I would like to present the case of a 38-year-old woman who suffered an ectopic pregnancy whilst using Implanon\textsuperscript{10} (Organon Laboratories Ltd, Cambridge, UK), the etonogestrel contraceptive implant, for contraception. Of interest, the patient reported an unplanned pregnancy 15 years ago following a true method failure of the combined oral contraceptive pill. The patient gave birth and delivered a healthy child. She then had a miscarriage and, following a condom accident, a further unplanned pregnancy that resulted in an abortion in April 2003.

Having had two unplanned pregnancies following contraceptive failures, the patient decided to use Implanon, the progestogen-only contraceptive implant. This was inserted on 5 August 2003. It is interesting to note that this patient had regular menstrual cycles whilst using Implanon, suggesting that she was ovulating regularly. Unfortunately, she contacted the Contraception and Sexual Health Clinic on 8 March 2006 following a laparoscopic salpingectomy for a left-sided ectopic pregnancy performed on 2 March 2006. Therefore this pregnancy had occurred after using Implanon for 2 years and 7 months. When the patient was reviewed she stated that she had not taken any liver enzyme-inducing drugs or herbal remedies. Her body mass index was 26 kg/m\textsuperscript{2}. The contraceptive implant was easily palpable on the medial aspect of her upper left arm. After discussion with Organon Laboratories blood was taken for a serum etonogestrel assay. The patient was also counselled about her future contraceptive needs. She decided to use Depo-Provera\textsuperscript{110} (Pfizer Ltd, Tadworth, UK), the progestogen-only injectable. A week later the patient returned to the clinic to have the implant removed and this was again sent for analysis.

The serum etonogestrel assay showed a quantitative level of 46.8 pg/ml. The lower level of quantification is 30 pg/ml and the minimal level needed to inhibit ovulation is 90 pg/ml. Studies have shown that after 2 years of Implanon use a mean serum etonogestrel concentration of 190 ± 43 pg/ml is to be expected. Organon Laboratories’ manufacturing technology department inspected the implant. The measured \textit{ex vivo} release rate of 43.9 µg/day was well above the declared minimum release rate of approximately 21 µg/day expected for the \textit{in situ} period of 951 days. Moreover, the residual content of etonogestrel in the implant (and hence the \textit{in vivo} release amount) was within the expected range.

Discussion

A number of case reports have been published reporting pregnancies with Implanon.\textsuperscript{1,2} Most often, these have been linked with failure to insert the implant or incorrect timing of insertion (women who were either pregnant or became pregnant very soon after implant insertion).\textsuperscript{3} Liver enzyme-inducing drugs, including natural therapies like St John’s Wort, are known to affect the efficacy of hormonal contraceptives including Implanon.\textsuperscript{3} However, there are a small number of true method failures being reported. The present case demonstrates that these true method failures may result from rapid hormone metabolism.

During the research and development of new hormonal contraceptive methods a safety window is built in to take account of individual metabolic variation. Initial studies with Implanon demonstrated that less than 5\% of women ovulated whilst using this contraceptive method.\textsuperscript{4} Although Implanon’s main contraceptive mode of action is to induce anovulation, it also exerts its contraceptive effects by altering the cervical mucus to reduce sperm penetration and altering the endometrium to prevent sperm survival and implantation of the blastocyst.\textsuperscript{4}

This patient had previously reported a method failure whilst taking the combined oral contraceptive pill. It can only be concluded that this unplanned pregnancy resulted from very low circulating levels of etonogestrel. Although Implanon is probably one of the most effective long-acting reversible methods of contraception (with failure rates quoted as <1 in 1000 women over a 3-year period)\textsuperscript{5} this case demonstrates that there is a small group of women who may report repeated unplanned pregnancies whilst supposedly using effective hormonal contraceptive methods.

Where do we go from here? Organon Laboratories are supportive of investigating women with true method failures. If similar cases are identified then it would be helpful if the medical adviser at Organon Laboratories is contacted. Arrangements can be made to collect serum to be assayed for etonogestrel (prior to removing the implant) and if the implant is removed this too can be analysed. This small cohort of women may agree to further investigation in the future to aid contraceptive technology development.

At the present time the most satisfactory and effective contraceptive methods available to this group of women are progestogen-only injectables, copper intrauterine devices, the levonorgestrel intrauterine system or permanent fertility control methods.

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References

Implanon® failure or a natural event?

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