Counting the costs: Comparing depot medroxyprogesterone acetate and norethisterone oenanthate utilisation patterns in South Africa

ABSTRACT

Providing IPCs on the basis of age is not appropriate or cost effective. Rational use of these products should include consideration of the cost of prescribing one over another.

INTRODUCTION

Introduction Affordability of drugs by developing countries is currently a topic of heated debate. In South Africa, where financial resources for health care are limited, and where health care costs are expected to soar as the HIV epidemic escalates, it becomes increasingly important to ensure that all drugs are rationally provided and used. The injectable progestagen-only contraceptives (IPCs) depot medroxyprogesterone acetate (DMPA) and norethisterone oenanthate (NET-EN) are by far the most widely utilised contraceptives in South Africa, especially amongst younger users and women living in rural areas. Both drugs are on the South African Essential Drug List and are available free of charge at public sector primary health care facilities. Although not extensively documented, it is claimed that there has been a shift away from the predominant use of DMPA, which is given every 12 weeks, to NET-EN, given every 8 weeks, especially amongst younger, nulliparous women. Combined injectable contraceptives (CICs), which contain a combination of oestrogen and progestagen, are not registered for use in South Africa. The World Health Organisation's general criteria - safety, affordability, necessity and efficacy - for inclusion on the Model List of Essential Drugs (EDL) provide a useful basis upon which to make decisions about drug selection and rational use. Taking into account published findings on efficacy, reversibility, side effects and safety, this paper analyses IPC supply patterns and costs from four pharmaceutical depots, and describes a case study of IPC utilisation patterns and side effects in a rural sub-district of KwaZulu-Natal, South Africa. Based on these analyses, appropriate recommendations for the rational use of IPCs are made. What the literature tells us Published clinical trials and reviews on efficacy, side effects, reversibility and safety of DMPA and NET-EN were sought by means of computerized and hand searches. Copies of relevant publications and citations from these publications were obtained and reviewed. Relevant international and South African policy documents were also reviewed. This extensive search revealed that: DMPA is better researched than NET-EN, few studies directly compare DMPA and NET-EN, few clinical trials have been undertaken in Southern Africa, few clinical studies have been undertaken amongst young users, and most published studies, upon which review after review are based, were undertaken in the 1970s and early 1980s. Methodological differences in subject recruitment, exclusion criteria, frequency and nature of procedures for follow-up, types of observations made, method of recording, methods of analysis and large intersite variability in some studies, make it difficult to evaluate the published data. Trussel et al. provide a useful account of difficulties in analysing and comparing contraceptive efficacy trials. Nevertheless, to the extent that this is possible, a comparative synopsis of the efficacy, side effects, delay in return to fertility and safety of DMPA and NET-EN is provided in this section. It is not the purpose of this paper to provide a detailed review, but merely to highlight relevant findings. The authors can be contacted for a more extensive bibliography. Both IPCs are demonstrably highly effective. There are minor differences in published efficacy rates of both drugs depending on the study, timing of the first

injection, the population, body weight, dosage regimen and provider training. An illustration of the high efficacy of these two products is provided by a World Health Organisation (WHO) comparative trial. According to this study the efficacy of DMPA given every 90 days and NET-EN given every 60 days are comparable, with a cumulative 2-year pregnancy rate of 0.4 per 100 woman-years. In an evaluation of 5 large controlled multicentre studies, Kaunitz reported that there were only 24 pregnancies among 7 849 women using DMPA for 122 496 patient-months. Trussel et al. provide "summary estimates of contraceptive failure" and give the lowest expected, and typical percentage, of accidental pregnancies in the United States, during the first year of use, as 0.3 for DMPA and 0.4 for NET-EN (unspecified dose interval). There is little direct comparative data on the reversibility of DMPA and NET-EN. While return to fertility is reported by some reviewers to be more rapid with NET-EN, more recently, Bigrigg et al. in examining early data, suggest that there is no delay in return to fertility with DMPA use, if one considers the methodological bias of early studies, which did not take in to account the date of the last DMPA injection. They state further that "if there is a delay it is not statistically significant and is less than 30 days". Kaunitz gives the shortest reported time before fertility is returned with DMPA, as 4 months after the last injection i.e. 4 weeks after the due date of the next injection and, according to Hatcher et al. return to fertility is delayed by DMPA for about 4 months longer on average, compared with the combined oral contraceptive method, intrauterine contraceptive device, and condoms. The poor side effect profile of progestagen-only injectables is extensively documented. The most frequently reported side effects, and those most likely to result in discontinuation, are menstrual disturbances such as amenorrhoea, irregular bleeding and heavy bleeding. Menstrual irregularities are reported to occur more often with DMPA than with NET-EN use. For instance, the WHO clinical trial undertaken in 1983 compared menstrual disturbances resulting from DMPA given at 90-day intervals, with NET-EN given every 60 days and with NET-EN given every 60 days for 6 months and then every 84 days. Significantly less amenorrhoea was reported by NET-EN users (on both dosage regimens), than by DMPA users. Amenorrhoea was also found to result in significantly higher discontinuation rates with DMPA users than with NET-EN. During the first six months of use, both dosage regimens of NET-EN were reported to result in more defined cyclic patterns and fewer prolonged bleeding and spotting episodes than DMPA, but similar discontinuation rates were found with the two products. However, in a study undertaken in Egypt, despite the more frequent occurrence of menstrual irregularities with DMPA, better one-year continuation rates were found with DMPA than with NET-EN. Weight gain is also a commonly reported side effect and in comparing DMPA and NET-EN, the findings on weight gain appear to be similar. A multinational WHO comparative clinical trial found no statistical difference in weight gain between NET-EN and DMPA (both administered at 12 week intervals) after a year of use - the weight gain with NET-EN was reported as 1.5 kg and with DMPA was 2.0 kg. Headache was the most common non-menstrual side effect reported in this comparative trial and was more frequently reported by DMPA users than NET-EN users, however, it is important to note that in this study, NET-EN was administered every 12 weeks. IPCs are considered to be relatively safe contraceptive methods and recent studies indicate that there is little reason to be concerned about either DMPA or NET-EN causing an increased risk of breast cancer. However, the possible effect of DMPA on bone density, particularly in adolescents and long-term users is cause for concern. Little is published on the possible effect of NET-EN on bone density. Findings from prospective studies in progress are awaited. The World Health

Organization's Medical Eligibility Criteria for Contraceptive Use classifies DMPA and NET-EN together, and makes no differentiation between the two in regard to their side effects or contraindications. The only restriction this document makes about age, for IPC use, is that "For women under 16 years of age, there are theoretical concerns regarding hypo-oestrogenic effects...." p.54. The WHO states further that there is no need to restrict use of progestagen-only contraceptive methods for nulliparous women. The Primary Health Care Essential Drugs List for South Africa provides no guidelines with respect to the circumstances under which DMPA rather than NET-EN should be prescribed (or vice versa).

CONCLUSION

Conclusions and Recommendations Providing IPCs on the basis of age is not appropriate or cost effective. Training of health workers and counselling of clients to correct this misconception is clearly required. Where clients require immediate return to fertility upon discontinuing contraception, neither IPC preparation is ideal. Since DMPA is a cheaper option than NET-EN, health worker training about the rational use of injectable contraceptives should include consideration of the cost implications of prescribing one product over another. DMPA should be considered as the first option, but where DMPA is not well tolerated, NET-EN should be available as a second option. It is also recommended that a comparative systematic review of DMPA and NET-EN be undertaken. Based on the outcome of this review, consideration may be given to conducting a comparative clinical trial of NET-EN and DMPA when used by African women. Consideration should be given to encouraging the registration of the combined injectable contraceptive in South Africa, which has a better side effect profile than the IPCs. This would be an expensive option thus combined injectable contraceptives should only be provided where side effects with the IPCs are intolerable. A better contraceptive option, especially for young people, might however be the male or female condom with back up of emergency contraceptive pills to provide dual protection against unwanted pregnancy and HIV and other sexually transmitted infections.