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Research Article

EVALUATION OF THE EFFECT OF TOPICAL ATORVASTATIN SOLUTION FOR THE TREATMENT OF PAPULOPUSTULAR ACNE

EHAB M. MIKHAEL[1]* AND MAHDI Y. MOHAMMAD[2]

[1]University of Baghdad, College of pharmacy, Clinical pharmacy department, [2]Abu - Gharib hospital, Chairman of dermatology department.

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ABSTRACT

Acne is a very common human skin disease that affects individuals around the world. It clinically characterized by seborrhea, comedones, papules, pustules, nodules and, in some cases, scarring. It may be caused by increased sebum production, follicular hyperkeratinization, colonization of the pilosebaceous unit with Propionibacterium acnes and the production of inflammation. Atorvastatin is a hydroxymethyl glutaryl CoA reducatase inhibitor that decreases cholesterol and triglyceride synthesis and possesses anti inflammatory activity. This study aimed to evaluate the benefit of using atorvastatin solution in treating patients with papulopustular (inflammatory) acne. Atorvastatin solution was prepared by addition of atorvastatin powder to 1:1 solution of propylene glycol and ethanol. 15 patients with papulopustular acne were enrolled in a double blinded clinical trial and were clinically evaluated and followed up by dermatologist for 1 month. After 1 month, 71.4% of patients in atorvastatin group were showed a good improvement and 75% of patients in placebo group showed a good improvement, however, there was no any statistical difference between the effect of atorvastatin and placebo on acne improvement, and thus atorvastatin solution was no more effective than placebo for treating acne.

Keywords: Inflammatory acne, Atorvastatin.

INTRODUCTION

Acne is a very common human skin disease that affects individuals around the world [1]. It is a disease of the pilosebaceous units, clinically characterized by seborrhea, comedones, papules, pustules, nodules and, in some cases, scarring [2]. Four key factors have been identified in the etiology of acne: increased sebum production, follicular hyperkeratinization, colonization of the pilosebaceous unit with Propionibacterium acnes and the production of inflammation [3]. Sebum is a lipid rich secretion of sebaceous gland that made of a mixture of lipids mostly triglycerides [4]. Propionibacterium acnes, colonizes the pilosebaceous ducts, breaks down triglycerides releasing free fatty acids, produces substances chemotactic for inflammatory cells and induces the ductal epithelium to secrete pro-inflammatory cytokines. The inflammatory reaction is kept going by a type IV immune reaction to one or more antigens in the follicular content [5].Additionally there is an important role of matrix metalloproteinases (MMP) in pathogenesis of inflammatory acne [6].

Atorvastatin is one of statins that act by inhibiting hydroxymethyl glutaryl CoA (HMGCoA) reductase enzyme, thus interrupting the conversion of HMG-CoA to mevalonate, which is the rate limiting step in de novo cholesterol biosynthesis, so decease cholesterol and LDLc synthesis and not only cholesterol but also it has a potent effect to lower TG level [7,8]. Moreover, atorvastatin as well as other statins have many pleiotropic effects like antiinflammatory activity and decreased matrix metalloproteinase activity [8, 9]. However till now there is no any study evaluating the topical use of atorvastatin in inflammatory acne, so this study aimed to evaluate the benefit of using atorvastatin solution in treating patients with papulopustular (inflammatory) acne.

MATERIALS AND METHODS

Preparation of atorvastatin solution

Atorvastatin calcium is slightly soluble in ethanol and freely soluble in methanol [10], additionally, it has a good solubility in propylene glycol [11].

Atorvastatin solution was prepared by addition of 50 ml of propylene glycol to 1gm of atorvastatin calcium powder which purchased from (Hetero labs limited, India), the resultant mixture stirred for 1 minute, then 50ml of ethanol that were purchased from (Tiba company, Iraq) were added, then the final mixture were stirred for 5 minutes and then left to settle down for 30 minutes and then stirred for additional 1 minute to produce a clear solution of atorvastatin.

The blank vehicle or placebo solution was prepared by mixing 50 ml of propylene glycol with 50ml of ethanol.

Study design

This study was a randomized double blinded placebo controlled clinical trial conducted in out patient clinic, Baghdad, Iraq from March 2012 to September 2012.

Fifteen patients (12 Females and 3 males) with papulo-pustular acne were randomly allocated to receive either atorvastatin or blank solution in addition to their treatment with doxycycline capsule (obtained from Medochemie, Cyprus) 100 mg twice daily, plus, Adapalene gel 0.1% (obtained from Galderma Laboratories Company, Switzerland).

Sample selection

Eligible patients who were examined by dermatologist and shown to have papulopustular acne (grade 3 acne) according to James and Tisserand [12] grading system were included in this study. Pregnancy, breast feeding, poly cystic ovarian syndrome and systemic use of steroid were considered as exclusion criteria for the current study.

Clinical evaluation

Clinical evaluation of patients for the number and severity of acne was done by specialized dermatologist who was blinded to treatment at zero time (baseline) and after 1 month.

Reduction in acne severity by 75% - 99% was considered to be as good improvement whereas 50 – 75% was considered as moderate improvement and less than 50% considered as poor improvement [1].

Statistical Analysis

Chi square test used for statistical analysis in this study, using a web version of chi square calculator from the following link:

http://www.quantpsy.org/chisq/chisq.htm

RESULTS

There is no any statistical difference in demographic data between atorvastatin and placebo group as shown in (table 1).

Table 1: Demographic data of acne patients

Parameter	Atorvastatin group	Placebo group	P Value
Number of patients	7	8	0.715
Female/Male ratio	5/2	7/1	0.437
Age	22.57± 3.1	22.38± 2.88	0.9

Table 2: Response of patient to the investigated solution

Improvement	Group 1 (Atorvastatin group) N = 7	Group 2 (Placebo group) N = 8	P value
Good	5	6	0.876
Moderate	0	0	1
Poor	2	2	1

After 1 month, 71.4% of patients in atorvastatin group were showed a good improvement and 75% of patients in placebo group showed a good improvement, as shown in (table 2), however, there was no any statistical difference between the effect of atorvastatin and placebo on acne improvement.

DISCUSSION

The results of the current study showed that there was no any statistical difference between the effect of atorvastatin in comparison to placebo to improve acne features, this result in contrast with the claims of many other researchers which highlight the importance of statin for treating many inflammatory dermatological diseases such as alopecia areata, vitiligo, lichen planus, subacute cutaneous lupus erythematosus, erythema multiforme, psoriasis [13], and acne [14] in patients with polycystic ovarian syndrome by the use of statin orally for 3 consecutive months [14]. In Addition to systemic effect, topically statin ointment has an anti-inflammatory activity in both acute and chronic models of skin inflammation [15]. Moreover, W ladys law Hajduk a pharmacist who argue that statin has the ability for treating acne when used topically since statin can lower androgen level in addition to lowering serum cholesterol level [16-18]. However, most of the aforementioned trials focus on simvastatin and not atorvastatin, and since Brachet *et al* found that there is a difference in the anti inflammatory effect of different statins, whereas simvastatin was more powerful than atorvastatin [19] this may partly explain the absence of statistical significance by the use of atorvastatin in the current study.

Further limitation of the current study are the small sample size and the shorter period of follow up which was designed according to the rapid effect of concomitant therapy with Adapalene and doxycycline that usually obtained within month [20], so further studies with longer follow up periods and on larger scale are needed to confirm the obtained result from this study.

CONCLUSION

Atorvastatin was no more effective than placebo when applied topically for papulopustular acne.

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