Original Research Article

Outcome of Adapalene and Isotretinoin in the treatment of acne vulgaris

ABSTRACT

Topical application of isotretinoin and adapalene has proved effective in treating acne vulgaris. Both drugs demonstrate therapeutic advantages and less irritancy over tretinoin, the most widely used treatment for acne. The objective of this study was to compare the efficacy and tolerability of adapalene cream 0·1% and isotretinoin cream 0·05% in the treatment of acne vulgaris.*Hundred* patients were enrolled and were instructed to apply adapalene cream 0·1% (50 patients) or isotretinoin cream 0·05% (50 patients) once daily over a 6-week treatment period. Efficacy determination included non-inflammatory and inflammatory lesions count by the investigator and global evaluation of improvement. Cutaneous tolerance was assessed by determining erythema, scaling, burning and pruritus.Adapalene and isotretinoin creams were highly effective in treating acne vurgalis. However adapalene was found significantly more effective than isotretinoin. Adapalene has faster onset of action of, which reflect on patients psychologically in term of improvements, comforts and good appearance. Significantly lower skin irritation was noted with adapalene, indicating that adapalene may begin a new era of treatment with low-irritant retinoids. It seems that, adapalene treatment is a good

choice for topical treatment of acne vulgaris with less side effects and high efficacy. Adapalene should be described as first line for treatment of acne vulgaris.

INTRODUCTION

Acne is an extremely common skin disease, and thus, individuals have various beliefs and perceptions about its treatment methods. In a recent community--based study, 68% of male and 66.8% of female teenage participants were reported to have acne(1).

Although less frequently encountered than in adolescence, a significant number of adults, and 20 years of age or older, also have acne(1). In many cases, acne is regarded as a physiologic phenomenon, which is likely to regress spontaneously after adolescence. However, in some, individuals, acne persists and substantially increases the likelihood of scarring(2). Because acne is a common skin condition, it has a great impact on quality of life. Thus, a detailed understanding of its more general aspects is important(3).Numerous clinical research studies have been undertaken on its epidemiology in western countries(1,4,5).However, comparatively few have been undertaken in African and Asian populations(6,7).

Acne is usually diagnosed by the patient. The physician needs to determine if the condition is non-inflammatory (open and closed comedones), inflammatory (papules or pustules) or a mixture of both , the most common situation.Topical treatment is sufficient in most patients with acne, but systemic therapy is required

in patients who have acne nodules and cysts(4). Topical retinoids such as tretinoin, isotretinoin, or adapalene are effective in many patients with comedonal acne.

Adapalene is a topical retinoid derived from naphthoic acid with a selective effect on the epidermis. It is indicated for treatment of acne vulgaris, alone or with other antiacneic topicals. It displays comedolytic and anti-inflammatory activities.

Topical retinoids are comedolytic and anti-inflammatory. They normalize follicular hyperproliferation and hyperkeratinization. They reduce the numbers of microcomedones, comedones, and inflammatory lesions and may be used alone or in combination with other acne medications. The most commonly prescribed topical retinoids for acne vulgaris include adapalene, tazarotene, and tretinoin. These retinoids should be applied once daily to clean, dry skin, but they may need to be applied less frequently if irritation occurs[(9)]. Skin irritation with peeling and redness may" be associated with the early use of topical retinoids. Alternate-day dosing may be used if, irritation persists. Topical retinoids thin the stratum corneum, and they have been associated with sun sensitivity. So patients should be Instructed about sun protection[(8)]. Retinoids are used in the treatment of many diverse diseases and are effective in the treatment of a number of dermatological conditions such as inflammatory skin disorders, skin cancers, disorders of increased cell turnover as psoriasis, and photoaging[(9)].

Adapalene is a third-generation topical retinoid primarily used in the treatment of mild-moderate acne and is also used (off-label) to treat keratosis pilaris as well as other skin conditions.[10]

Adapalene has been shown to enhance the efficacy of topical clindamycin, although adverse effects are also increased. [11] Application of adapalene gel to the skin 3–5 minutes before application of clindamycin enhances penetration of clindamycin into the skin, which may enhance the overall efficacy of the treatment as compared to clindamycin alone. [12]

Unlike tretinoin (Retin-A), adapalene has also been shown to retain its efficacy when applied at the same time as benzoyl_peroxide due to its more stable chemical structure.[89] Adapalene in small concentrations is a moderator of cellular differentiation, keretinization, and inflammatory processes. It has both exfoliating and anti-inflammatory effects. The exact mode of action of adapalene is unknown. Adapalene is applied topically to the skin, and its absorption into the blood through this medium is very low. Only trace amounts of adapalene have been found in the plasma of chronically treated patients [13].

Tretinoin is all-trans stereoisomer of retinoic acid, used topically for treatment of cases of acne vulgaris in which comedones, pustules, and papules predominate; it prevents comedo formation and suppresses keratin synthesis;

common adverse effects are erythema and desquamation. It is also administered orally in treatment of acute.[13]

In a Pakistani clinical study conducted by Iftikhar et al adapalene cream 0.1% was compared against isotretinoin 0.05% in the treatment of acne vulgaris. The study targeted comparing efficacy and tolerability of adapalene cream 0.1% and isotretinoin cream 0.05% in the treatment of acne vulgaris[14].

Both adapalene and isotretinoin demonstrated comparable efficacy. However, significantly lower skin irritation was noted with adapalene.

The only frequent adverse event is a mild skin irritation during the first two weeks of treatment.

Objective

The present study was undertaken to compare the efficacy and tolerability of adapalene cream 0.1% and isotretinoin gel 0.05% in the treatment of acne vulgaris of the face.

Materials and Methods

This is an observational, cross-sectional hospital-based study included the both genders attended Khartoum Teaching Dermatology Hospital with acne vulgaris from September 2010 to September 2011. Pregnant women, breast feeding women and patients on a previous treatment have been excluded

Sample size:

According to the Equation:

N = Z2(PQ)/D2

Where:
N= Sample size. Z = constant 1.96 2
P = Prevalence = 10% Q = (1-P).
D = allowable error = 4%

It was determined to be 90 patients , but 100 patients of mild to moderate acne irrespective of age, sex and social status were enrolled. After an informed consent, a detailed history was taken and scrupulous physical examination was performed in each patient.

Patients were randomized into two groups A and B (fifty patients for each). Patients in group A applied adapalene cream 0.1% and group B used isotretinoin cream 0.05% once daily at night for 6 weeks. Quantity of cream or gel remained the same i.e. equivalent to size of half a pea.

All patients were clinically diagnosed. Efficacy variables included non-inflammatory and inflammatory lesions and total lesion counts; global grade; and global assessment of improvement in acne severity. Skin tolerability variables included erythema, desquamation (scaling), dryness, pruritus, and stinging/ burning. Demographic data collected by direct interviewing to the intended subjects and clinical examination was done according to the attached questionnaire.

Data was analyzed by Statistical Package for Social Sciences (SPSS), version 10, t- test used to compare quantitative variables (score of nonmedical treatment according to socioeconomic status) . Analysis of variance ANOV A was used to compare score of nonmedical treatment according to education level.Chi-squared test was used to determine the statistical significances of association between qualitative variables. Test was considered significant, when P. value is less than 0.05.

RESULTS

Fifty patients were treated with Adapalene and fifty were treated with Isotretnoine. The means age of Adapalene and Isotretenoine groups were 27.42±10.15 and 24.28± 7.92.The gender distribution of Adapalene and Isotretenoine groups, in both groups the percentage of males was 22 % and female 78% . Among Adapline group the mild cases were 36% and moderate cases were 64%, while among Isotretenoine group the mild cases were 18% (9) and the moderate were 82 % . Cases with inflammatory lesions were 62% of Adapalene groups, while 76 % were of isotretenoine groups .Analysis indicated that Adapalene cream was significantly ($P < 0.01$) more effective in treating acne than Isotretinoin gel after 3 and 6 weeks from treatment. After 3 weeks of treatment with adapalene 2% was cured, 94 % were improved and 4 % were not improved, while within isotretenoine group 2% was cured, 46 % were improved and 52 % were not improved. After 6 weeks of treatment with Adapalene 90% was cured and 10 % were improved , while within isotretenoine group 8% was cured, 50 % were improved and 42 % were not improved . After 6 weeks of treatment with Adapalene 28 % of cases had lesions, while among Isotretenoine group they were 84 % .

The adverse drug reactions on skin based on scaling, erythema, burning sensation, pruritus and other assessment were significantly ($P<0.001$) high among isotretenoine group than adapalene one. The percentages were 20 % scaling, 28 % erythema, 10 % burning sensation, 10 % pruritus and 6% other of adapalene group and 74 % scaling, 48 % erythema, 42 % burning sensation, 32 % pruritus and 12% (+) others of Isotretenoine group.

Table 1: The mean age of Adapalene and Isotretenoine groups

Drug used	Age		
	N	Mean	Std. D.
Adapalene	50	27.42	10.15
Isotretenoine	50	24.28	7.92

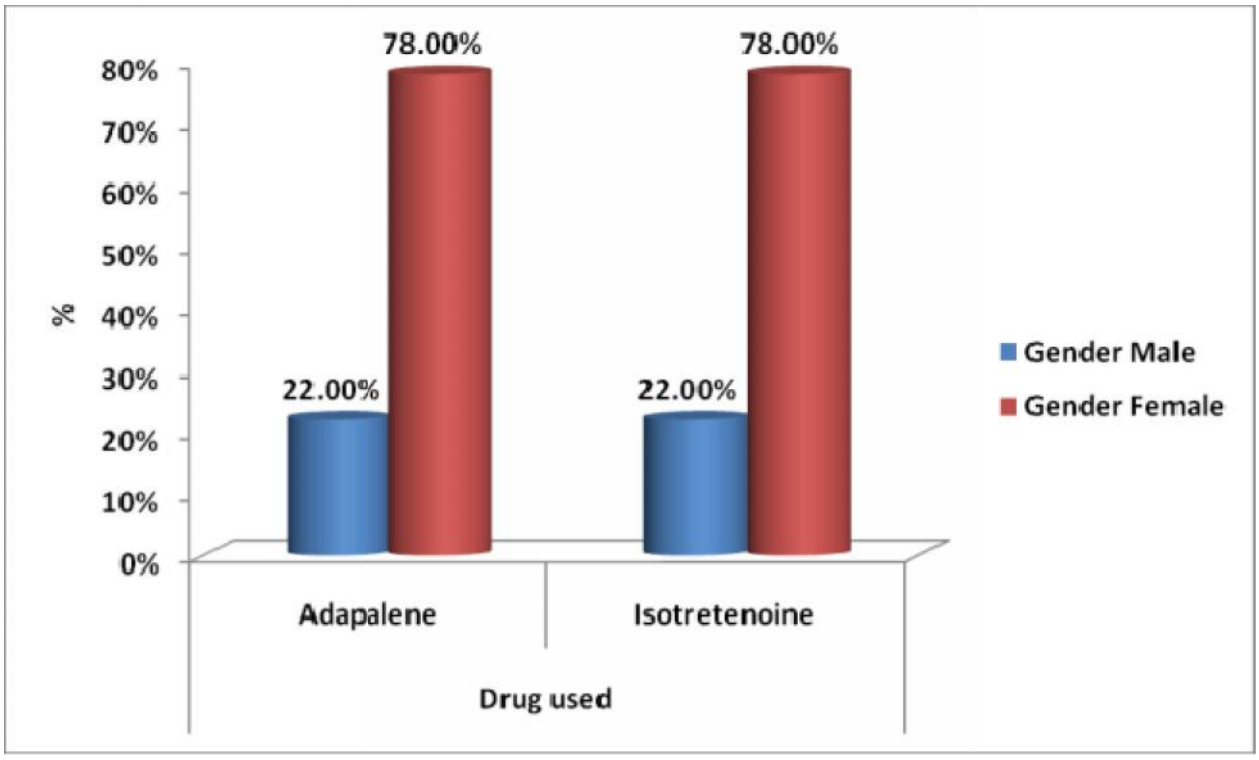

Figure 1: The gender distribution of Adapalene and Isotretenoine groups

Table 2: Distribution of type of drug used according to acne severity and inflammatory

		Drug used			
		Adapalene		Isotretenoine	
		N	% of Total N	N	% of Total N
Acne	**Mild**	18	36.00%	9	18.00%
	Moderate	32	64.00%	41	82.00%
Inflammatory	**Yes**	31	62.00%	38	76.00%
	No	19	38.00%	12	24.00%

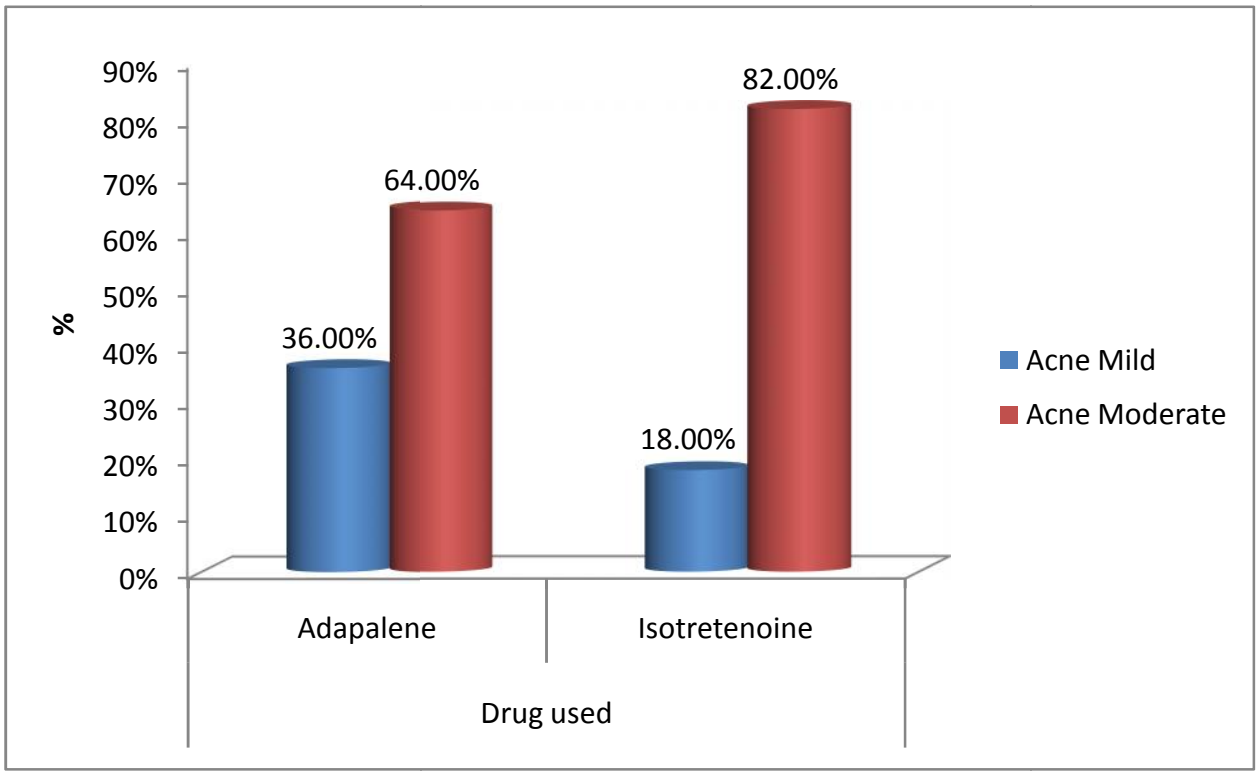

Figure 2: Distribution of type of drug used according to acne severity

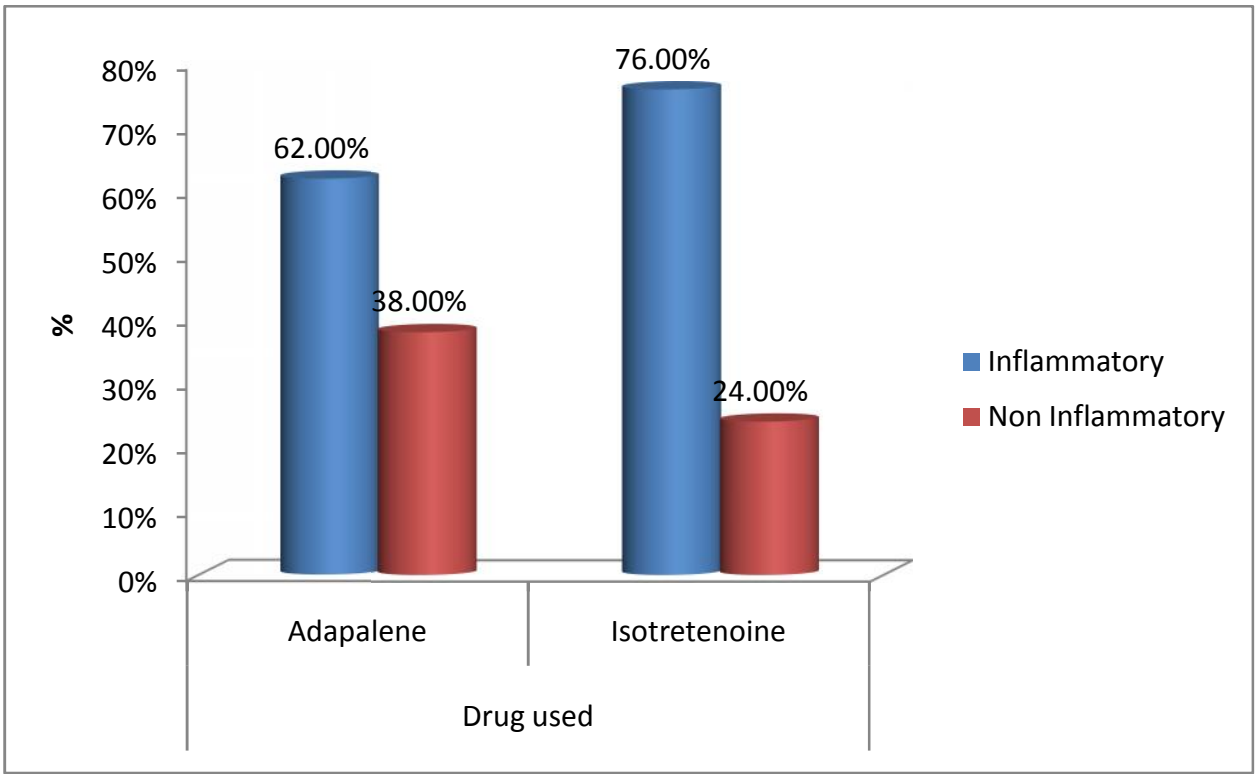

Figure 3: Distribution of type of drug used according to Inflammatory.

Table 3: Acne improvement according to type of drug used and duration of treatment

Improvement		Drug used			
		Adapalene		Isotretenoine	
		N	% of Total N	N	% of Total N
After 3 weeks	Cured	1	2.00%	1	2.00%
	Improved	47	94.00%	23	46.00%
	Not Improved	2	4.00%	26	52.00%
After 6 weeks	Cured	45	90.00%	4	8.00%
	Improved	5	10.00%	25	50.00%
	Not Improved	0	0.00%	21	42.00%

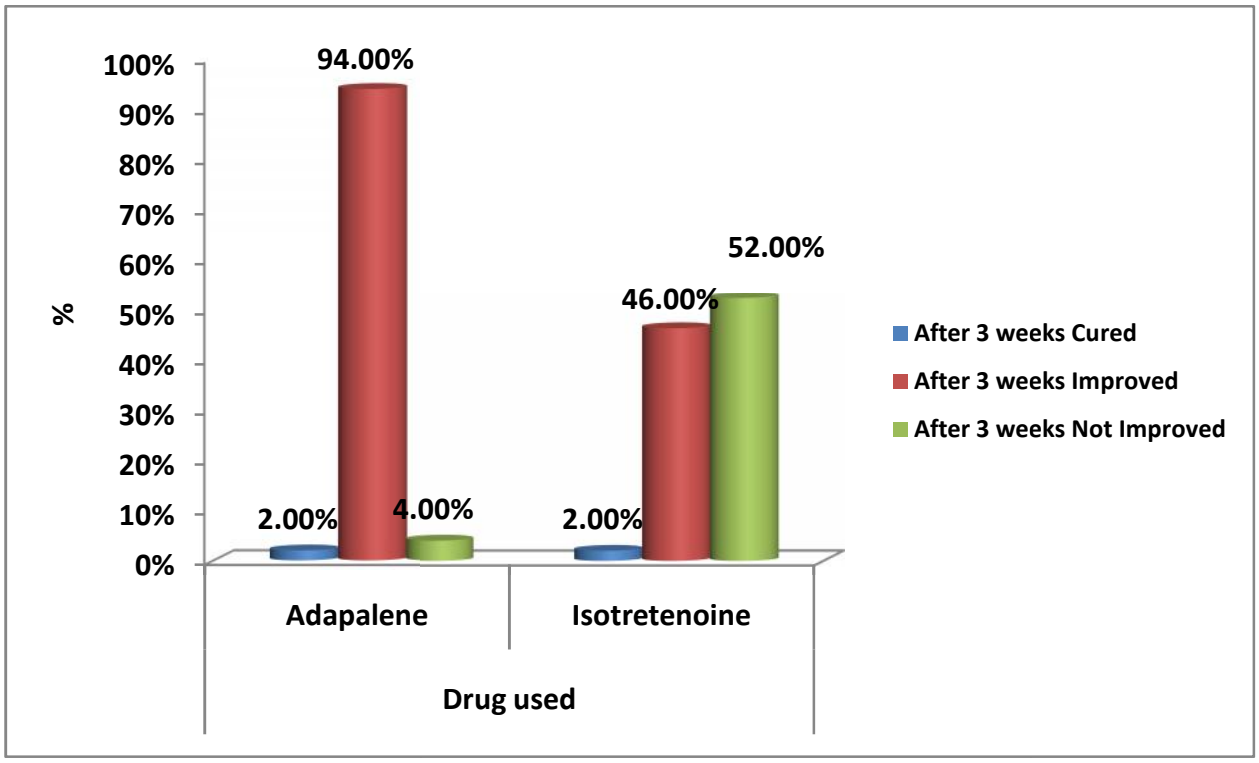

Figure 4: Acne improvement according to type of drug used after 3 weeks

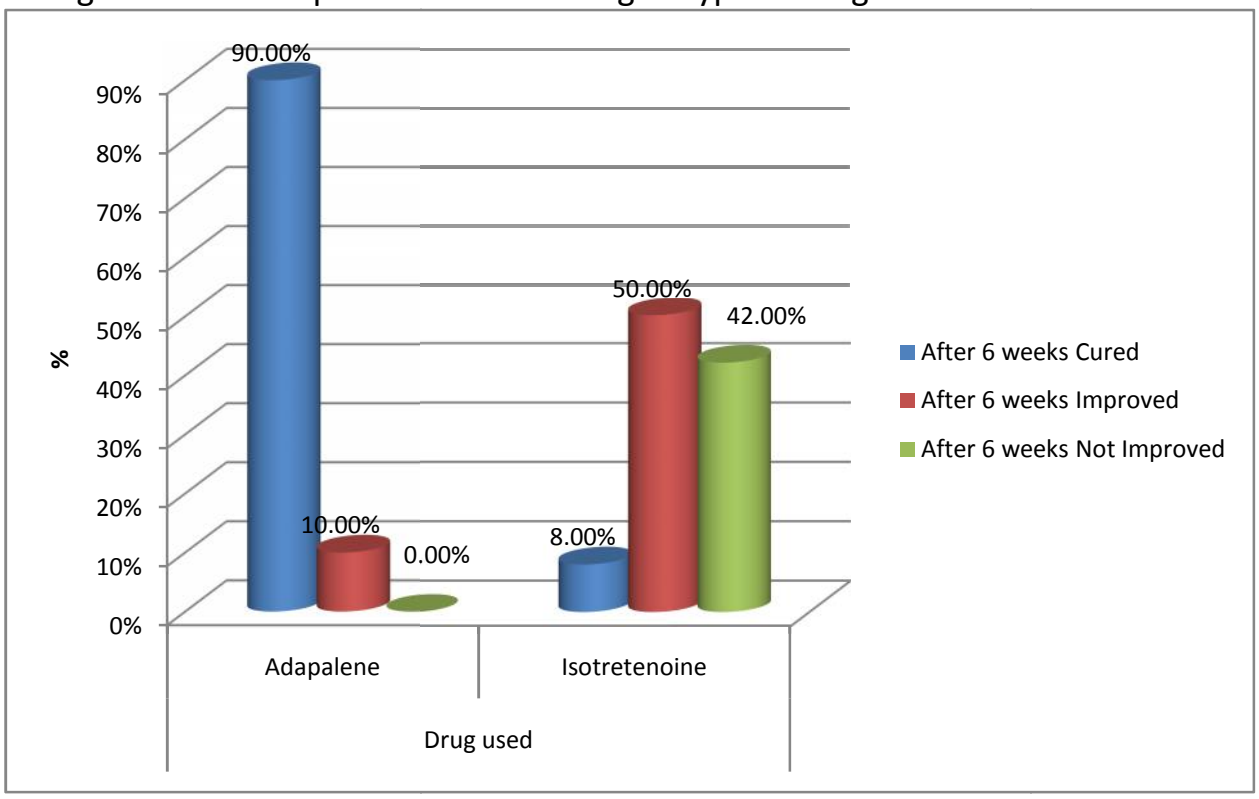

Figure 5: Acne improvement according to type of drug used after 6 weeks

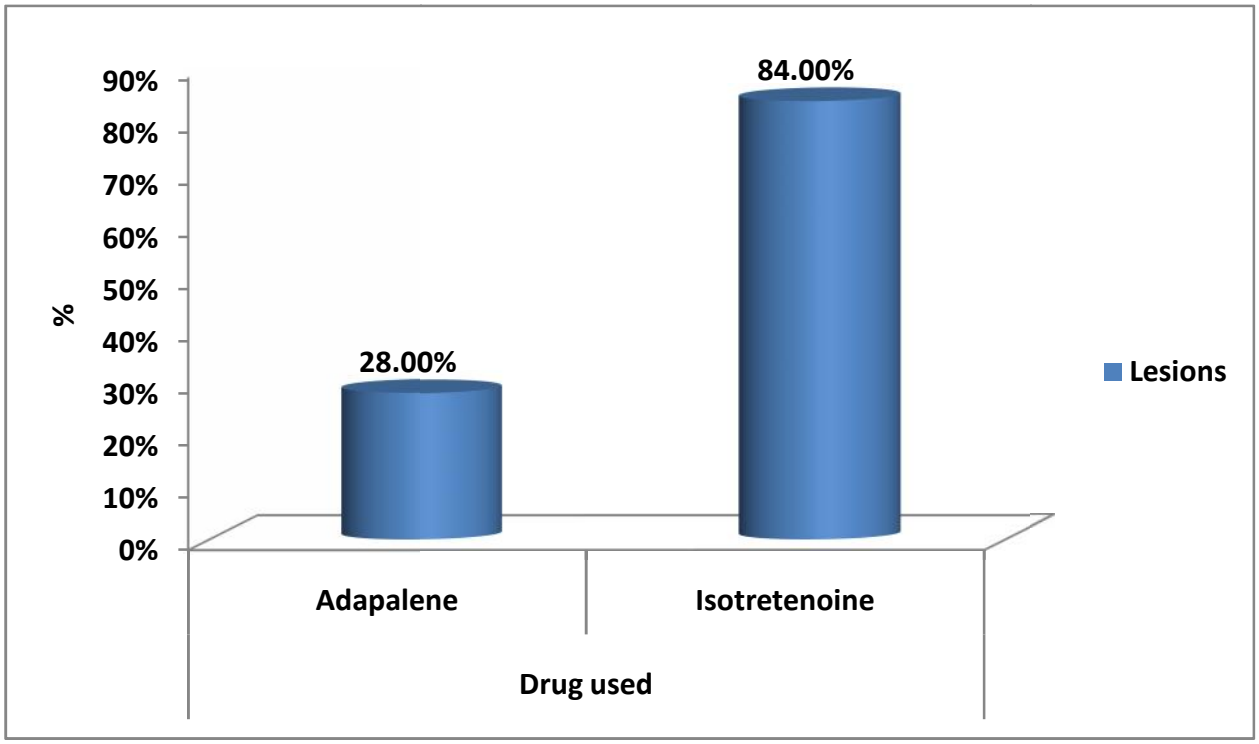

Figure 6: Lesions after treatment among Adapalene and Isotretenoine group

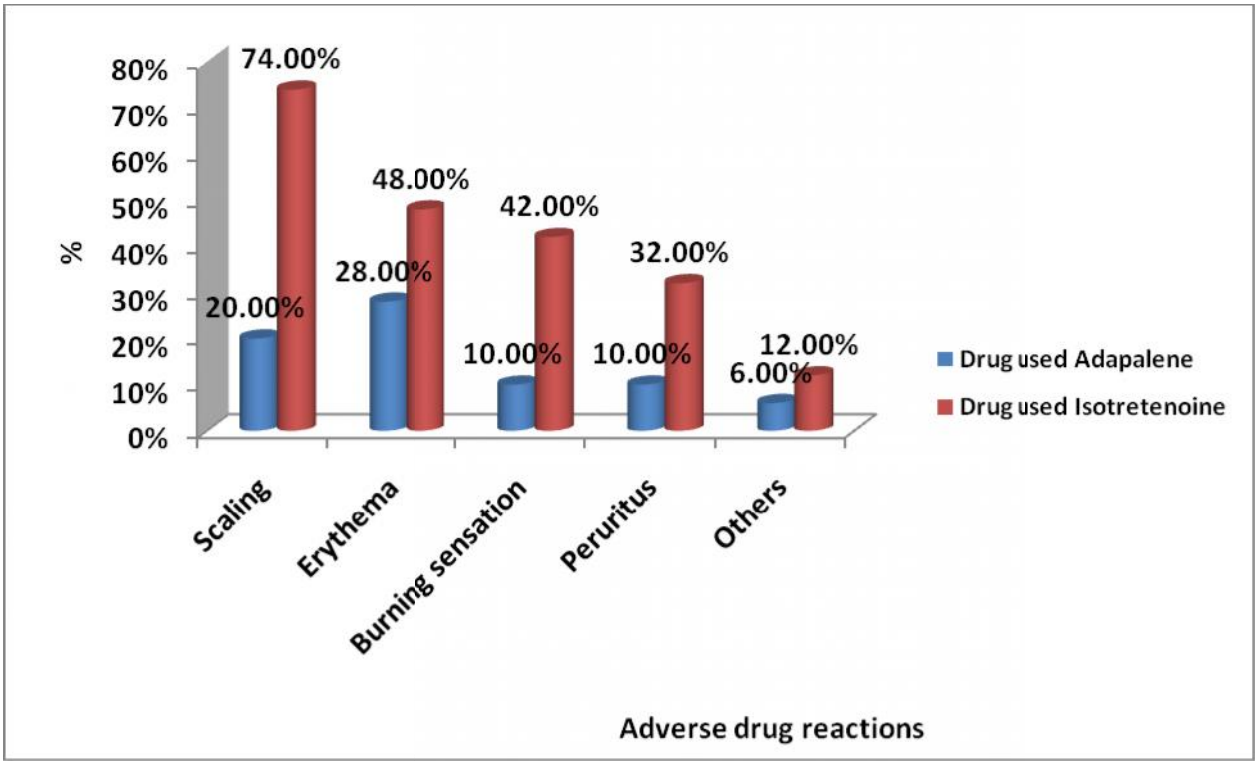

Figure 7: Adverse drug reactions according to type of drug used

DISCUSSION

Acne vulgaris is a chronic, inflammatory disease of the pilosebaceous unit, that affects seborrhoeic areas like face, back, and chest and characterized by comedones, papules, pustules, nodules, cysts, and scars. Almost every individual has some degree of acne during puberty with spontaneous resolution occurring in early adult life. Occasionally, the disease persists into the fourth decade or even remains a lifelong problem. Because of the involvement of the face with considerable cosmetic problems, acne is a major psychosocial problem for many teenagers and young adults[15, 16, 17].

The treatment of acne vulgaris is not curative. The purpose is to reduce discomfort due to inflamed lesions, to improve the appearance, and to prevent scars. Acne management is a long-term treatment and requires patience. The patient should be informed on the issue[15,18]. Topical treatment of acne vulgaris has changed over the years. Agents containing sulphur or resorcinol were used in especially first part of 20th century. Salicylic acid which is a keratolytic agent was popular in some time. Nowadays, the most popular topical agents were retinoids, benzoyl peroxide, azelaic acid, and topical antibiotics[19].

Topical application of isotretinoin and adapalene has proved effective in treating acne vulgaris. Both drugs demonstrate therapeutic advantages and less irritancy

over tretinoin, the most widely used treatment for acne. They both act as retinoid agonists, but differ in their affinity profile for nuclear and cytosolic retinoic acid receptors.

The objectives of this study were to compare the efficacy and tolerability of adapalene cream 0·1% and isotretinoin cream 0·05% in the treatment of acne.

Result indicated that both adapalene cream 0·1% and isotretinoin are effective in treating acne. However adapalene was found significantly more effective than isotretinoin, After 6 weeks of treatment all patient (Mild and Moderate) treated with adapalene were either cured or improved, while among isotretinoin group 42% of patients were not improved and 50% improved. Patients remained with lesions after 6 weeks of treatment among Adapalene group were significantly lesser than among Isotretenione group. This result with agrees with previous studies by Ioannides et al and Ahmed et al[20,21]. All these studies ensured the efficacy of Adapalene in comparison with other different retinoids.

The study demonstrated that Adapalene has faster effect than Isotretinoin. After 3 weeks of treatments 96 % of patients treated with Adapalene were either cured or improved, while among Isotretinoin group the percentage was 48 %.The faster onset of action of Adapalene was also recorded by considering the safety and tolerability and like many previous studies [20,21] Adapalene showed significantly higher safety and tolerability concomitant with Iftikar [14] The safety and tolerability

was assessed depending on the degree of scaling, erythema, burning sensation and pruritus. This anti-inflammatory effect is due to inhibition of the lipooxygenase activity and also to oxidative metabolism of arachidonic acid. These mechanisms may be the reason for decreased risk of irritation with adapalene. Adapalene has a very low percutaneous absorption once the drug has penetrated the stratum corneum, so that it becomes entrapped in the epidermis and hair follicle, which are targeted areas. Only trace amounts (0.25 ng/ml) of parent substance have been found in the plasma of acne patients following chronic topical application of adapalene in controlled trials. Excretion appears to be primarily by the biliary route. Erythema, peeling, dryness and burning are the most frequent encountered side effects accorded with Millikan results [22].

CONCLUSIONS

The purpose of treatment of acne vulgaris is to reduce discomfort due to inflamed lesions, to improve the appearance, and to prevent scars.Both adapalene cream 0·1% and isotretinoin are effective in treating acne, however adapalene was found significantly more effective than isotretinoin . Adapalene has faster onset of action of, which reflect on patients psychologically in term of improvements, comforts and good appearance. Significantly lower skin irritation was noted with adapalene, indicating that adapalene may begin a new era of treatment with low-irritant retinoids.

RECOMMENDATIONS

Adapalene treatment is a good choice for topical treatment of acne vulgaris with less side effects and high efficacy. Adapalene should be described as first line for treatment of acne vulgaris.

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