

## Isotretinoin Treatment of Rosacea

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Twenty patients with severe rosacea were treated with isotretinoin for 3-6 months. Six patients initially received 1.0 mg/kg and 14 patients 0.5 mg/kg of isotretinoin. The response was good or excellent in all patients and the papulopustular lesions in particular cleared promptly. Patients receiving 1.0 mg/kg of isotretinoin experienced more side-effects and the dose had to be lowered in five of the six patients. Seventeen of the 20 patients had no relapses during a follow-up of one year showing that isotretinoin has a long-lasting favourable effect in rosacea. (Received June 10, 1986.)

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The pathomechanism of rosacea remains obscure, and different systemic drugs, such as tetracycline, metronidazole and chloroquine, have been used with varying success (1, 2). Isotretinoin has proven very effective in severe acne, and in contrast to antibiotics, the disease activity remains low several months after treatment has ceased (3). This effect may be mediated through the altered function of sebaceous glands (4). Recent reports suggest that isotretinoin is also effective in rosacea (5-9). We treated 20 rosacea patients with isotretinoin and examined not only the efficacy and side-effects but also the relapse rates during a follow-up of one year.

### MATERIAL AND METHODS

Twenty patients, 10 males and 10 females, aged from 32 to 76 years were examined. The mean duration of rosacea was 10 years (range 2-25 years) and all patients had earlier received systemic treatment with tetracycline (20 patients), metronidazole (5 patients) or chloroquine (5 patients) with no or temporary effect. The study period was from September 1983 to November 1985, and all systemic and local treatment was stopped at least one month before start of the study period. Fourteen patients received 0.5 mg/kg of isotretinoin (Roaccutan®, Roche Ltd., Basle, Switzerland) and six patients 1.0 mg/kg. The initial treatment protocol included the same dosage for at least 3 months, after which the dose could either be changed individually or stopped. No local treatment was given. The clinical response was evaluated after 1, 2, 3, 4 and 6 months by scoring papules, pustules, cysts, redness and oiliness on a four-grade scale. After isotretinoin has been stopped, each patient was examined every three months for relapses for up to one year. The laboratory tests taken at 0, 1, 2 and 4 months and at the end of the treatment were total blood cell count, ASAT, ALAT, AFOS, creatinine, triglycerides and urine albumin and blood. All females of fertile age took contraceptive pills if they did not have an intrauterine device.

### RESULTS

Isotretinoin had an immediate effect on papules and pustules. In 13 patients these disappeared during the first month of therapy and in the remaining seven cases during the second month. Oiliness also diminished rapidly. The effect on erythema was slower and more incomplete. The total clinical score in the whole patient group was  $7.5 \pm 2.4$  at the beginning of the treatment and  $1.25 \pm 0.6$  at the end. The difference is significant ( $p < 0.001$ ,

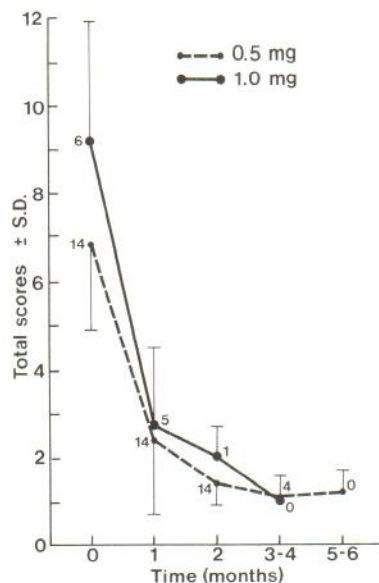


Fig. 1. Clinical effect of 0.5 mg/kg and 1.0 mg/kg of isotretinoin on rosacea lesions. Results are expressed as total scores. Numbers on curves indicate patients on active treatment.

Student's *t*-test). The response was the same during the first two months of therapy in the patients taking 0.5 mg/kg or 1.0 mg/kg (Fig. 1). Of the six patients who started with 1.0 mg/kg of isotretinoin, five could not continue this dosage for the scheduled three months because of various side-effects. The dose was reduced to 0.5 mg/kg in these five. All tolerated the new dosage well and, healing continued. All 14 patients initially taking 0.5 mg/kg of isotretinoin managed to go on taking this dose without any harmful side-effects. During the one-year follow-up, 17 patients remained in remission. Nine of these had no signs of active disease, but the remaining eight had a few minute papules and some oiliness. The total scores in these 17 patients at the beginning and at the end of one-year follow-up were  $1.3 \pm 0.6$  and  $1.2 \pm 0.9$ , respectively. Two patients relapsed after 3, and one after 6 months. Two of these had taken 0.5 mg/kg and one 1.0 mg/kg of isotretinoin and all three had excellent results when isotretinoin was stopped.

Some mucosal side-effects, such as dryness of the lips and nose, occurred in all patients. Six patients experienced musculoskeletal pain. Five of the six patients taking 1.0 mg/kg had such severe side-effects that the dosage had to be lowered: two had intolerable mucocutaneous symptoms, one had tinnitus and headache and two showed a prompt increase in triglyceride levels (6.04 and 3.64 mmol/l, normal below 1.7). In the whole patient group the mean triglyceride level rose during the treatment from  $1.26 \pm 0.56$  mmol/l to  $2.36 \pm 1.56$  mmol/l. This difference is significant ( $p < 0.005$ , Student's *t*-test). All six patients with high triglyceride levels of over 3.0 mmol/l showed nearly normal or normal levels one month after isotretinoin was stopped. No other laboratory abnormalities were seen.

## DISCUSSION

The patients had severe rosacea and had previously been treated unsuccessfully with various antibiotics and chloroquine. Results in all 20 patients were good or excellent after 2-6 months of treatment with isotretinoin. This is in agreement with previous similar studies reporting good results in 83-100% of the patients using isotretinoin in dosages



between 0.05 and 1.0 mg/kg (5-9). In the present study we found no difference in the efficacy of 1.0 or 0.5 mg/kg of isotretinoin. However, the patients starting with 1.0 mg/kg clearly had more prominent side-effects and the dose had to be lowered in five of six patients. Although our series was small it seems clear that 0.5 mg/kg is to be preferred to 1.0 mg/kg in rosacea patients, as also confirmed by Schmidt et al. (8). The dosage of 1.0 mg/kg of isotretinoin seems to cause harming side-effects as frequently in acne as in rosacea patients (10).

Data on the remission time after successful isotretinoin treatment in rosacea are scanty. Mahrle et al. (9) followed 18 patients for 1½ years and found that 13 were still in remission. In agreement with this, only three of our 20 patients had relapses during the one-year follow-up. Two of these had relapsed after 3 months and one after 6 months, but we could not find any reason for the relapses because the history and primary treatment effect were similar to those of the other patients. Suppression of sebaceous gland function is a typical finding in acne treated with isotretinoin (4). A similar effect seems to occur in rosacea (5, 8) and is consistent with the present findings of rapidly diminishing oiliness after treatment with isotretinoin has started and of a reversal one year after the treatment has ceased.

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