Subdermal implantable contraceptives versus other forms of reversible contraceptives or other implants as effective methods of preventing pregnancy

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Subdermal implantable contraceptives are highly effective, easy to use and carry a low risk of side-effects. These features make them a good option for women in under-resourced settings. However, data are lacking on the performance of contraceptive implants compared with other contraceptive methods.

RHL Commentary by Bahamondes L

1. EVIDENCE SUMMARY

The present review (1) is a revised version of a 1998 review (2). It sought to 'assess the effectiveness, tolerability and acceptability of subdermal implants' in comparison with other reversible methods of contraception. Since the authors were unable to identify any randomized controlled trials comparing contraceptive implants with other forms of contraception, the focus of the review shifted to a comparison of different types of implant.

The authors identified nine trials that met the inclusion criteria for the review. Eight trials compared Implanon (a single-rod etonogestrel-releasing implant) with Norplant (the 6-rod levonorgestrel-releasing implant), and one compared Implanon with Jadelle (the 2-rod levonorgestrel-releasing implant) (3–7). It is worth keeping in mind that currently a WHO trial is under way in which Implanon and Jadelle are being compared with a copper-bearing intrauterine device (IUD).

The main finding of the review was that Norplant, Jadelle and Implanon are highly effective methods of contraception: only two, three and zero pregnancies were recorded in 4377, 2307 and 2068 women–years of follow–up, respectively. These figures represented pregnancy rates of 0.05, 0.13, and 0 per 100 women–years of use for Norplant, Jadelle and Implanon, respectively. There were no statistically significant differences between the three implants with respect to contraceptive efficacy. The age range of the women in the trials was 18–40 years.

The review also evaluated bleeding disturbances and amenorrhoea associated with subdermal implantable contraceptives. Bleeding disturbances and amenorrhoea constitute one of the most important side-effects, which could lead to premature discontinuation of the method, possibly resulting in unintended pregnancy if the woman does not switch over to another contraceptive method. With respect to bleeding disturbances, infrequent bleeding [odds ratio (OR) 1.30; 95% confidence interval (CI) 1.04–1.63] and prolonged bleeding (OR 1.49; 95% CI 1.09–2.03), per a 90-day reference period, were more likely to occur among Implanon
users compared with Norplant users (8–10). In addition, amenorrhea was found to be statistically significantly higher in users of Implanon compared with those of Norplant (OR 1.87 and 95% CI 1.45–2.42 for 1 year of use; and OR 2.14 and 95% CI 1.63–2.81 for 2 years of use), and increased with number of years of use. Nevertheless, it is possible that the rate of amenorrhea may be affected by the number of discontinuations. For this reason, caution is required in the interpretation of these data and women should be informed with respect to the differences between the different types of implant.

Method continuation rates for the three implants were similar at 1, 2, 3 or 4 years. However, continuation rates varied with the type of setting: overall, at two years, 90.6% of Implanon users and 91.4% Norplant users were continuing with their methods in developing countries compared with 55.4% of Implanon users and 47.5% of Norplant users in developed countries.

Regarding hormonal side-effects or adverse events, no significant differences were found between the three types of implant evaluated. The time required to insert and remove the different types of implant was also evaluated in the review, although only limited data were available. Implanon was significantly quicker to insert and remove compared with Norplant, probably because Implanon is a single-rod implant whereas Norplant consists of six rods. Similarly, Jadelle was significantly quicker to remove compared with Norplant, probably also because Jadelle contains only two-rods.

Even though no trials were available to answer the authors' original question, the quality of the included studies and the methods employed by the review authors are sound. The selection of studies was independently evaluated by the three authors of the review and the quality of the trials was assessed independently by two of them. In general, the authors followed the methodological guidelines for calculating method failure rates recommended by Trussell (11). They also contacted the authors of some of the studies, as well as the pharmaceutical companies that manufactured the two models of implants, to obtain additional data.

2. RELEVANCE TO UNDER-RESOURCED SETTINGS

2.1. Magnitude of the problem

During the last 30 years there has been a global decline in total fertility rate (TFR), even in countries in which TFR was high in the 1960s. TFR declined worldwide from around six in the 1950s to around three at the beginning of the new millennium. In addition, TFR simultaneously declined to the same extent in most of the developing countries (12). Nevertheless, the unmet need for contraceptive methods and services in the developed and developing world remains high.

The rate of unintended pregnancies around the world is extremely high, not only in developing countries, but also in the developed world. For example, in the USA almost half of all pregnancies are unintended or unplanned and over one third result in an abortion (13). About 60% of unplanned pregnancies occur in women using some form of contraception, even during the month in which they conceived (14), and this probably occurs due to the difficulty that some women have in correctly and consistently using some of these methods (13).

One of the advantages that implants and other methods such as the IUD offer over other contraceptive methods is that they are not user-dependent in the way that condoms, injectables and combined oral contraceptives (COC) are. Hence, implants and IUDs do not have differences in efficacy rates between “perfect use” and “typical use” (15). Norplant was the first contraceptive implant system to become available and has been on the market since 1983, after which the other two were developed. Implants are approved in more than 60 developed and developing countries and are currently being used by millions of women worldwide (16). Owing to their high contraceptive efficacy (which begins almost immediately after insertion), low rate of complications and side-effects, possibility of long-term use following a single intervention and the rapid return of fertility after removal, contraceptive implants are good candidates for
inclusion in the method mix offered by family planning programmes, especially in under-resourced settings (17).

2.2. Applicability of the results

The findings of this review are important because they apply equally to developed and developing countries. Much of the data included in the trials covered in this review were gathered in developing countries. The reported continuation rates for implants were high, with almost 80% of the women still using the method two years after insertion. However, this figure must be interpreted with caution because women in clinical trials tend to be more enthusiastic about persisting with a method than those in real-life conditions of use.

Caution should also be exercised in interpreting the efficacy of Implanon based on the findings of the review. Although the review authors reported no pregnancies among Implanon users, the actual situation is slightly different. During the period between the introduction of Implanon in 1998 and March 2007, a total of 1688 pregnancies were reported, resulting in an overall postmarketing Pearl Index of 0.024 (data on file, Organon International, Roseland, NJ, USA). In fact, the actual number of pregnancies that have occurred worldwide among Implanon users is unknown; the Organon figures are a compilation of spontaneous reports, not figures reported in randomized controlled trials. Most of the pregnancies were attributable to three causes: (i) insertion of the implant in women who were already pregnant or insertion after the recommended first few days of the cycle; (ii) concomitant use of hepatic enzyme-inducing antiepileptic drugs; and (iii) failure to insert the implant (18, 19). This implies that, like all contraceptive methods, subdermal implants are also prone to failure, although failure rates of implants are extremely low.

In addition, it has been demonstrated that among women participating in trials and those in developing countries are more likely to continue with implantable contraceptives compared with those in developed countries. If we take into account that the most common side-effect is bleeding disturbances and that this side-effect is responsible for many of the early discontinuations, we can speculate that women in developing countries are more willing to accept this inconvenience, perhaps because they are benefiting from being able to use a highly-effective contraceptive method. Moreover, women's decision to remain in a study and continue using the same method may be related to their having received accurate information about the method.

2.3. Implementation of the intervention

The number of users of implants is still low, especially in developing countries. One explanation for this may be that the cost of implants is high and at the beginning of use compared with other contraceptive methods. However, it may be worth noting that organizations such as the United Nations Population Fund help developing countries to obtain these methods at low, public-sector prices. Consequently, many countries are able to provide the method free of charge or at a very low cost to low-income users.

On the other hand, contraceptive implants could be considered inexpensive and cost-effective if the number of years of use is taken into account. However, if the number of women who discontinue prematurely is high, then the cost may be correspondingly high. For this reason, counselling is crucial to inform potential users about possible side-effects and to reassure them about the method, especially with respect to side-effects. Amenorrhoea/irregular bleeding is one of the most common side-effects of progestogen-only contraceptives. The acceptability of bleeding disturbances induced by implantable progestogen-only contraceptives varies in different cultures. Good counselling before implant insertion is very important and can increase the continuation rate. Different strategies have been used to treat bleeding irregularities in users of progestogen-only contraceptive implants, but without much success (20).

Insertion and removal of implants requires well-trained health-care providers. In addition, adequate infection prevention and control, and waste disposal must be implemented at the service delivery points, and personnel must be available every day to perform removals upon request. Moreover, adequate information, education and communication materials must be provided to avoid women being influenced by
misinformation.

3. RESEARCH

This systematic review was unable to compare the effectiveness and side-effects of different implants with other contraceptive methods. Fortunately, WHO is currently conducting a trial in which Implanon and Jadelle are being compared with each other and with a copper-bearing IUD. Data from this study can be expected by the middle of 2009.

In the case of contraceptive implants, more studies are needed on the perspectives of users regarding the method and the perspectives of women and their partners regarding the amenorrhoea provoked by the method. In addition, in this review the authors used continuation rate of the method as a marker of acceptability, while reported side-effects were used as a marker of tolerability. Continuation rate is not synonymous with acceptability because users in real life may be different from participants in clinical trials. Likewise, side-effects do not necessarily reflect tolerability for the same reasons mentioned above. It should be noted that not all women with side-effects will discontinue the method, since their decision to discontinue may in fact reflect other factors as observed by the substantial differences in the discontinuation of implants in developing countries (90.6% of women continuing to use Implanon and 91.4% Norplant at 2 years) compared with developed countries (55.4% for Implanon and 47.5% for Norplant at 2 years) (1). However, these findings may also be interpreted as women in developing countries not having a wide choice of contraceptive methods.

References

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