The Comparison Effects of Autologous Serum and Autologous Serum with Doxycicline Peak in the Blood on Treatment for Acne Vulgaris

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Muhlis Yunus MD[1] Muh. Nasrum Massi MD,PhD[2], Anis Irawan Anwar MD,PhD[1], Khairuddin Djawad MD,PhD[1], Siswanto Wahab MD,PhD[1], Rahmawati Minhajat MD,PhD[3], Uleng Bahrun MD,PhD[4], Ilhamjaya Patellongi MD,PhD[5], Gemini Alam PharmD, Ph.D[6], Ni Nyoman Sri Budayanti MD,PhD[7]

[1]Dermatology and Venereology Department, Faculty of Medicine, Hasanuddin University, Makassar. Indonesia
[2]Clinical Microbiology Department, Faculty of Medicine, Hasanuddin University, Makassar. Indonesia
[3]Internal Medicine Department, Faculty of Medicine, Hasanuddin University, Makassar. Indonesia
[4]Clinical Pathology Department, Faculty of Medicine, Hasanuddin University, Makassar. Indonesia
[5]Physiology Department, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia
[6]Pharmacy Department, Faculty of Pharmacy, Hasanuddin University, Makassar. Indonesia
[7]Clinical Microbiology Department, Faculty of Medicine, Udayana University, Denpasar, Bali. Indonesia

Abstract

Introduction: Acne vulgaris is a chronic inflammatory disease that occurs with a variety of factors, both intrinsic and extrinsic. Treatment is topical, systemic or a combination of both depending on degree severity. Recently, treatment using products from human blood has been widely studied, including the field of dermatology because it has a unique composition.
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Introduction

Acne vulgaris is a chronic inflammatory disease that occurs with the multifactorial etiology. Treatment can be topical, systemic or a combination of both depending on the degree of severity.[1] Acne vulgaris is disease of the

polisebaceous unit, the sebaceous glands are found throughout of the human skin and in greater concentration on the face and scalp and absent on the palms and soles. These glands deposit sebum in the hair, and carry it to the surface along the hair shaft. Sebum provides lubrication, hydration, consists of triglycerides and free fatty acids, aliphatic hydrocarbons found in human sebum.[2]

Acne Vulgaris cause the interaction of four major pathogenic factors, hyperproliferation of sebaceous glands, hyperproliferation of keratinocytes, colonization of p.acnes and inflammation. These pathogenic factors influence each other and should not be looked at individually. Although the interaction of pathogenic factors is known etiology of the acne, certain trigger factors can worsen or cause acne to appear, for example premenstual, cosmetic use, etc. [3] The Treatment can be topical, systemic or a combination of both depending on the degree of severity. Recently, treatment using products from human blood has been widely studied, including in the field of dermatology because of its unique composition.

Objective

The therapeutic modalities used to treat acne vulgaris are topical therapy and systemic therapy. Topical therapy includes the use of topical antibiotics, vitamin A derivatives, as well as systemic therapy such as oral antibiotics, vitamin A derivatives and the use of hormonal drugs. Based on the pathomechanism of acne vulgaris, the current therapeutic modality can be given topical, systemic or a combination of both.[5] However, in certain cases these drug preparations cannot be administered, for example, allergies,

causing side effects.[6] Researchers want to see the effect of autologous serum doxycicline in autologous serum in the treatment for acne vulgaris.

Material and Methode

Clinical trials Pre and post treatment using autologous serum in 2 treatment groups, each group totaly 10 people suffering from acne vulgaris based on the type of lesion and photography. The method of taking autologous serum is by taking 50 cc of blood from the vein and then inserting it into a tube without a coagulant which is then carried out by the centrifuge process for 10-15 minutes at a speed of 3000 rpm. The clear blood will be separated by the blood clot that has formed. While the other group was given doxycicline oral 200 mg single dose after 2 hours, 50 cc of venous blood was taken and the same centifuge process was performed. Serum obtained from the centrifuge process is put into a small bottle containing 1-2 cc for one application. The serum is stored in a refrigerator at 0 degrees and is applied every night to areas of the face that have acne lesions for 28 days. Before being applied, patients are asked to wash their face without using soap and not using other cosmetic products. To see the changes that occur, the calculation of lesions (comedos, papules, pustules) is carried out using a comparison of photography before and after application.

Result

In the autologous serum application group after 28 days gave improvement of comedones lesions, when compared to before and after application there was a decrease in lesions by 15%, papules 8%, pustules

5%. In the table below, you can see the results of the Wilcoxon test for the number of comedos, papules, pustules between the results of day-1 and day-28 observations. This shows that there is a significant decrease (p <0.05).

Tabel 1. Group Autologous Serum Application

Variabel	D1 – D 28	
	Mean (SD)	**p***
Decreased Number of Comedones (%)	60,2 (11,7 %)	<0,001
Decreased Number of Papules (%)	54,4 (15,0 %)	<0.001
Decreased Number of Pustules (%)	78,9 (15,4 %)	<0,001

Superscripts Different on the same line showed significantly different Wilcoxon test results (p <0.05); if the same means not significantly different (p> 0.05)

Figure 1.Before and after 28 days of autologous serum application

Tabel 2. The Autologous Serum with Doxycicline Peak in The Blood Application Group

Variabel	D1 – D 28	
	Mean (SD)	p*
Decreased Number of Comedones (%)	98 (18,8 %)	<0,001
Decreased Number of Papules (%)	37(26,6 %)	<0.001
Decreased Number of Pustules (%)	18 (56,0 %)	<0,001

Superscripts Different on the same line showed significantly different Wilcoxon test results ($p < 0.05$); if the same means not significantly different ($p > 0.05$)

Figure 2. Before and after 28 days of autologous serum had been given doxycicline 100 mg oral single dose application

Discussion

In patients with acne vulgaris, hyperproliferation of keratinocytes occurs with a buildup of desquamated abnormal corneocytes along the

sebaceous follicles with lipids and monofilaments, a phenomenon that results in comedogenesis. P.acne is an anaerobic bacteria, colonizing gram-negative pathogens in sebaceous follicles. Blood draws were taken 2 hours after oral doxycycline administration, it is based on the pharmacokinetics of doxycycline, it is known that doxycycline reaches peak plasma concentrations reported 2 hours after oral administration of 200 mg. Doxycycline is an oral antibiotic drug that is very effective for inflammatory acne so it can be used as an acne therapy because it effectively inhibits the growth of P.acne and has anti-inflammatory properties. The use of oral antibiotics is generally indicated for moderate-severe inflammatory acne, resistant to previous topical therapies. Oral antibiotics such as macrolides, tetracyclines (doxycycline, minocycline and limesycline). These antibiotics are agents that inhibit the recovery of P. acnes and synthesize inflammatory mediators from P. acnes tetracyclines groups are used frequently because they are effective and cheap.[7]

Doxycycline and minocycline are preferred because of their low gastrointestinal irritation effect, and they are fat soluble, and their penetration of the polysebaceous follicles is more efficient. In addition, lower resistance to P. acnes was reported compared to the macrolides group. Androgen hormones increase sebum production and follicular keratosis which are the main keys of acne vulgaris etiology.[8] Androgen hormones stimulate increased production and secretion of sebum. Increased sebum production is directly related to the incidence of severe acne lesions. The hormone estrogen has a mechanism of opposition to androgens in the sebaceous glands. One of the ingredients in autologous serum is the hormone estrogen. The most important

natural estrogens are estradiol, estrone, and estriol. Biologically, estradiol is the most active. Oral contraceptives used to treat acne vulgaris contain estradiol with a mechanism of action of reducing 5-α reductase activity, reducing sebaceous gland activity. High levels of estradiol have been shown to be used as a treatment for acne vulgaris. [9]

Some of the unique ingredients of serum include growth factor, platelet rich plasma (PRP), vitamin A, estogen hormon and many more. As we know that topical acne vulgaris treatment uses topical vitamin A derivatives (tretinoin) which works as an anti-inflammatory, suppresses sebum production, increases skin turnover.[10] In this study measuring serum vitamin A and Estadiol content using the ELISA (Enzyme Linked Immunosorbent Assay) test found serum vitamin A levels between 0.16-0.72ug / dl. In this study, the higher the level of vitamin A in serum, the better the reduction in inflammatory and non-inflammatory lesions.

In this study, menstrual estradiol levels (follicular phase) were obtained levels ranging from 20.8 to 200.5 pg / mL. The concentration of estradiol levels is lowest during the menstrual phase with serum concentrations around 40 to 200pg / mL. Meanwhile, the level of estradiol during preovulation was around 250 to 500 pg / mL, so it was concluded that the estrogen levels in the menstrual phase were lower than that of the preovulatory phase. Low estrogen levels are associated with the severity of acne. Androgen hormone increases sebum production, so that the sebum level in patients with acne vulgaris is higher than in normal people.[9,10] There is a relationship between sebum excretion and the severity of acne vulgaris because the sebum level in patients with severe acne vulgaris is found to be higher. The hormone

estradiol can inhibit sebum production so that it can reduce sebum levels. The use of oral contraceptives to treat acne vulgaris contains estradiol.[11]

Platelet Rich Plasma works through alpha-granule degranulation in platelets containing growth factors. It is ideal for collecting blood PRP in a tube containing sodium citrate as an anticoagulant to keep growth factor active. Biologically active cellular components such as preserved growth factors, when the platelets are held in an inactive state so that premature degranulation does not occur, therefore the cellular components are held in a container that can protect the platelets. After platelet activation, the granules then fuse into the cell membrane by a degranulation process, activating growth factors, which bind to target cell transmembrane receptors, such as mesenchymal stem cells, fibroblasts, endothelial cells, and epidermal cells. This binding activates intracellular signaling proteins that express gene sequences resulting in cell proliferation, collagen synthesis, cell extracellular formation, and many other pathways to promote healing and repair processes. Platelets are damaged with degraded cellular components or are unable to induce this response. [12,13]

Platelet Rich Plasma can be used for skin rejuvenation because it can activate growth factors that result in cell proliferation, collagen synthesis which can lead to healing and repair processes. In addition, PRP is reported to be associated with collagen expression, hyaluronic acid production, and fibroblast proliferation, which are the main mechanisms of skin rejuvenation. The mechanism may be Insulin-like growth factor, Epiderma growth factor which binds to the outer surface of the fibroblast cell membrane to activate signal proteins to realize extracellular matrix synthesis and collagen

repackaging. Transforming Growth Factor b1 (TGF-b1) and PDGF were able to increase hyaluronic acid synthesis by increasing regulation of hyaluronic synthase expression. Hyaluronic acid can draw water into the space between cells and retain intracellular water so as to achieve skin elasticity. [14,15]

The improvement of acne lesions in this study was thought to be due to the involvement of growth factors, platelet rich plasma, vitamin A, estradiol. Vitamin A works as an anti-inflammatory, reduces sebum production, and increases skin turnover, estradiol works to inhibit androgens so that it can control reducing sebum production, growth factor works as an anti-inflammatory. Based on these contents it is assumed that in the autologous serum that works together according to the pathegenesis of acne vulgaris.

Conclusion

Autologous serum has many components including growth factors, platelet rich plasma, vitamin A, and estradiol which work together to inhibit the pathomechanism of acne vulgaris. the addition of doxycicline 100 mg orally as a single dose provided an improvement in the manifestation of inflammatory lesions in acne vulgaris compared to autologous serum alone but did not have a significant difference.

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