SHORT ARTICLE

Treatment Outcome of Acne Vulgaris with Oral Isotretinoin

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ABSTRACT

Objective: To determine the clinical efficacy of oral isotretinoin in the treatment of severe acne and assess its effect on total serum cholesterol, triglycerides, HDL-cholesterol and Low-Density Lipoprotein-cholesterol (LDL-cholesterol).
Study Design: A cohort, descriptive, hospital-based study.
Place and Duration of Study: Al-Ain Medical District, Tawam Hospital, United Arab Emirates, from 1994 to 2002.
Methodology: A total of 198 patients seen at Tawam Hospital, referred with acne vulgaris for a minimum of 6 weeks, were treated by isotretinoin for the first time, were included in the study. Variables studied were as per objectives apart from demographics and distribution.
Results: The study included 63 (32%) males and 135 (68%) females of mean age (±SD) of 21.3±5.6 years. Majority (81%) of patients was under 25 years. Of them, 26 patients had family history of acne. The most common site of acne was on face (66.7%), followed by trunk (26.2%) and neck (9.1%). Of 198 patients treated, 32.8% were cured, 19.1% markedly improved, 11.1% moderately improved and 24.2% of patients were advised for further treatment. There was no marked change in total and LDL-cholesterol, while LDL and triglycerides changed markedly.
Conclusion: In acne patients, isotretinoin is effective in producing remission. In addition, it was safe and its effect on serum lipids was transient, especially in healthy and young patients with normal liver functions.

Key words: *Isotretinoin. Acne vulgaris. Treatment.*

INTRODUCTION

The efficacy of isotretinoin in the treatment of acne has been widely established. Broad scale administration of isotretinoin has demonstrated that some patients are resistant to this treatment, either during the first treatment course or after successive courses.[1,2] Several studies investigated the role of the Total Cumulative Dose (TCD) of isotretinoin,[2,3] explored the predictive factors of resistance to isotretinoin, and determined the role of the mean daily dose on relapse of acne after isotretinoin discontinuation while taking into account patient characteristics and the TCD.[1]

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Besides its clinical efficacy in the treatment of severe acne, the clinical and laboratory adverse effects of the medicine has been well-delineated.[4,5] Over the past two decades, it has revolutionized the treatment of acne vulgaris and became a standard therapeutic agent including a long-lasting remission.[6]

Little is known about treatment outcome of acne vulgaris with oral isotretinoin in Arabian Gulf countries.[7,8] Treatment of various diseases has been noted to vary by patient demographics.[9] There might be gender and racial differences in response to treatment of acne.

The aim of the present study was to determine the clinical efficacy of oral isotretinoin in the treatment of severe acne, and to assess its effect on the variations of total serum cholesterol, triglycerides, HDL-cholesterol and low-density lipoprotein-cholesterol (LDL-cholesterol).

METHODOLOGY

It was a cohort, hospital-based, descriptive study performed at Dermatology Clinic of Tawam Teaching Hospital, Faculty of Medicine and Health Sciences at the Al-Ain University UAE between 1994 and 2002. All patients were referred with acne vulgaris for a minimum of 6 weeks and who were treated by isotretinoin for the first time, were included in the study. Patients who failed to keep scheduled follow-up visits or take their medication regularly, and patients with incomplete or non-informative data were excluded from the final analysis. The study was performed on 198 patients. Data on patient's age, gender, nationality, family history

of disease, and history of clinical examination was noted. Also data included site, duration and severity of acne, dosage (average daily dose and TCD) and response to isotretinoin, time taken to relapse, subsequent and indication of treatment, and antibiotic use. Those with either complete or partial (> 80%), clearance were considered as cohort because of the difficulty in categorizing them accurately due to retrospective nature of the study. The serum lipid profile including cholesterol, triglycerides, HDL, and LDL laboratory was done routinely at regular 4-6 weeks intervals in Dermatology Clinics of Tawam Hospital for all patients receiving isotretinoin.

The statistical package for social science version 11 was used to calculate chi-square to ascertain the association between two or more categorical variables. The significance difference between pair comparisons was tested using a paired t-test and Wilcoxon signed-rank test was performed for non-parametric test. The level $p<0.05$ was considered as the cut-off value for significance.

RESULTS

The study included 198 patients. There were 63 (32%) males and 135 (68%) females. Their mean age was 21.3±5.6 ranging from 12 to 42 years. Majority of patients was under 25 years (81%). Of the total sample, 85.4% were UAE nationals and 14.6% were expatriates. Twenty-six patients had family history of acne.

Table I gives the clinical characteristics of patients studied. Commonest site of acne was facial (66.7%), followed by truncal (26.2%) and the least at neck (9.1%). Regarding treatment response, 65 (32.8%) patients were cured, 38 (19.1%) markedly improved, 22 (11.1%) moderately improved, and 48 (24.2%) required further treatment.

Table II depicts the pre- and post-treatment serum levels of various serum lipids.

Table I: The clinical characteristics of 198 patients studied.

Variables		Frequency	Percentage
Treatment type			
	Isotretinoin–alone	144	72.7
	Isotretinoin-topical treatment	21	10.6
	Isotretinoin-systemic antibiotics	22	11.1
	Isotretinoin-2nd course	11	5.6
Site of acne*			
	Facial	132	66.7
	Neck	18	9.1
	Truncal	52	26.2
Global clinical evaluation			
	Completely cured	86	43.4
	Improved	60	30.3
	Unchanged	20	10.1
	Deteriorated	32	16.2
Further treatment			
	Yes	48	24.2
	No	129	65.2
	Lost follow-up	21	10.6

**Multiple sites: Percentages may not add to 100%*

Table II: Mean values of lipid and lipoprotein levels in a group of 198 patients, before and after isotretinoin treatment for acne.

Serum lipid	Serum level (mean±SD) (mmol/L) Before treatment	After treatment	p-value
Total cholesterol	4.27±0.96	4.85±0.98	<0.001
HDL-cholesterol	1.32±0.34	1.13±0.30	<0.001
LDL-cholesterol	2.69±0.81	3.09±0.79	<0.001
Triglycerides	0.76±0.56	1.15±0.67	<0.001

DISCUSSION

Most of the patients reported in this study had isotretinoin as their first-time therapy. In contrast with current therapy, these protocols dictated that treatment for acne vulgaris could not be continued beyond 6 weeks.

The effectiveness of isotretinoin in the treatment of severe acne has been well-documented.[1-3,6,8] Excellent clinical results have been obtained in the treatment of severe inflammatory acne with oral systemic isotretinoin.[1-3,10-13] A study by Jones reported a 70% response rate to isotretinoin therapy for severe nodulocystic acne.[14] In the study by Shahidullah *et al.* in Singapore, patients' response was excellent and good in 50.8% and 34.4% respectively.[11]

Acne is so common that it can almost be regarded as a physiological phenomenon of adolescence. However, upto 30% of teenagers develop acne of such severity to require isotretinoin treatment.[11] In this study population, 64% of patients were under 20 years of age and most were between 18 and 24 years of age.

In severe papulopustular and in nodulocystic/conglobate acne, oral isotretinoin is the treatment choice.[15] It is also required for patients with moderate to severe acne, especially when acne scars start to occur, a new therapeutic approach consists of a low-dose regimen of isotretinoin. More recently, it was reported that a total dose upto 120 mg/kg should be reached for optimal results and avoidance of relapses. The low-dose regimen leads to fewer adverse effects and offers an excellent effect on pre-existing scarring. Furthermore, a total dose $\leq$ 120 mg/kg as the therapeutic regimen of isotretinoin has proven to be the most successful in preventing relapses and scarring.

Oral isotretinoin, since its introduction more than 20 years ago, is the only approach to acne with possibility of a permanent "cure" or long-term remission. The role of isotretinoin has evolved with higher dosage schedules and used earlier in the course of the disease. One has still to consider the potential adverse effects of the drug especially on serum lipids. It tends to elevate VLDL and LDL, and decrease chylomicron metabolism.[16] These changes seem to be mild, reversible and transient, and should be interpreted in the context of clinical findings and normalcy of hepatic enzymes.[17,18]

Contraceptive measures have become a more prominent facet of oral retinoid therapy leading to

increased safety for its use in females of child-bearing potential.[19] In Philippines, oral isotretinoin is currently the gold standard in the treatment of moderately severe to severe acne vulgaris and approximately 50-85% of patients achieve permanent cure with one course based on 1.0-2.0 mg/kg/body weight,[20] which is consistent with this study results. Although, the profile of acne patients in the Philippines requiring a second course of oral isotretinoin is seen in those taking a mean cumulative dose (actual total dose) less than 120 mg/kg/body weight, with a mean actual duration of 6.7 months.

CONCLUSION

In acne patients, isotretinoin was effective in producing remission. It is safe and its effects on serum lipids are transient especially in healthy and young patients with normal liver functions.

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