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Isotretinoin: 10 Years On

Isotretinoin is now a well-known drug, and its place is established in the treatment of severe acne. Side effects, particularly teratogenicity, have been reviewed [1–3]. Several long-term studies have situated the long-term benefit of isotretinoin [3–5], and it appears from these observations that about 60% of the patients are in stable remission following one single course of treatment. Two and more courses are necessary for the rest of the patients.

From a clinical point of view some questions presently remain.

Which Is the Best Dose Regimen?

We have demonstrated [6] that the total cumulative dose (TCD) is the best parameter to determine the dose necessary to obtain stable remissions and found that the threshold is at about 100 mg/kg. More recently [4, 7] higher TCD of 120–150 mg/kg have been recommended. Age of the patients and severity of acne increase the risk of relapse [5, 6]. For this reason the TCD should be adapted to the risk factors. However, no supplementary benefit can be obtained with TCD higher than 150 mg/kg, which is clearly demonstrated in the study of Lehucher-Ceyrac et al. [7] in this issue. The daily doses given in order to reach the appropriate TCD vary between 0.5 and 1.0 mg/kg. Cunliffe et al. [4] insist that daily doses of 1.0 mg/kg are related with a lesser relapse rate. This has not been confirmed in other studies [2, 5, 7].

Which Acne Patient Should Be Treated with Systemic Isotretinoin?

It has been postulated that only patients with severe nodulocystic acne should receive isotretinoin. Actually, as the experience with this drug is progressing, there is a tendency to extend the strict indications. So subjects with less severe acne who do not respond to conventional treatment are treated with isotretinoin [4]. Young patients (11–15 years) with a positive family history of severe acne may be treated before important inflammatory lesions develop and therefore heal without scarring [2]. Cunliffe et al. [4] even proposed to give isotretinoin to depressed patients with dysmorphophobia.

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What about Women Who Do Not Respond to Systemic Isotretinoin as Well as Expected?

In this issue Lehucher-Ceyrac and Weber-Buisset [7] report their experience in a long-term study with a follow-up period of 9 years. This paper is of particular interest because the authors deal with a large group of patients including an important number of women (75 of a total of 188). These women (1) had a higher mean age (28 years) than that of the male group (23 years), (2) 22 out of 75 had associated endocrinological problems and (3) had a significantly higher relapse rate, even after several treatment courses. It was also in this group of women that a complete remission could not be obtained, unless cyproterone acetate was administered simultaneously with isotretinoin. Lehucher-Ceyrac and Weber-Buisset [7] underline that in women, particularly with late acne onset, endocrinological problems should be suspected and if present treated with antiandrogens. Isotretinoin may be considered in these cases only as an adjuvant treatment.

In conclusion isotretinoin is presently the best drug for acne treatment. If efficient contraception is assured in females, no reason remains to exclude moderate acne from treatment with isotretinoin. TCD should be adapted to the risk factors. Special attention should be focused on female patients with late acne who may have endocrinological problems which should be detected and treated with antiandrogens.

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