Sonar findings of the uterus in patients on medroxyprogesterone acetate (Depo Provera) 150 mg injection

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Abstract

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Background: Depo Provera (medroxyprogesterone acetate) 150 mg intramuscular injection every 12 weeks is one of the most common, effective, affordable and popular methods of contraception. Depo Provera shows excellent results in comparison to oral contraceptive agents as well as the contraceptive patch.

Objective: The aim of the study was to determine the effects of the chronic use of medroxyprogesterone acetate 150 mg injections on the endometrium and myometrium of the uterus as measured by means of ultrasound.

Methods: An analytical case-control investigation was performed. Two groups were included and participants were actively selected and recruited by the researcher. Patients in both groups were similar with regard to socio-economic background, age and clinical profile. Each patient in the study group was paired with a patient in the control group. During patients' visits, measurements were performed by means of a Medison Sonoace 5500 digital ultrasound apparatus. A structured interview was conducted with each participant in order to obtain relevant patient information.

Results: Fifty participants were recruited and selected for both the study group and the control group. All the participants were women from the Thaba Nchu and Botshabelo municipal areas in the Free State Province, served by the researcher's private general practice in Botshabelo. Participants in the study group (20–46 years; median age 31 years) were treated with Depo Provera, while the control participants (19–48 years; median age 30.5 years) were not on any chronic medication or hormonal contraception, did not have intrauterine devices and were not pregnant or breastfeeding during the 12 months preceding the study. The medians of all the parameters (uterus length and width; endometrial thickness) were determined in the patients selected from the researcher's practice. The presence of uterine myomata was documented and compared between the two groups. Statistically significant differences with regard to all the measurements of the uterus and presence of myomata were observed between the study and the control group.

Conclusions: It was concluded that intramuscular administration of 150 mg medroxyprogesterone acetate was responsible for these differences.

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Introduction

Depo Provera (depot medroxyprogesterone acetate; DMPA) 150 mg intramuscular injection every 12 weeks is one of the most common methods of contraception used by the female population in Botshabelo, Free State Province.[1] The endometrial thickness of the uterus is affected by Depo Provera to such an extent that it creates an unfavourable environment for implantation of a fertilised ovum, should ovulation occur. It is therefore regarded as one of the most effective contraceptive methods available. During the postpartum period it has some influence on lactation yet allows the mother to continue with breastfeeding. Depo Provera has the best Pearl Index value (i.e. 0–1) when compared to oral contraceptive agents or the contraceptive sticker (patch).[2]

This specific contraceptive method poses benefits as well as disadvantages.[3] Currently some of the disadvantages of Depo Provera are actually utilised from a therapeutic perspective. Therefore, patients regularly present to the general practitioner with signs and symptoms related to side-effects of Depo Provera 150 mg injection.[4]

Depo Provera affects the endometrium and myometrium of the uterus.[1] Some of its side-effects, for example amenorrhoea, may be a cause of concern to some patients, while in others, for example women who suffer from endometriosis, it may have a therapeutic effect.[5] Other side-effects of Depo Provera include acne, fluid retention, changes in weight and libido, depression, breast tenderness and breakthrough bleeding, which represent the most common reasons for seeking medical attention.[6] Breakthrough bleeding usually occurs during the first six months of using Depo Provera. A study in California reported that mifepristone (50 mg every second week for 24 weeks), a progesterone receptor antagonist, could be administered to limit breakthrough bleeding to a large extent.[7]

Ultrasound is used to measure endometrial thickness. It is a cost-effective, non-invasive procedure that is frequently used in the field of obstetrics and gynaecology.[8,9] It does, however, require expertise, operator skill, training and experience to obtain accurate findings of clinical value.

In endometrial adenocarcinoma, ultrasound, in particular transvaginal ultrasound combined with MRI, is of great value in staging of the

specific case. Although most cases of endometrial adenocarcinoma occur in postmenopausal women, up to 25% of cases are reported in premenopausal patients. In selected cases, abdominal and transvaginal ultrasound is used to follow up on patients who have already received tumour regression therapy. When such patients do not want to fall pregnant, they can be placed on Depo Provera with periodic ultrasound evaluation to monitor endometrial thickness.[10] Depo Provera has also been used with success for preoperative regression of uterine myomata.[11]

The aim of the study was to determine the effects of chronic use of Depo Provera 150 mg injection on the endo- and myometrium of the uterus by means of ultrasound.

Methods

An analytical case-control study was performed. All the participants were female patients from the Botshabelo and Thaba Nchu municipal areas in the Free State Province, who voluntarily visited the private general practice of the researcher in Botshabelo between October 2006 and May 2007. This practice renders services to approximately 2 500 patients per month, of whom 60% are female. Sixty-six Depo Provera 150 mg injections are administered each month. Active recruitment and selection of the participants was done by the researcher. Patients of similar socio-economic background, age and clinical profile were selected for both the study and control groups. Participants in the study group were matched to participants in the control group by age (within two years).

The study group consisted of 50 women of reproductive age (20–46 years) who had been on Depo Provera 150 mg for longer than 12 months. Participants in the study group underwent a lower abdominal sonar investigation and received a Depo Provera 150 mg injection at the first visit. Both the investigation and the contraceptive injection were repeated 12 weeks later. Both visits were free of charge. Any local or systemic side-effects resulting from the Depo Provera injection or the lower abdominal sonar were managed free of charge.

Fifty women (19–48 years) who were not on any chronic medication or hormonal contraception, did not have intrauterine devices and were not pregnant or breastfeeding during the 12 months preceding the first ultrasound investigation were included in the control group. Participants in the control group underwent two lower abdominal sonar investigations 12 weeks apart, free of charge. No Depo Provera was administered to the control group.

A structured interview was conducted with each participant during the consultation.

Uterine measurements were performed by means of a Medison Sonoace 5500 digital ultrasound apparatus. Measurements included uterine length and width, endometrial thickness and the presence or absence of uterine myomata. The researcher, who had formal training in gynaecological ultrasound procedures, conducted all the measurements. No invasive procedures were performed as part of the study.

The size of the uterus was determined by taking two measurements, from both left and right lateral views, measuring the length of the uterus from the fundus to the internal os of the cervix and the largest diameter of the fundus from left to right. Measurements were annotated on a specially designed data sheet.

In the event of detecting any pathology during the ultrasound investigation, patients were either treated by the general practitioner (researcher) in his practice or referred for specialised evaluation and treatment if necessary.

Descriptive statistics, namely medians and percentiles for continuous data and frequencies and percentages for categorical data, were calculated for each group. The results for the two groups were compared by means of 95% confidence intervals for paired data.

A pilot study was performed using three patients to test the information leaflet, the questionnaire and the document designed to annotate the measurements. These patients' findings were excluded from the study.

An information leaflet compiled in three languages (Afrikaans, English and Sesotho) was handed to each of the participants selected for the study. Since the researcher is fluent in all three these languages, information was also conveyed verbally to each participant in her language of choice.

Participation was voluntary and participants gave written informed consent to be included in the study. Refusal to participate was not penalised and patients who refused to participate continued to enjoy full benefits as clients of the private practice. All information was handled with confidentiality. Ethical approval to conduct the investigation was granted by the Ethics Committee of the Faculty of Health Sciences, University of the Free State (ETOVS number 169/06).

Results

The study group and the control group consisted of 50 participants each. All the participants were residing in either Thaba Nchu or Botshabelo in the Free State Province, both towns being included in the drainage area served by the researcher's private general practice situated in Botshabelo.

Only 46 of the participants could be matched by age. The median age of the participants was 31 years (range 19–46 years).

Ninety-two per cent of the study group were Sesotho speaking, while the rest were English speaking. In the control group, 96% of the participants were Sesotho speaking and 2% were English speaking, while one (2%) participant was isiXhosa speaking.

The median number of years that the study group participants had been receiving Depo Provera 150 mg injection every 12 weeks as a contraceptive measure was four years (minimum one year; maximum 13 years). As noted in the Methods section, none of the control group participants were on Depo Provera.

None of the participants in the control group reported amenorrhoea as opposed to 85% of the study group who reported amenorrhoea of at least six months duration preceding the study. The difference was statistically significant (95% CI [69.7%; 92.4%]).

Fifty-two per cent of participants in the study group reported breakthrough bleeding, while it was reported by only 8% of the control group. Breakthrough bleeding occurred significantly more in the study group with 95% CI [31.3%; 61.6%].

The medians of all the uterus measurements (length, width and endometrial thickness) were calculated. These findings are shown in Table I.

Table I: Uterus measurements in the study and control groups as determined by lower abdominal ultrasound.

Measurement	First sonar		Second sonar 12 weeks later	
	Study group	Control group	Study group	Control group
Uterus length				
Minimum (mm)	37.6	44.1	37.6	43.8
Median (mm)	54.7	60.6	56.4	60.6
Maximum (mm)	81.7	88.7	81.4	88.3
Uterus width				
Minimum (mm)	21.4	24.8	21.2	24.6
Median (mm)	31.2	33.9	30.9	33.7
Maximum (mm)	44.9	47.6	44.7	47.1
Endometrial thickness				
Minimum (mm)	0.2	0.8	0.2	1.0
Median (mm)	1.2	2.9	1.2	2.9
Maximum (mm)	2.7	3.7	2.6	3.7

Statistically significant differences between the study group and the control group were found with regard to uterus width on first measurement (95% CI [0.1; 0.2]) and endometrial thickness on first measurement (95% CI [0.1; 0.1]). The difference between the two groups with regard to uterus width on second measurement was not significant (95% CI [–0.4; 0.2]), endometrial thickness second measurement (95% CI [–0.1; 0.1]), uterus length on first measurement (95% CI [0; 0.2]) as well as second measurement (95% CI [–0.1; 0.3]).

Changes in uterus length and width as well as endometrial thickness from the first to the second measurement were documented for each participant and compared between the study group and the control group. Statistically significant differences were observed with regard to uterus width (95% CI [0.1; 0.6]). On the other hand, the difference between the two groups in changes in uterus length and endometrial thickness from the first to the second measurement was not significant (95% CI [–0.1; 0.2] and [0; 0.2] respectively).

In the study group, no uterine myomata were found in 96% of participants with the first ultrasound examination, while 4% of participants presented with a single myoma. These two patients had been on Depo Provera 150 mg for three and 6.5 years, respectively. With the second ultrasound examination 12 weeks later, these findings remained unchanged. In comparison, 94% of control group participants were free from uterine myomata. Three (6%) of the control participants, however, had myomata on first examination, of which one patient presented with a single myoma and the other two with two myomata each. On second ultrasound examination, 92% of the control group did not have myomata, while three participants (6%) presented with a single myoma and one (2%) with two myomata. Statistically there was no significant difference between the two groups (95% CI [–14.5%; 4.0%]).

Discussion

Statistically significant differences between the study group and the control group were observed in some of the uterus measurements and endometrial thicknesses, which could be attributed to the intramuscular administration of medroxyprogesterone acetate 150 mg every 12 weeks.

The measurements of the study group participants for uterine width and endometrial thickness were significantly lower than the measurements observed in the control group. These findings are supported by the 95% confidence interval for the median differences. It was determined that the use of Depo Provera caused chemical ablation of the endometrium.

The study group also presented with significantly more breakthrough bleeding than the control group, which led to the conclusion that Depo Provera was responsible for this observation. This finding is corroborated by the literature. Different options are available to limit this side-effect of medroxyprogesterone acetate, for example mefenamic acid 500 mg t.i.d., Ovral® therapy, mifepristone 50 mg every two weeks for 24 weeks (although this is an expensive option) or even intravenous Cyklokapron® (tranexamic acid) in severe, acute cases of breakthrough bleeding.

The incidence of uterine myomata in the study group was lower than in the control group, although no significant differences were observed. In retrospect, the 12-week period is, according to the literature, not a sufficient length of time to determine whether Depo Provera had any impact on the development or regression of uterine myomata.[12] A larger study including more participants and conducted over a substantially longer period could shed more light on this matter.

The findings of this study confirm that Depo Provera may cause significant decrease in the volume of the uterus and in endometrial thickness, which may be of value in clinical practice when patients are treated with medroxyprogesterone acetate as contraceptive agent.

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