ISOTRETINOIN IN TREATMENT OF ACNE: ITS EFFICACY, SIDE EFFECTS, AND RECURRENCE RATE OF DISEASE

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Background: Acne is a chronic inflammatory disease of pilosebaceous units. In addition to an unpleasant appearance, it may result in scarring in some cases. Despite the introduction of different treatments, oral isotretinoin is the most effective treatment and affects all the factors involved in the pathogenesis of this disease. This study was performed on patients with acne to examine the therapeutic effects, recurrence rate, and adverse effects of this drug.

Methods: One hundred patients with acne, who were visited at the Bou-Alli Hospital during 2000 – 2001, and found eligible to take part in this study were selected. The severity of acne was graded at the beginning, during, and after a 6-month treatment course with oral isotretinoin. Necessary laboratory tests were done.

Results: The data of 83 of 100 patients who continued the treatment for 6 months were analyzed. The mean ± SEM severity score of acne improved from 3.15 ± 0.10 to 0.58 ± 0.09 (P < 0.0001). Complete cure was achieved in 65% of patients. The mean ± SEM follow-up was 8.7 ± 2.3 months and the acne severity score was 1.04 ± 0.13 during the follow-up period. Overall, the recurrence rate was 19%; 4% of patients had to undergo retreatment. A rise in triglyceride level was the only significant laboratory alteration observed.

Conclusion: Oral isotretinoin appears to have favorable results and the least adverse effects in treatment of carefully-selected patients with acne.

Keywords: Acne vulgaris • isotretinoin

Introduction

Acne is a chronic inflammatory disease of pilosebaceous units, which is characterized by the development of comedones in the form of erythematous papules, pustules, and less commonly nodules, or pseudocysts. Four important factors involved in the pathogenesis of acne are 1) increased sebum production, 2) disordered microbial flora, 3) hyperkeratinization of pilosebaceous ducts, and 4) inflammation. Currently, different treatments are used, based on the severity of lesions, among which topical antibiotics, topical tretinoin, benzoyl peroxide, oral antibiotics, and some hormonal compounds are more commonly used. Regarding the increased resistance of microorganisms involved in pathogenesis of acne to common antibiotics, application of oral isotretinoin has become more common. It is necessary to mention that oral isotretinoin is the only drug that affects all the factors involved in the pathogenesis of acne. However, several adverse effects, including cutaneous side effects and laboratory alterations have been reported to associate with consumption of this drug. The indications of isotretinoin therapy in acne vulgaris are dysmorphophobia, unsuccessful rational treatment for more than three months, moderate to severe acne, and early recurrence after complete therapeutic courses.

In this study, we evaluated the therapeutic effects, recurrence rate, and adverse effects of this
drug on patients with acne vulgaris who were visited in Dermatology Clinic of Bou-Ali Hospital in 2000 – 2001.

Patients and Methods

This study was a quasi-experimental clinical trial, with sequential sampling, in such a way that all patients with acne vulgaris, who attended the Dermatology Clinic of Bou-Ali Hospital were examined by a dermatologist. Those who fulfilled the criteria of treatment with oral isotretinoin and had no previous history of renal, hepatic, or hematologic disease, were chosen. Those patients with normal complete blood count, red cell sedimentation rate, AST, ALT, ALP, triglyceride, bilirubin, and cholesterol, could enter the study. Women in the child-bearing age were examined by an obstetrician and after being confirmed to have a safe contraception, as well as giving a written consent, entered this study and received an oral daily dosage of 0.5 mg/kg of isotretinoin (Ro-Accutane; Roche Company, Switzerland), prescribed under direct supervision of a dermatologist. Patients were examined at the beginning and after six months of treatment. They were then classified, based on the type and site of lesions (laboratory results were seen at the end of the first, forth, and sixth months). The grading system used was as follows:

Grade I (mild): Comedones and papules on the face and trunk.

Grade II (mild to moderate): Papules and pustules on the face and trunk.

Grade III (moderate): Papules and pustules with back and chest involvement; or papules and pustules and nodular lesions of face (nodules on the face and papules and pustules and fewer nodules on the trunk).

Grade IV: Nodulocystic lesions on the face and trunk.

Grade zero: This was used at the end of treatment and during the follow-up and defined as nonexistence of the lesions.

Adverse effects were recorded at monthly visits. For cheilitis and skin dryness, the following grading was used:

Mild: Emollients were sufficient for treatment.

Moderate: Intermittent topical steroid was necessary.

Severe: A potent steroidal ointment and oral antibiotics, together with antiseptics, were necessary.

For mucosal dryness, the following grading was applied:

Mild: Emollients were sufficient for treatment.

Moderate: Topical mupirocin was necessary.

Severe: Mupirocin and oral antibiotics were both necessary.

Variable recurrence was defined as an increase in the severity of acne grade during follow-up, in comparison with that at the end of treatment.

The criteria for starting oral isotretinoin were 1) acne with a moderate or high grade; 2) lack of response to common drugs, including oral antibiotics in grade I or II acne; and 3) dysmorphophobia in patients with grade I or II acne.

Statistical analyses

Continuous variables were compared using repeated measures one-way analysis of variance (ANOVA). A P value of <0.05 was considered statistically significant. Continuous variables are presented as mean ± SEM.

Results

One hundred patients entered this study, of whom 83 finished the six-month treatment course. Forty-eight (58%) patients were females and 35 (42%) were males. The mean ± SD age of patients was 25.3 ± 8.8 (range: 16 – 42) years.

The grading of lesions was recorded before the treatment, during the follow-up, and after the 6-month treatment, based on the method mentioned earlier (Table 1). The mean ± SEM grade was 3.15 ± 0.10 before treatment. After six months, 54 patients had complete cure (clearance rate of 65%). Acne was improved to grade II in 19 and to grade I in 10 patients (Table 1).

All who did not have complete cure used only nonretinoid topical treatment. The follow-up period was longer than 6 months in 74 patients (mean ± SEM: 8.7 ± 2.3 mon).

Recurrence was observed in 14 (19%) patients

<table>
<thead>
<tr>
<th>Stage/Severity</th>
<th>Acne severity n(%)</th>
<th>Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>After treatment</td>
<td>54 (65%)</td>
<td>10 (12%)</td>
</tr>
<tr>
<td>During follow-up</td>
<td>35 (42.2%)</td>
<td>11 (13.3%)</td>
</tr>
</tbody>
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Table 1. Severity of acne before and after treatment and during the follow-up.
of whom, only three developed the same primary severity. The mean ± SEM grade was 1.04 ± 0.13 during follow-up (Table 1).

Triglyceride and total cholesterol levels before and after the treatment were also compared (Table 2). Although triglyceride level increased significantly (P < 0.05), the mean cholesterol level had no significant change.

Cheilitis occurred in 76 patients, which was mild in 69 and moderate in 7 patients. Skin dryness was observed in 24 patients; mild in all cases. Mucosal dryness occurred in 13 patients, which was mild in 11 and moderate in 2 patients (Table 3).

**Discussion**

Introduction of isotretinoin has led to an extensive modification in treatment regimens of acne. The most important advantage of this drug is its effect on all four factors involving in the pathogenesis of acne, though its adverse effects and rather high price have resulted in its limited use. In our study, the rate of complete cure was 65% after 6 months of treatment. The recurrence rate was also found to be only 19% after a mean follow-up of almost 9 months. The acne severity score was the same as the primary lesions only in 3 patients. In other words, represcription of the drug was only necessary in 4% of patients. In another study, it was shown that complete cure took place in 39% of patients and was sustained during three years after treatment. In 17% of patients, acne improved from severe to moderate and retreatment was needed in 19% of patients. However, this study was limited to severe acne. Also, the criteria used for the severity of acne were not objective. Of patients, only three developed the same primary severity. The mean ± SEM grade was 1.04 ± 0.13 during follow-up (Table 1).

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**References**