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Review

Executive summary

Implantable contraceptives (subdermal implants and hormonally impregnated intrauterine systems) versus other forms of reversible contraceptives: two systematic reviews to assess relative effectiveness, acceptability, tolerability and cost-effectiveness

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Background

Research on progestogen-only contraceptive subdermal implants and hormonally impregnated intrauterine systems (IUSs) started in the mid-1970s, with some, including Norplant® and the LNG-20 IUS (Mirena®), receiving licences for use in the UK by the early 1990s. Implanon® became available in the UK in autumn 1999. Since this review was commissioned Norplant has been withdrawn from the UK market because of adverse publicity.

Aims

- To assess the contraceptive efficacy, tolerability and acceptability of subdermal implants and IUSs in comparison with other reversible contraceptive methods.
- To use these data to determine the relative cost-effectiveness.

Methods

Data sources

Literature was identified through electronic database searches, reference lists and contacting individuals/organisations working in the field.

Study selection

All prospective intervention studies that compared subdermal implants or IUSs with other forms of reversible contraceptives and reported pre-determined outcomes in women of reproductive years were included. The primary outcomes measures reviewed were pregnancy due to method/user failure and continuation of contraceptive method.

Data extraction

The quality assessment of studies and data extraction were completed independently by two blinded reviewers. A quality check list was designed to identify general methodological and contraceptive-specific factors which could bias results. Events per women months and single decrement life-table probabilities were extracted for pregnancy, continuation, adverse events and reasons for discontinuation. Events per total number of women at follow-up were collected for hormonal side-effects, menstrual disturbance, and planned pregnancy after discontinuation of method.

Data synthesis

When appropriate, data were pooled at the same time points of follow-up and rate ratios were calculated to determine the relative effectiveness of contraceptive methods. For single decrement life-table probabilities, probability differences were pooled to determine the absolute difference in effectiveness. Interventions were combined only if the contraceptive methods were similar (e.g. studies comparing IUSs with copper intrauterine devices (IUDs) > 250 mm^3 were combined, and studies comparing IUSs with copper-bearing IUDs ≤ 250 mm^3 were combined). (The categorisation of copper-bearing IUDs was based on the surface area of the copper wire.)

Results

Subdermal implants

Thirty-four comparative studies met the inclusion criteria. The majority of studies were comparisons of different types of implant, although there was a broader range of comparisons in the non-randomised controlled trials (non-RCTs). In many of the non-RCT studies the intervention groups were often dissimilar at baseline. It was possible to combine the data from only a few studies as it was deemed inappropriate to use data from investigations of prototypes.

- For Norplant, the most common comparison was with other types of subdermal implant, followed by comparisons with IUDs. There was no significant difference in the pregnancy rate among users of Norplant compared with users of other contraceptive methods (Level 1a* for Norplant versus Implanon – there were no pregnancies with either method; level III versus other methods). Norplant users were about twice as likely to continue with the method compared with women using oral contraceptive pills, vaginal rings or depomedroxyprogesterone acetate (DMPA) injections (III).
- There was no evidence of differences between Norplant users and users of other contraceptive

*Type of evidence (based on Agency for Health Care Policy and Research (USA), 1994). Ia: evidence obtained from the meta-analysis of RCTs. Ib Evidence obtained from at least one RCT. IIa: evidence obtained from at least one well-designed controlled study without randomisation. IIb: evidence from at least one other type of well-designed quasi-experimental study. III: evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case–control studies.

methods in relation to planned pregnancy following removal (IIa), hormonal side-effects (III), or adverse clinical events (Ib). Norplant users were significantly less likely than IUD ≤ 250 mm^3 users to expel the device (III). When Norplant was compared with IUDs > 250 mm^3, there were significantly lower rates of dysmenorrhoea, spotting, menorrhagia and prolonged bleeding (III). Norplant users were significantly more likely to experience amenorrhoea than users of IUDs > 250 mm^3 or the contraceptive pill (III).

- Norplant users were 90% less likely to discontinue for menstrual reasons compared with women having DMPA injections (III). The only other significant difference observed was that Norplant users were less likely than pill uses to discontinue the method for personal reasons.

Hormonally impregnated IUSs

- Twenty-nine intervention studies with IUSs met the inclusion criteria. With one exception (a study that compared the LNG-20 IUS with Norplant-2) all were comparisons between different types of IUS or between IUSs and IUDs. It was possible to pool data from only a few studies.
- There was no evidence that LNG-20 IUS users differed from users of IUDs > 250 mm^3 (Ia) in terms of unplanned pregnancy. In the comparison of the LNG-20 IUS with IUDs ≤ 250 mm^3 (Ia), LNG-20 IUS users were significantly less likely to have either intrauterine or extrauterine pregnancies when rate ratios were calculated (i.e. events per women months).
- Calculation of differences in single decrement life-table probabilities indicated that after 5 years women assigned to the LNG-20 IUS were significantly less likely to continue with the method than were women assigned to the IUD > 250 mm^3. However, this difference was not evident when rate ratios were pooled (Ia).
- LNG-20 IUS users were more likely to experience amenorrhoea (Ib) and device expulsion (Ia) compared with IUD > 250 mm^3 users. There was no evidence of other significant differences between methods, in terms of the occurrence of acne, headaches, breast tenderness, nausea, prolonged bleeding, embedded device, or pelvic inflammatory disease (Ib).
- LNG-20 IUS users were more likely than other IUD users to discontinue because of hormonal side-effects (Ia) or menstrual disturbance (Ib) (specifically amenorrhoea [Ib]). No other significant differences in reasons for discontinuation were observed.

Cost-effectiveness analysis

The economic evaluation was informed by the results of the systematic review and meta-analyses, which provided data on the effectiveness and the duration of use of the compared alternatives.

Generally the cost-effectiveness ratios for subdermal implants and IUSs were quite high, indicating that they were on balance more costly per pregnancy averted than the contraceptive methods with which they were compared. This was explained by the low incremental effectiveness of these methods relative to the other contraceptive methods.

Conclusions and recommendations

There was insufficient evidence from the comparative studies included in these systematic reviews to suggest that one type of subdermal implant was any more or less effective in preventing pregnancy than another, that implants were any more or less effective than the other methods with which they were compared, or that the LNG-20 IUS was any more or less effective than IUDs > 250 mm^3. LNG-20 IUS users were significantly less likely to experience either intrauterine or extrauterine pregnancies than were IUD ≤ 250 mm^3 users. Women using the LNG-20 IUS were more likely to experience amenorrhoea, and this event was a notable reason for discontinuation of IUSs.

Poor study design, lack of clarity in measurement of contraceptive effectiveness and heterogeneity between studies hindered synthesis of data. The following recommendations are made on the basis of the evidence from these reviews.

1. Standardisation of methods and measurements used in contraceptive research should be encouraged.
2. Well-designed prospective cohort studies should be carried out to follow up women using different contraceptive methods.
3. An RCT is required to assess the impact of counselling on discontinuation rates of subdermal implants and IUSs, particularly in relation to the effect of amenorrhoea.
4. There should be consumer involvement in the development of contraceptive research to identify user-related questions.
5. Evaluation should be carried out to determine the most effective training for healthcare workers in the insertion and removal of implantable contraceptives.
6. Economic endpoints should be included in primary research on methods of contraception.

Publication

French RS, Cowan FM, Mansour DJA, Morris S, Procter T, Hughes D, *et al.* Implantable contraceptives (subdermal implants and hormonally impregnated intrauterine systems) versus other forms of reversible contraceptives: two systematic reviews to assess relative effectiveness, acceptability, tolerability and cost-effectiveness. *Health Technol Assess* 2000;**4**(7).

NHS R&D HTA Programme

The overall aim of the NHS R&D Health Technology Assessment (HTA) programme is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and work in the NHS. Research is undertaken in those areas where the evidence will lead to the greatest benefits to patients, either through improved patient outcomes or the most efficient use of NHS resources.

The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

This report is one of a series covering acute care, diagnostics and imaging, methodology, pharmaceuticals, population screening, and primary and community care. It was identified as a priority by the Pharmaceutical Panel and funded as project number 95/41/01.

The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In particular, policy options in the area of screening will be considered by the National Screening Committee. This Committee, chaired by the Chief Medical Officer, will take into account the views expressed here, further available evidence and other relevant considerations.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

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Reports are published in the HTA monograph series if (1) they have resulted from work either prioritised by the Standing Group on Health Technology, or otherwise commissioned for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

The editors have tried to ensure the accuracy of this report but cannot accept responsibility for any errors or omissions. They would like to thank the referees for their constructive comments on the draft document.

Copies of this report can be obtained from:

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