INTRODUCTION

The potential for weight gain is an important issue when considering contraceptive methods. One reason for this concern is the increasing rates of obesity in developed, affluent societies.1,2 Despite the availability of numerous types of contraceptives, there remains a need for effective and reliable contraceptive options with improved adverse event profiles. Recently, a subcutaneous formulation containing a lower dose of active compound Depot medroxyprogesterone acetate has been developed, which is expected to provide an improved adverse event profile and potentially to increase compliance by eliminating the need for periodic return to the health care system for injections.1,2 Depot medroxyprogesterone acetate has been approved for use as a contraceptive in more than 100 countries worldwide.3

ABSTRACT

Objective: To determine the 1-year efficacy of contraception, changes in bleeding pattern and weight with the use of Depot medroxyprogesterone acetate-subcutaneous injected subcutaneously once every 3 months.

Study Design: Descriptive case-series.

Place and Duration of Study: Gynaecology and Obstetrics Unit, Holy Family Hospital, Rawalpindi, from March 2003 to June 2004.

Methodology: Twenty five patients were selected by purposive sampling and followed up in Holy Family Hospital, Gynaecology and Obstetric Unit for a one-year period using DMPA-SC every three months. Hospital Ethical Committee permission was obtained prior to commencement of the study. Informed written consent was taken. Body weight was measured at baseline and every 3 months thereafter. Bleeding analysis in terms of blood flow and severity of bleeding was also done at 3 months interval using a 5-point scale.

Results: DMPA-SC showed 100% efficacy in preventing pregnancy in the 25 patients who were followed up. Mean and SD of age was 34.24±3.57 years. Mean and SD of weight was 63.44±13.81 kg. There was a mean weight gain of 0.1 kg at visit 1-3 (first 3 months) and an average weight gain of 1.036 kg at the end of the year. There was a trend towards amenorrhea with 56% of the patients included in the category of bleeding less than usual at the end of treatment period.

Conclusion: DMPA-SC can be used in women desiring reversible contraception with unremarkable weight gain and overall bleeding pattern leading towards amenorrhea.

Key words: DMPA-SC. Contraception. Body weight. Amenorrhea.
progestosterone acetate-subcutaneous (DMPA) injections offer estrogen free contraception without the need for frequent dosing. Prolonged use of DMPA may lead to a decrease in bone mineral density, which may not be completely reversible. The potential impact on bone mineral density should be considered when assessing DMPA as a contraceptive option. A common effect is irregular menstrual bleeding, which decreases with time, usually resulting in amenorrhea. 

This article presents the results of 25 patients who were a part of two large, pivotal Phase 3 contraceptive trials of Depot medroxyprogesterone acetate-subcutaneous (DMPA-SC). One of these multinational trials was conducted in North and South America; the other in Europe and Asia. Pakistan was part of the Asian countries trial in which we have presented the data of 25 patients who underwent the one year trial of DMPA-SC (March 2003 to June 2004) and completed it successfully at the Holy Family Hospital (Gynaecology and Obstetrics Unit). Permission from the respective company was obtained to present the data of these patients from the Holy Family Hospital. Formal Ethical Committee permission was also obtained from the concerned authorities of the hospital before the commencement of the study.

The objective was to determine the one year contraceptive changes in bleeding pattern and weight changes with the use of Depot medroxyprogesterone acetate-subcutaneous which was injected (104 mg/0.65 ml) once every 3 months.

**METHODODOLOGY**

This study was a descriptive case series. It was a Phase 3, multinational, one year trial of DMPA-SC 104, conducted in 5 centres of Pakistan as part of the Asian Trials (Europe/Asia N=1065); two centres in both Karachi and Lahore each and one centre in Rawalpindi. Twenty five patients were followed up at the Rawalpindi centre (Holy Family Hospital, Gynaecology and Obstetrics Unit) for a one-year period as part of the Asian trial as they successfully completed their contraception for the one year (March 2003 to June 2004). Ethical Committee permission was obtained prior to the commencement of the study. Informed written consent was obtained from the patients before their enrollment in the study.

The patients were selected by purposive sampling for the study and included women who were in the reproductive phase of their lives i.e. women with child bearing potential (CBA’s). These women had normal 28-35 day menstrual cycles with no history of menorrhagia. Their partners were using a barrier method of contraception, namely condoms, and these women had not used any hormonal contraceptive pills at least for the last 3 months. They also did not receive any DMPA-SC injection nor an IUD (intrauterine contraceptive device) in the last one year. Clinical and gynaecological examination were done in these women to rule out any co-morbid disease like diabetes, hypertension, raised or abnormal liver function tests or menorrhagia. Their Pap smears showed normal cytology and all the women who were above 35 years were required to undergo mammography for screening and selected if found normal. Informed written consent was taken.

The first dose of Depot medroxyprogesterone acetate-subcutaneous (DMPA-SC) was initially injected at visit 1. It was ensured that the woman was still menstruating and it was administered at day 5 of the regular menstrual cycle. Its dose was 104 mg/0.65 ml. The injection was then administered subsequently after every 3 months for a year. The route was subcutaneous usually administered on the anterior abdominal wall or anterior thigh.

Body weight was measured at baseline and every 3 months thereafter (at each injection visit). Changes from baseline in body weight among women receiving DMPA-SC 104 in each study were analyzed. Analyses included summary changes (means and SD) from baseline at each visit. During each trial, subjects recorded their bleeding patterns in diaries at the end of each day using a five point scale, 0=no flow, 1=spotting (mini pad or no protection required), 2=bleeding less than usual (requiring sanitary pads or tampons), 3=bleeding approximately the same amount as usual and 4=bleeding more than usual. The data was analyzed according to 90 days intervals starting from the date of the first dose of study medication. The 90 day interval was chosen to identify changes over time (cumulative bleeding pattern analysis over a 3-month period showing bleeding changes in every month). Visit 2 was an exception, where bleeding pattern analysis was done after one and half month.

All analysis was done in SPSS version 13. Mean, SD were calculated for quantitative data and frequency percentage were calculated for all qualitative data. Demographic data was presented. Frequencies and percentages were calculated for categorical variables like bleeding pattern changes. Mean and SD were calculated for the numerical variables like age, weight, height and BMI (body mass index).

**RESULTS**

A total of 25 patients were included in the study. The mean age in years at the time of visit one was 34.24 years with SD of 3.57 years. Mean weight in kilograms was 63.44 kg and SD was 13.81 kg (at visit 1). Mean height at baseline was 156 cm.

The average weight gain at each visit was 0.1-0.2 kg till visit 3 (three months) but then there was an average total weight gain of 0.66 kg at visit 4 (six months), 0.84 kg at visit 5 (nine months), and then 1.036 kg at
visit 6 (at twelve months) from baseline Depot medroxyprogesterone acetate-subcutaneous (104 mg/0.65 mL) was injected once every 3 months at visit 1 and from visit 3 to visit 6, (visit 2 was a follow-up without the injection). A majority of the patients were in the category of bleeding less than usual. About 44% of the patients were in this category at visit 4 (six months) and 56% patients at visit 5 (nine months).

As is apparent from Figure 2, there was a trend over the period of one year towards bleeding less than usual and some blood drops ultimately leading to amenorrhea in some cases.

**DISCUSSION**

Figure 1 shows weight change analysis with an average weight gain of 0.1 kg at visit 1, the trend remaining consistent till visit 3. There is a slight increase of at visit 4 and eventually mean weight gain of 1.036 kg at visit 6 or end of the year. Several studies reported no significant weight changes in women using DMPA-IM 150 for upto one year, while other studies reported substantial mean weight gains, ranging from approximately 1.35-4.50 kg over one year. Injectable contraceptive methods have been proved to be safe, highly efficacious, and commonly used worldwide.

Depot medroxyprogesterone acetate (DMPA) should be available as a first line method to all those who wish to make an informed choice about reversible methods of contraception. Pre-use counseling is essential to minimise the effect of menstrual change which occurs in most patients.

It is ideal for patients with contraindications to estrogen use and certain medical conditions. Side effects with this method even when they are negligible, including irregular bleeding, breast tenderness, weight gain, and the impact on bone mineral density should be taken into consideration when prescribing the method.

In this study, on the average, 28% of the patients were in category 2 belonging to bleeding less than usual. Then from visit 4 onwards, the percentage of patients in this category increased, going upto 44%, with a maximum of 56% at visit 5 (9 months into the study). After that, the trend declined with 36% patients in this category at visit 6 (month 12) as shown in Figure 2. Irregular menstrual bleeding has been a common side effect of Depo-Provera injection, which decreases with time.

Overall, in a multitude of different studies, changes in bleeding patterns associated with DMPA-SC 104 use have showed no consistent differences according to the subject's age or BMI. Among women experiencing bleeding and/or spotting while on DMPA-SC 104, the likelihood of achieving amenorrhea has increased with each injection, as shown by the bleeding shift analysis.

Figure 2 shows the bleeding pattern on each visit. In the beginning, till visit 2, patients’ bleeding cycles were mostly unaffected. Then from visit 3 onwards, there was a trend towards amenorrhea, which became apparent from visit 4 (month 6). The percentage of patients belonging to the category of excessive bleeding also declined after visit 3 (month 3).

All progestin-only methods, whether low or high dose, lead to menstrual disturbances. Although troublesome, the menstrual disturbances which occur in DMPA users very rarely require operative or medical intervention, and can often be improved simply by short courses of estrogen or shorter injection intervals. Again, women need to know what can be done so that they are aware that they should seek early medical advice, rather than anxiously waiting for their 12 week appointment. DMPA
Body weight and bleeding pattern changes in women using DMPA-SC

has no appreciable effects on blood pressure or thrombosis risk. In this, it has an advantage over the combined oral contraceptive pill, and provides a simple, effective alternative for women who cannot use the pill for these reasons. DMPA-SC is just as effective as the formulation injected into the muscle, and the patterns of bleeding changes and amount of weight gain are similar. One year continuation rates in clinical trials were high, 68% on average at sites in North and South America and 80% in Europe and Asia. Despite the lower dose, DMPA-SC is effective for overweight or obese women.

Limitations: The sample size of this study is small as only 25 patients were followed up in the Rawalpindi centre. Also, this is a descriptive case series, and there is no comparison group. The study period was only one year and patients were followed up for another 3 months. Strict parameters could not be followed for the weight gain as BMI was determined at every visit but BMR and nutritional evaluation could not be done.

CONCLUSION

DMPA-SC (Depot medroxyprogesterone acetate-subcutaneous injection can be used in women desiring contraception who have no co-morbid medical conditions. Over a period of time, with the use of DMPA-SC, the overall bleeding pattern in patients leads towards amenorrhea and an unremarkable weight gain. Pre-use counseling is essential to deal with the effects of menstrual changes which occur in most patients.

REFERENCES