Letter to the Editors

Suggestions for effective contraception in isotretinoin therapy

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We read with interest the paper 'Isotretinoin, pregnancies, abortions and birth defects: a population-based perspective' by Bérard *et al.* [1], published in your Journal last year. Our interest stems, in particular, from our experience of managing three cases of pregnancy exposed to isotretinoin during the last 12 months. Each of these occurred after careful compliance with established guidelines.

Bérard *et al.* conclude that the overall annual incident pregnancy rate while on isotretinoin is 32.7 per 1000 women-years of treatment [1]. The authors also confirm the teratogenic effects of the drug [1]. Although isotretinoin is a widely prescribed drug, few studies exist that demonstrate the incidence of pregnancy during isotretinoin therapy. Mitchell *et al.* [2] found an annual incidence of 8.8 pregnancies per 1000 women-years of treatment. The Slone Accutane Survey has reported similar findings with an annual rate of 7.4 per 1000 women-years [3].

Isotretinoin is an effective drug for acne, and there is no doubt that millions of people have benefited from it. One could argue that it is also a safe drug provided that all necessary precautions are taken. However, at-risk pregnancies continue to occur. Given the known teratogenic effects of isotretinoin, even one unwanted pregnancy should be viewed as a failure of the existing pregnancy preventing programmes. Current European and US guidelines [4, 5] require that patients should have a negative pregnancy test before commencement of the treatment. They will also have to undergo regular pregnancy tests during and 5 weeks after the end of treatment. Regarding contraception, it is suggested that patients should agree to at least one and preferably two complementary methods of contraception, including a barrier method, before the initiation of therapy, during treatment and for 5 weeks after the end of it. Furthermore, female patients will be given only a 30-day supply. The necessity for effective contraception cannot be overemphasized. In the UK, the choice of contraception is usually left to the patient's general practitioner (GP). A popular choice seems to be the

oral contraceptive pill in combination with a barrier method, such as the condom or the diaphragm. However, the effectiveness of contraception methods varies and is influenced by the characteristics of the method itself as well as patient compliance. Obviously, failure to comply – unintentionally or not – with the instructions relevant to each different contraceptive method results in a high risk of pregnancy. Our aim should be to eliminate that possibility.

Our personal experience reveals that none of our pregnancy cases could have been prevented by closer adherence to the guidelines (either UK or US protocols).

Therefore, we suggest that parenteral progestogen-only contraceptives (injectable preparations, implants, intrauterine system or device) be adopted as a standard approach to contraception for female patients considered for isotretinoin therapy. These methods are >99% effective and are independent of the patient's individual compliance. We realize, however, that there are some disadvantages regarding the use of these contraceptive methods, such as irregular bleeding, headaches, weight gain, etc.

In particular, injectable preparations of medroxyprogesterone acetate have been linked with a temporary decrease in bone mineral density (BMD), which occurs in the first 2–3 years of use. After cessation, BMD recovers and there is no evidence of increased risk of fracture [6]. Given the fact that it will be used only for a relatively short period of time (6–9 months), we believe that the possible risks do not outweigh the benefit.

After the end of isotretinoin treatment, contraceptive methods could be evaluated by the GP or specialist and, of course, patients' needs and preferences should always be considered.

Another suggestion, and a challenge that we direct towards the pharmaceutical industry, would be the development of a combined pill containing both isotretinoin and a contraceptive. The requirement to maintain the correct dose of each component would require very

careful consideration and may require some alteration to established treatment regimens, but this problem does not seem insuperable.

Competing interests

ST has provided consultancy advice, received lecture fees and undertaken contract work for pharmaceutical companies. All of his work is related to myometrial contractility and does not overlap with the current article.

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