The relationship of testosterone and cortisol level with acne vulgaris in the adolescent men

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Acne vulgaris is a common chronic skin disease that occurs when hair follicles are clogged with dead skin cells and skin oil from forming blackheads, papules, pustules, nodules, and cysts. Approximately 85% of people have acne at some point in the course of their lifetime with the highest incidence is in the age of 14-19 years. The disease causes significant morbidity and affects patients physically and psychologically in terms of scarring, depression, anxiety and low self esteem. Genetic, hormonal, and psychological stress plays an important role in pathogenesis of acne vulgaris. Follicular hyperkatinization, sebum production, presence of Propionibacterium acnes, inflammatory mediators, and androgens have been identified as a major component of acne. To determine the association of the blood testosterone and cortisol levels with the occurrence of acne vulgaris in adolescent men, we conducted an observational study with case control study design in 70 adolescent men in the age of 17-18 year old. They were divided into two groups of acne and control groups, 35 each. Blood samples were obtained from the cubital vein at 8:00 am to measure testosterone and cortisol hormones by using ELISA method. The study was approved by Research Ethics Committee of Medical Faculty Andalas University. The results showed that high testosterone levels were present in 40% of the acne group and 60% of the control group. There was no significant correlation between testosterone levels and acne vulgaris ($p > 0.05$), but it seem that at the low levels of testosterone tended to have acne vulgaris 0.44 times greater than the low levels (OR <1). The High level of cortisol were present in 54.3% of the acne group and 51.4% of the control group. There were no significant different, but the tendency for acne seem 1.12 times greater at high level of cortisol than the low level (OR> 1). From this study, we conclude that there were a tendency that acne vulgaris occurs in groups with low level of testosterone and high level of cortisol

Key words: acne vulgaris, cortisol, testosterone

INTRODUCTION

Acne vulgaris is a common chronic inflammatory disease of the pilosebaceous unit that comprising the hair follicle, hair shaft and sebaceous gland, the density of which is greatest on the face and scalp and least on the extremities (Ewadh et al,2011; Suh and Kwo , 2015). Acne is sufficiently common that it often has been termed physiologic and become a disorder predominantly of late childhood and adolescence. Most cases occur between the ages of 14 and 19 years despite the fact that it may persist into, recur, or begin during adulthood. Mild degrees of acne are frequently seen at birth, probably resulting from follicular stimulation by adrenal androgens, and may continue into the neonatal period (Bergfeld,2004). Prevalence of acne reached its peak during the middle teenage to late teenage period, with affected more than 85% of adolescents, and then become decreases. However, acne may persist through the third decade or even later, particularly in women (Evanse et al,2005).

Before early sexual maturation, referred as adrenarche that occurs at around 10-12 years of age, the adrenal gland starts to produce a precursor for testosterone. The principal physical consequences are androgen effects, especially pubic hair and the change of sweat composition that produces adult body odor, increased skin oiliness, and mild acne may occur. Pilosebaceous units consist of soft, fine, unpigmented vellus hairs and small sebaceous glands. At the time of adrenarche, androgen levels increase dramatically especially in males, mediate the development of secondary sexual characteristics. In sebaceous areas, such as the face, pilosebaceous units become sebaceous follicles while the hair remains vellus (Miller,2009; Wei et al,2014; Utriainen et al, 2015).

Androgens stimulate the enlargement of the sebaceous glands and increase the production of sebum. This androgen-dependent secretion of sebum is mediated by potent androgens such as testosterone and Dihydrotestosterone (DHT). Sebum and abnormal keratinase materials that accumulate in microcomedo, causing increased pressure. This increasing of pressure and recruitment of inflammatory mediators, cause rupture of microcomedo and release keratinogen and immunogenic sebum, that stimulate the inflammatory response (Ewadh et al,2011; Balachandrudu et al,2015). This microenvirontment allows the proliferation of Propionibacterium acnes, the normal flora of the follicle to activate complement, resulting an increase of pro-inflammatory cytokines, including chemoattractants for neutrophil which may cause suppurative pustules or inflamed

papules, nodules, or cysts. If inflammation is followed by tissue damage, post-inflammatory scarring will develop and it lead to hyperpigmentation. Although the course of acne may be self-limiting, the sequelae can be lifelong with pitted or hypertrophic scar formation, that may causes significant morbidity and affects the patients on physically and psychologically such as depression, anxiety and low self-esteem (Bergfeld , 2004; Bellew et al,2011; Elsaie,2016).

The cause of acne vulgaris is multifactorial and includes pathophysiologic mechanisms such as altered sebaceous gland activity associated with hyperseborrhea, follicular hyperkeratinization, bacterial insult, induction of inflammation cascades, genetics, and dysregulation of the hormone microenvironment (Zouboulis et al.,2002). External factors occasionally contribute to acne, including mechanical trauma, cosmetics, topical corticosteroids, and oral medications such as corticosteroids, lithium, iodides, some antiepileptics. Endocrine disorders resulting in hyperandrogenism may also predispose patients to developing acne. Acne can also be triggered or worsened by ultraviolet radiation and other environmental factors, dietary factors, smoking, stress and the modern lifestyle. (Evans et al.,2005; Albuquerque et al.,2014).

Acne vulgaris typically affects the areas of skin with the densest population of sebaceous follicles, therefore acne lesions usually occur on the face,neck, back, chest, and shoulders. Development of acne vulgaris involves many processes, which the initial step in the development of acne is the formation of the microcomedo. Comedogenesis occurs when abnormally desquamated corneocytes accumulate in the sebaceous follicle and form a keratinous plug. When the keratinous plug enlarges below a very small follicular pore at the skin surface, it becomes visible as a closed comedone (whitehead). An open comedone (blackhead) occurs if the follicular pore dilates (Kubba et al.,2009; Cunliffe et al., 2015).

Skin lesions of acne vulgaris can be described as inflammatory or non-inflammatory, with local symptoms may include pain, tenderness, or erythema. There is no single uniform, standardized, and reproducible grading system for severity of acne. Acne is commonly classified by type such as comedonal, papular, pustular, nodulocystic, and/or severity such as mild, moderate, moderately severe and very severe. Severe acne, characterized by multiple comedones, without the presence of systemic symptoms, is known as acne conglobata. This severe form of acne frequently heals with disfiguring scars. Severe acne with associated systemic signs and symptoms, is referred to as acne fulminans. Acne fulminans is a rare acne subtype that presents with variable systemic manifestations, including fever, arthralgias, myalgias, hepatosplenomegaly, and osteolytic bone lesions (Cunliffe et al.,200).

MATERIALS AND METHODS

Seventy adolescent males in the age of 17-18 years old were collected from outpatients of Dermato Venereology Department in Arifin Ahmad Hospital. There were divided into two groups, the first group includes 35 patients with acne vulgaris and the second group include 35 patients without acne vulgaris as control group. Those patients were not suffering from serious systemic illness. The severity of acne through the combined assessment of the types of acne lesions (comedones, papules, pustules, nodules and cystic) and their anatomic location (forehead, cheeks, nose, chin, chest, and back). Blood was collected in the morning to measure cortisol and testosterone levels. Testosterone level was measured by human testosterone enzyme immunoassay ELISA test kit, as well cortisol, was measured by human cortisol enzyme immunoassay ELISA test kit. The data of this case control study were analyzed by using Chi-square, Odds ratio and logistic regression to determine the dominant factor associated with the occurrence of acne vulgaris. The study was approved by Research Ethics Committee of Medical Faculty Andalas University.

RESULTS

In this study, our data shows that the adolescent men of the group with acne vulgaris and the control group were a senior high school students and college students, in the aged between 17-18 years, and have normal body mass index (BMI). Clinical features of acne vulgaris in acne vulgaris group were at most located on the face (forehead and cheeks), and in the form of papulopustula type (94.29%), while in the form of comedones type were 5.71%, and no subject with nodulocystic, as shown in table 1.

Table 1: Characteristic of Subject

	Acne		Control		Total	
	No.	%	No.	%	No.	%
Age (years)						
- 17	18	51,43	15	42;86	33	46,14
- 18	17	48,57	20	57,14	37	52,86
Body weight (Kg)						
- < 58	18	51,43	21	60,00	39	44,39
- ≥58 kg	17	48,57	14	40,00	31	55,71
Type of Acne						
- Comedones	2	5,71	0	0	2	2,86
- Papulo-pustula	33	94,29	0	0	33	46,14
- Nodulocistic	0	0	0	0	0	0

The levels of cortisol in the group with acne vulgaris were 53.01 ± 8.02, there were no significantly different with the control group (51.98 ± 11.83) (p> 0.05). Similarly, testosterone levels, in which the group with acne vulgaris (16.19 ± 3.12) were no significantly different with the control group (16.54 ± 4.54) (p> 0.05) as shown in Table 2. There were also no relationship between cortisol and testosterone level with acne vulgaris.

Table 2: The mean of cortisol and testosterone levels in group with acne vulgaris and control group

	n	Mean±SD	p
Cortisol			
- Acne	35	53,01 ±8,02	0,67
- Control	35	51,98 ±11,83	
Testosterone			
- Acne	35	16,19 ±3,12	0,71
- Control	35	16,54 ±4,54	

Table 3 shows that the number of subjects in the group with acne vulgaris who has high cortisol levels were 57.29% and those with low cortisol levels were 45.71%. While in the control group, the subjects who has high cortisol levels were 51.39% and those with low cortisol levels were 48.61%. There were no statistically significant difference between groups (p> 0.05), but it seem that the subjects with high cortisol levels have 1,12 times greater to have acne vulgaris compared with those with low cortisol (OR> 1)

Tabel 3: The number of subjects who had a high and low levels of cortisol and testosterone in the acne and control groups

	Low		High		Total	
	No	%	No	%	No	%
Cortisol						
- Acne	16	45,71	19	54,29	35	50
- Control	17	48,61	18	51,39	35	50
- Total	33	45,71	37	54,29	70	100
Testosterone						
- Acne	20	57,14	15	42,86	35	50
- Control	14	40,00	21	60,00	35	50
- Total	34	48,57	36	51,43	70	100

The group with acne vulgaris who has high testosterone level were 42,86 and low testosterone level were 57,146. While in the control group the subjects with high testosterone

levels were 60% and those with low testosterone levels were 40%. There was no statistically significant difference between groups ($p > 0.05$), but there was a tendency for protection of acne vulgaris 0,44 times greater in subjects with high testosterone levels than those with low cholesterol (OR <1).

DISCUSSION

From the data, we found that the vast majority of subject had moderate acne, and a little had mild acne vulgaris. This is because the subject of acne vulgaris group were the adolescent who came to because the acne is in need of treatment. The comparative studies obtained by Ogedegbe and Henshaw, 2014, Hanishah et al.,2009, and Agheai et al,2006, found that in hospital-based studies most cases were in moderate or severe of acne compare to mild acne vulgaris, while in population- based studies in the students, they founded more frequency of mild acne, respectively. Acne ranges from mild acne, which may not need any help from doctors, to severe acne that can form cysts and scar formation. All forms of acne may be distressing for the person, even mild acne can be distressing due to its appearance and self-esteem that it often affects the adolescence when they begin developing relationships. (Purdy,2011).

The location of acne vulgaris in this study were most on the face. This may be related to air pollution where the subject is located. Car exhaust and other noxious fumes in the urban is teeming with tiny dust particles. These particles causes blackheads, increased oil production and a build-up of dead cells, essentially creating for acne. Pollution can cause blackheads to become more visible and new blemishes to appear. Exposure of ultra violet has an additive effect with airborne pollutants and O3. UV irradiation is known to compromise the skin barrier and O3 seems to heighten this phenomenon by disturbing stratum corneum lipid constituents that are known to be critical determinants of the barrier function. UV exposure and O3 have also been found to have an additive effect on antioxidant depletion such as vitamin E and on lipid peroxidation levels that lead to additional additive effects of severity of acne vulgaris (Valacchi et al,2012). On the other hand, the interest that has recently emerged is the action of vitamin D in the skin. The pilosebaceous unit is capable of metabolizing and producing provitamin D in the skin. Furthermore, vitamin D analogs may potentially be useful in normalizing sebaceous gland physiology in patients with acne (Toossi et al,2015)

This study found that the level of serum cortisol were not statistically different between acne group in compare to control group. Cortisol known as stress hormone, because the level changes in response to psychological stress. Reactions to stress are associated with enhanced secretion of a various hormones including glucocorticoids, catecholamines, growth hormone and prolactin, the effect of which is to increase mobilization of energy sources and adapt the individual to its new circumstance. In our study the cortisol level were measured in the morning because of diurnal cycles of cortisol levels in human. The amount of cortisol present in the blood undergoes diurnal variatio in which the level peaks in the early morning around 8 am (Ranabir and Reetu,2011).

In this study we did not measure the stress level of adolescents as research subjects. Psychological stress may exacerbate acne vulgaris although it is still not known whether the perceived association between stress and acne exacerbation is due to increased sebum production. Sebum production is thought to play a major role in acne vulgaris in adolescents. Study of Yosipovitch et al, 2007 found that in adolescents, psychological stress does not appear to affect the quantity of sebum production, but its suggests a significant association between stress and severity of acne vulgaris, especially in males. Increased acne severity associated with stress may result from factors other than sebum quantity.

Testosterone belongs to a class of male sex hormones called androgens. This hormone has the effect of increasing sebum production at the base of hairs, the oily substance that protect and lubricate the skin. The production of testosterone rises during puberty, causes greasy skin because it increases and can trigger acne vulgaris by over-stimulating oil glands. In this study we found that testosterone level were no difference between acne vulgaris group with control group. The high testosterone levels were obtained in the control group found in acne vulgaris group and in control group. This indicates the presence of other factors that trigger acne vulgaris beside the high levels of testosterone. Testosterone alone doesn't cause acne vulgaris, but too much of this androgen can make acne worse. Lifestyle and personal behaviors can also be risk factors for acne development or worsening. A 'western' diet, typically rich in high glycemic load food, is considered to cause chronic hyperinsulinemia, potentially provoking a growth factor response via IGF-1 receptor, thereby potentiating hyperseborrhea and androgen signaling (Bickers et al, 2006)

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