Initial UK experience of the levonorgestrel-releasing contraceptive intravaginal ring

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Abstract

A study was performed to establish the tolerance, acceptability and associated efficacy of a levonorgestrel-releasing intravaginal ring (IVR) in a sample of British women requiring contraception. This was achieved with an open non-randomized prospective study of 1710 women aged 18–40 years, recruited in 75 centers geographically spread around the UK using an IVR designed to release 20 μg/day of levonorgestrel. Assessments were made at baseline, after 6 weeks, after 3 months and then 3-monthly. After initial insertion of the IVR, it was changed at 3-monthly intervals. A total of 1591 women were eligible for analysis, with 572 available after 12 months and 34 after 24 months of use. Life-table analysis revealed pregnancy rates of 5.1% and 6.5% at 12 months and 24 months, respectively. The IVR was rated as acceptable or very acceptable as a form of contraceptive by 60.7% of women at 12 months. The most common adverse events were menstrual disturbance, headache and vaginal discharge. No significant pattern of biochemical, hematological, microbiological or cytological abnormalities was found but vaginal erythematous lesions were noted at some centers. This IVR was found to be a generally well-accepted method of contraception with a failure rate comparable to some other progestogen-only methods. On this basis, further development of hormone-releasing intravaginal rings is justified.

Introduction

Interest has grown in the use of intravaginal rings (IVR) as novel delivery systems for
pharmaceutical compounds including steroid hormones [1–5] and the first intravaginal ring, releasing estradiol, has been licensed in Scandinavia and the UK for the treatment of local menopausal symptoms.

There may be considerable advantages to the delivery of steroid hormones per vagina compared with the oral route. These include the avoidance of first-pass hepatic metabolism, reducing the amount of hormone that needs to be administered to achieve an effective blood level, and perhaps increased compliance, as the intravaginal ring can be left in situ for a number of months without the need for daily action on behalf of the user. Unlike some long-acting non-oral delivery systems, such as subdermal implants or intrauterine devices (IUDs), the use of the intravaginal ring does not require any particular skill to insert or remove. In addition, in common with oral contraception, the user can discontinue use of an intravaginal method herself, without the need for medical intervention.

The IVR discussed in this study was developed by the World Health Organisation in association with the Population Council. This IVR is made from medical-grade silastic and its dimensions are 55.6 mm in toroidal diameter and 9.5 mm in cross-section. Its core contains 5 mg of levonorgestrel and the total weight is approximately 11 g. It was designed to release approximately 20 μg of levonorgestrel over a 24-h period and to be left in the vagina for 3 months (although it could be removed for short periods of time) at the end of which it could be replaced by another IVR. Previous studies of this IVR have been performed in more than 1000 women, largely in developing countries [6].

This open study was designed to provide tolerance, acceptability and associated efficacy data from a sample of women in the UK requiring contraception.

Methods and subjects

Following Local Ethics Committee approval, subjects were recruited into this open study from 75 UK centers, which were either general practices or family planning clinics (both community and hospital-based). The study was conducted in accordance with the Declaration of Helsinki (Hong Kong Amendment 1989) and the Association of the British Pharmaceutical Industry Guidelines for Good Clinical Practice.

Subjects were aged 18–40 years with a need for contraception (those engaging in sexual intercourse at least, on average, once a week were eligible unless excluded by one or more criteria detailed in Table 1). Baseline assessment consisted of history taking, full physical examination, a cervical smear (unless one had been performed in the preceding 3 months), microbiology swab and standard hematology and biochemistry. Further assessments at the study center were then performed 6 weeks and 3 months after initial insertion of the IVR and thereafter every 3 months. During each assessment, information was recorded on clinical examination, any adverse events, bleeding patterns, expulsion of the IVR, voluntary removal of the IVR and acceptability of the method. Where indicated, repeat vaginal microbiology, cervical smear and standard hematology/biochemistry testing was performed (these, except for microbiology, were repeated routinely after 12 and 24 months of IVR use).