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An overview of reports concerning implantation complications and unintended pregnancy while on etonogestrel

Introduction

Recently, the media has paid considerable attention to unintended pregnancies during treatment with etonogestrel (Implanon®). Etonogestrel was approved for the Dutch market on August 28th 1998 for the following indication: *contraception*. It is a contraceptive implant, to be placed just under the skin on the inside of the upper arm. The duration of its effectiveness is three years. Unintended pregnancy can be caused by implantation complications or by lack of efficacy of the implant.
The SPC advises that a barrier contraceptive is used after insertion of the implant until the moment that the implant can be palpated. In case of non-palpable implants, the SPC advises checking the implant by ultrasonography, MRI, and lastly hormonal assay as supplied by the MAH[1].

Reports

Three cases that have been reported to the Netherlands Pharmacovigilance Centre concerned unintended pregnancy. Additionally, 37 reports of unintended pregnancy were received from the Marketing Authorisation Holder (MAH). One of these reports had been sent to both Lareb and the MAH. Two reports probably referred to women who were already pregnant before the insertion of the implant.
Of the remaining 37 cases 11 pregnancies were terminated and in 5 cases a spontaneous abortion occurred before the 10th week. One instance of a foetal death was reported (gestational age 20 weeks) and in two cases a healthy baby was born. Information about the outcome of the other 18 pregnancies was not available.
In two reports the implant was found to be in situ. In 11 cases the implant was reported not to be in situ, based on negative etonogestrel levels. For the remaining 24 cases information was either not available or controversial: in four instances the implant was not palpable and in three cases the implant could not be detected by ultrasound and additional etonogestrel levels were lacking.

Other sources of information

Literature

A Medline search yielded one publication about the tracing of non-palpable implants. MRI is considered the best technique to detect the rod, although the SPC advises ultrasonography as the primary and MRI as a secondary detection method[2]. Reports on untraceable rods or unintended pregnancies due to implantation complications could not be found. Concerning therapeutic failure, a recent publication states that “No study has yet reported any failures with Implanon”[3].

Databases

The WHO database shows statistically significant disproportionalities associated with different ADRs (see Table 1). Assuming that etonogestrel exclusively refers to Implanon®, we think it is remarkable that implantation complications have only been reported twice. Although unintended pregnancy is statistically significantly associated with etonogestrel (ROR 16.0 (95%CI 9.2-28.2)), it must be emphasised that this association is the weakest in the list of associations with contraceptives for which more than three reports have been received.

Mechanism

In the media, it is suggested that unintended pregnancies might be due to implantation complications. These articles possibly refer to cases in which the rod failed to enter the body although the physicians in question were convinced that it had been placed correctly.

Conclusion

Based on our data and the data in the literature, an association between unintended pregnancies and implantation complications (i.e. untraceable implants) could not be supported. Moreover, the WHO database suggests that implantation complications should not be seen as a major problem since they do not occur on a global scale and unintended pregnancies are rare. Nevertheless, the incidence of untraceable implants in the Netherlands is high.

References

1. Dutch summary of product characteristics of Implanon® version (7-2-2002) http://www.cbg-meb.nl.
2. Merki-Feld GS, Brekenfeld C, Migge B, Keller PJ. Nonpalpable ultrasonographically not detectable Implanon rods can be localized by magnetic resonance imaging. Contraception. 2001 Jun;63(6):325-8.
3. Glasier A. Implantable contraceptives for women: effectiveness, discontinuation rates, return of fertility, and outcome of pregnancies. Contraception. 2002 Jan;65(1):29-37.