antioxidants" due to its benefits such as to regulate the immune response system, repair organs and skin, and stimulate the production of other antioxidants. Patients with AV treated with oral glutathione would probably improve their acne condition clinically. Three cases of female patients aged 19 and 20 years with mild to moderate acne vulgaris were administered single therapy of 500mg glutathione taken orally for four weeks to see if there is clinical improvement of their acne vulgaris condition. All three patients came to Dermatology-Venereology Department in Prof. RD Kandou Hospital, Manado Indonesia, in different times. Three female patients, one patient with mild severity and two patients with moderate severity of AV. All patients had no history of atopy, no drug allergic reactions, no chronic disease, were not taking routine medications, and were not being treated with any acne therapy in the last 1 month. During the consumption of this supplement, there were no significant complaints experienced by the patients. Face photographs was performed on the 1st day and on the 29th day. Oral glutathione 500mg single dose may provide a clinical improvement of mild to moderate acne vulgaris.



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1. INTRODUCTION

Acne vulgaris (AV) is one of the most common chronic skin diseases which is still a major problem in most of the population, especially in adolescents and young adults, which urges patients to find treatments to

overcome this condition. The cause of AV is still unknown, but there are four main pathogenesis factors in the process of AV, namely follicular hyperproliferation, increase of sebum secretion, colonization of *Propionibacterium acnes* (*P. acnes*), and inflammation and immune response [1].

In recent years, researchers have begun to look at the role of oxidative stress in the pathophysiology of acne. Several studies have shown an increase in oxidative stress in the skin and systemic conditions found in acne patients. Recent research, the pathogenesis of AV has emphasized the importance of oxidative stress which affects the work and defense mechanisms of antioxidants. Found a higher serum level of malondialdehyde and xanthine oxidase in acne patients compare to controls proposing that oxidative damage may play a role in the pathogenesis of acne [2]. In their study of measuring serum level of glutathione in acne patients found highly significant result compared to healthy volunteer clearly suggests the existence of oxidative stress in patients with acne vulgaris and that condition along with inflammation play a critical role in acne pathogenesis [3].

Oxidative stress condition has the reactive oxygen species known with oxidants. Since it is considered as part of AV pathogenesis, the use of antioxidant to treat AV could be a successful option. Glutathione is known as the "mother of antioxidants" due to its benefits, namely as a producer and regulator of the immune response system, protect and repair cell damage, toxin metabolism, carcinogens, xenobiotic, detoxification, repair organs and skin, and stimulate the production of other antioxidants [4]. Glutathione utility has been known as an anti hyperpigmentation therapy and proven to increase skin condition [5], [6]. Several studies have shown a low level of glutathione in acne vulgaris patients which proves that decreasing glutathione contributes to the development of acne vulgaris. Hence, glutathione could be used to treat AV.

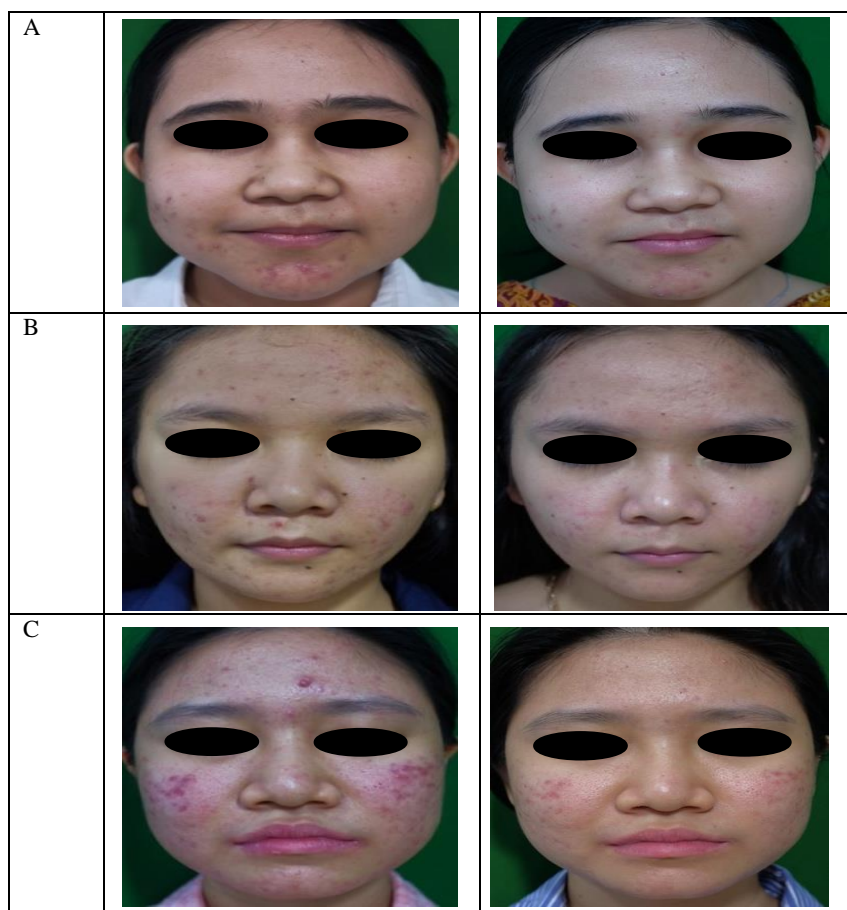
2. Case Reports

The following were 3 cases of female patients with mild to moderate acne vulgaris who were administered single therapy of 500mg glutathione taken orally for four weeks to see if there is clinical improvement of their acne vulgaris condition. All three patients came to Dermatology-Venereology Department in Prof. RD Kandou Hospital, Manado Indonesia, in different times.

Three female patients aged 19 and 20 years, one patient with mild severity and two patients with moderate severity of AV. The severity of AV was assessed through Investigator Global Assessment (IGA) criteria [7]. All patients had no history of atopy, no drug allergic reactions, no chronic disease, were not taking routine medications, and were not being treated for acne in the last 1 month.

The patients were administered a single therapy of 500mg oral glutathione for 4 weeks. During the consumption of this supplement, there were no significant complaints experienced by the patients. Facial documentation was performed on the 1st day before the patients took oral glutathione, on the 15th day after taking oral glutathione for 14 days, and on the 29th day after taking oral glutathione for 28 days.

Patient	Day 1	Day 29
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All patients whose AV condition was at grade 2 (mild severity) in patient A and grade 3 (moderate severity) in patient B and C experienced clinical improvement after consuming 500 mg of oral glutathione for 4 weeks. Based on the IGA score assessment, patient A experienced clinical improvement from score 2 to score 1 on day 29, and patient B and C experienced clinical improvement from score 3 to score 2 on day 29.

These three patients were not given any other therapy to treat acne other than monotherapy of 500mg oral glutathione for 4 weeks, as the purpose of this treatment was to see whether clinical improvement of acne vulgaris condition could be achieved solely from oral glutathione consumption, although acne vulgaris involves several factors of pathological mechanisms that require combination of therapy. It turned out that all of the patients experienced clinical improvement as assessed by the IGA.

3. Discussion

Acne vulgaris is a multifactorial disease in which there are several pathologic mechanisms involved that yield several clinical degrees. Treatment of acne requires treatment that includes all its pathological aspects. Several recent studies have focused on the effect of reactive oxygen species that cause oxidative stress conditions on the tissues that can trigger inflammatory reactions and thus emerges acne. Glutathione could give protective effect against this products of oxidative stress which is known as reactive oxygen species. In these three cases, 500mg of oral glutathione monotherapy was administered to see the clinical response of patients with mild to moderate acne vulgaris condition. There was a clinical improvement after 4 weeks treatment in all patients. This suggests that oral glutathione may have a role in treating acne condition since no other acne medicines were given. Glutathione monotherapy probably overcome oxidative stress, the condition recently established as one of the mechanisms for pathogenesis of acne.

Several studies have shown that oxidative stress plays a role in the pathogenesis and progression of acne vulgaris. Glutathione has the property of antioxidants which prevents cell damage caused by reactive oxygen species such as free radicals and peroxides.

A study by found that the endogenous antioxidant glutathione is sensitive to the squalene monohydroperoxide (Sq-OOH). It could be used to protect tissues and cells from the oxidative stress caused by Sq-OOH [8]. Perceived at the quantity of glutathione in the stratum corneum of acne vulgaris patients compared to healthy patients. Glutathione levels were found to be very low in patients with acne vulgaris. This suggests that the systemic glutathione level decreases in patients with acne vulgaris [9]. Reported that levels of glutathione peroxidase, one of the body's antioxidative peroxidase enzymes, decreased in acne vulgaris patients [10]. Also reported that the activity of the enzyme superoxide dismutase, which is also an antioxidative enzyme in the body, decreased in papulopustular acne [11].

In acne pathogenesis, there are several mechanisms that can occur in all four mechanisms that lead to the formation of reactive oxygen species. A study by explained that *P. acnes* bacteria causes the release of several chemotactic factors that increase the accumulation of neutrophils, causing follicular epithelial damage after the release of several inflammatory factors such as lysosomal enzymes as a result of the phagocytosis process. The reactive oxygen species are then released by active neutrophils in the inflammatory tissue. These oxidants attack lipid membranes and cause chemical damage to all surface molecules including normal tissue [12]. Stated that the burden of oxidative stress can also be a contributing factor to the development of acne. It can trigger the production of lipid peroxidation, which helps in driving the acne process. The environment that promotes the growth of *P. acnes* is created by the oxidation of sebum. This is also known to play a leading role in the development of acne [13]. Statement by Bowe and Logan in their review on lipid peroxidation theory, emerging studies have shown that patients with acne are under increased cutaneous and systemic oxidative stress. Indeed, there are indications that lipid peroxidation itself is a match that lights an inflammatory cascade in acne [14]. Evaluated the serum of 50 patients with acne vulgaris. Their findings support an association between oxidative/nitrosative stress and acne. Biomarkers of oxidative/nitrosative stress may be useful in evaluating the progression of acne and in elucidating the mechanisms of disease pathogenesis [15].

Based on some of these studies, it is possible that a decrease in the amount of antioxidants and a decrease in antioxidative ability in the body due to the low quantity of antioxidants plays an important role in the pathogenesis of acne vulgaris, hence the administration of antioxidants such as glutathione can help the healing process or improve clinical complaints of acne vulgaris.

4. Summary

This is the first report of mild-moderate acne vulgaris using monotherapy of 500mg oral glutathione with clinical improvement clearly seen in all 3 patients with mild to moderate acne vulgaris. It is necessary to conduct further study on the usage of oral antioxidant glutathione in patients with acne vulgaris to assess in more detail about how the effect of oral glutathione on the clinical improvement of acne vulgaris.

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