Contraception With Medroxyprogesterone Injections in Port Harcourt, Nigeria.

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Abstract

Context: Depot medroxyprogesterone acetate (Depo Provera®) contraception is effective but associated with menstrual side effects that cause discontinuations among acceptors. Experience with its use in **Port** Harcourt has never been reported before.

Objective: Evaluation of the effectiveness, acceptability and side effects of Depo Provera in Port Harcourt clients and comparison with experience elsewhere.

Methods: Collection of data on Depo Provera contraception at the University of Port Harcourt Teaching Hospital (UPTH) Family Planning Clinic between 1st August 1986 and 31st July 1995 from client records. Information obtained included proportion of new clients accepting Depo Provera, socio-demographic characteristics, number of injections received, side effects including accidental pregnancies, and discontinuations.

Results: Depo Provera (1870 new acceptors) accounted for 32% of all non-barrier contraception during the study period. The mean $[\pm SD]$ age and parity of the 1541 acceptors whose files were available were 31.6 \pm 3.3 years and 5.8 ± 2.3 respectively. Multiple side effects (total 1611 episodes) occurred with 87% of these, mostly related to menstruation. Secondary amenorrhoea was reported by 53.7% of the study subjects. Five accidental pregnancies occurred (Pearl Index 0.22 per hundred woman years). Defaults from scheduled injections and discontinuations of use were common with a low continuation rate (7.6%) at the end of the observation period. Secondary amenorrhoea was responsible for 33.3% of discontinuations.

Conclusion: The efficacy and side effects of Depo Provera in Port Harcourt are similar to those reported elsewhere. Defaults from injections and high discontinuations in our study subjects suggest low motivation for contraception.

Key Words: Contraception, Progestin, Depo Provera, Acceptability, Injectable. [Trop J Obstet Gynaecol, 2002, 19: 107-111]

Introduction

Medroxyprogesterone acetate (MPA), given as a depot injection (Depo Provera®), is the commonest depot progestogen used for contraception. Acting primarily by inhibition of ovulation ¹, it has a low failure rate and user effectiveness is almost identical with its theoretical effectiveness^{2,3}. Some menstrual abnormalities — irregular periods, secondary amenorrhoea, and menorrhagia⁴ - during its use occasionally cause discontent and discontinuation among users. Decrease in libido, bloating, dizziness, breast symptoms, headaches, weight gain and delay in return to fertility following use many also occur ⁵.

Major concerns over the safety of this contraceptive (possible carcinogenicity, adverse metabolic effects, cardiovascular risks and induction of a menopause-like state with excessive bone matrix loss) have been expressed. However, studies in users have revealed no increased incidence of any type of cancers ^{6,7,8,9}. Also demonstrated is a protective role of this contraceptive against endometrial carcinoma and uterine fibroids ^{10,11}. Despite an increase in serum high density lipoproteins during its use, no increased

incidence of ischaemic heart disease or cerebrovascular accidents have been reported ^{12,13}. The hypooestrogenic state during its use is usually temporary, and resolves spontaneously after discontinuation ^{14,15,16,17}.

Previous reports on Depo Provera contraception in Nigeria ^{18,19,20,21} agree with worldwide experience on the issues of effectiveness and side effects. In addition, its use for long-term contraception in women who do not want surgical sterilization¹⁹ is noted. This is the first review of clinical experience with medroxyprogesterone contraception from the University of Port Harcourt Teaching Hospital where it was introduced at the inception of the Hospital's Family Planning Clinic on 1st August 1986. The contraceptive's efficacy, acceptability and side effects in our clients are evaluated to ascertain if experience here differs from those of other centers.

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<u>Table 1</u>

<u>Pattern of Discontinuation of Depo Provera® by Number of Injections Received</u>

Number of Injections Received	Number of Subjects	Discontinuations of Depo Provera by Number of Injections Received	Percentage Discontinuing Depo Provera by Number of Injections Received	Cumulative Discontinuation Rate (%)	Continuation Rate (%)
1	387	387	25.1	25.1	74.9
2-4	515	515	33.4	58.5	41
5-8	283	260	16.9	75.4	24.6
9-12	167	124	8.0	83.4	16.6
13-16	74	57	3.7	87.1	12.8
17-20	49	29	1.9	89.0	11.0
21-24	25	15	1.0	90.0	10.0
25-28	11	10	0.6	90.6	9.4
29-32	17	15	1.0	90.0	8.4
33-36	10	9	0.6	90.6	7.8
37 and above	3	3	0.2	91.6	7.6

Materials and Methods

The case records of all the acceptors of Depo Provera® (MPA) at the UPTH Family Planning Clinic during the period August 1st 1986 to July 31st 1995 were reviewed. During this period, nurse practitioners and physicians provided contraceptive services. After counselling and clinical assessment to exclude contraindications, especially pregnancy, practitioners injected 150 mg of MPA into the deltoid or gluteal muscle within the first seven days of a normal menstrual period where menstrual dates were known. It was also given post-abortion and six weeks postpartum in lactating mothers who were still amenorrhoeic. Follow-up observations and repeat injections were done every 90 days. Data collection was aided by a purpose-designed worksheet applied to each acceptor's clinic folder.

The proportion of women reporting secondary amenorrhoea of three months or more during use of medroxyprogesterone acetate by number of injections received was calculated. The values obtained represent the conditioned probabilities of developing secondary amenorrhoea after a given number of three monthly injections. Woman-months of contraceptive protection was calculated as the product of three and the total number of injections received. The Pearl Index, a measure of contraceptive effectiveness, was calculated with the formula:

Pearl Index =
$$\frac{A \times 100}{B/12}$$

Where A is the number of accidental pregnancies during use of Depo provera and B is the number of woman months of contraceptive protection.

Results

The six main methods of contraception available at the UPTH during the study period, and the proportion of clients who accepted them were:Depo Provera®: 32%; intrauterine contraceptive devices: 24%; combined oral contraceptive pills: 17%; levonorgestrel subdermal implant (Norplant): 9%; norethisterone enanthate injections (Noristerat): 9%; bilateral tubal ligation: 5%; and progestogenonly pills: 4%. Acceptors of the condom, spermicides and diaphragm were excluded from the analysis.

Depo Provera® was the most commonly accepted method of contraception during the study period, with 1870 acceptors. The family planning case files of 1541 (82.4%) of these acceptors were retrieved. The family planning case files of the remaining 329 clients had been attached to their hospital folders and could not be traced. The age range and mean \pm SD of the clients were 18-52 years and 31.6 \pm 3.3 years respectively. Clients with parity 1 to 4 and those with parity above 5 were 28.4% and 68.1% respectively. Parity was not stated by 2.7% of the subjects. The parity ranged from 0-14 (mean 5.8 \pm 2.3 SD). Twelve subjects (0.8%) were nulliparae who accepted MPA injections after treatment of complications of induced abortion.

The number of injections received by each study subject ranged from one to thirty eight. subjects achieved the latter, corresponding to 114 woman-months of use. Among the clients, 387 (25.1%) did not return for a second injection while 515 (33.4%) discontinued after receiving two to four injections; 74 (4.8%) received thirteen to sixteen injections. At the end of the period of observation, 117 subjects (7.6%) were still attending the clinic. although in default of several infections. Discontinuations were common (an aggregate total of 902 clients), giving a cumulative discontinuation rate of 58.5%. The high cumulative discontinuation rates and low continuation rates are seen in Table 1.

Table 2 presents the side effects observed during the study period. There were multiple side-effects totalling 1611 episodes. Most were related to menstruation. Secondary amenorrhoea was the commonest side effect reported. Some of the subjects had more than one side effect. Two women each had an injection abscess. Some of the side effects reported were noticed at routine assessment such as urinalysis, weight and blood pressure measurements during follow-up visits.

The probability (risk) of the study subjects developing secondary amenorrhoea after receiving injections of MPA are shown in Table 3. The probability increased from 0.13 for one injection of MPA to 0.90 by the eighth injection. Incomplete records made, it impossible to exclude clients with lactational amenorrhoea.

Voluntary discontinuation without any specific reason occurred in 302 (19.6%) clients. In 513 clients (33.3%), the reasons for discontinuation were menstrual abnormalities, secondary amenorrhoea contributing 72% of these. The other reasons for discontinuations and the percentage of clients involved respectively were specific medical disorders - 3.4%; weight-related complaints - 1.4%; pregnancy-related complaints - 1.6%; psychological and vasomotor complaints - 1.0%; preference for other methods - 1.0%; and miscellaneous reasons -1.3%. Spouse-related reasons, inconvenience with clinic visits and non-availability of the drug caused discontinuation in 0.9% of cases. Some of the clients (11.1% of the 1424 discontinuers) switched method to another type of contraceptive. Only one of these accepted bilateral tubal ligation.

Five accidental pregnancies occurred. Three of these were in 1986 (the first year of the clinic) and the remaining two in 1993. Four of these subjects terminated the pregnancies while the fifth had a spontaneous abortion. All five subjects subsequently discontinued the injections.

The 1541 subjects received 9056 injections of MPA for a total of 27168 woman-months of contraceptive protection. With five accidental pregnancies, the Pearl Index was 0.22 per 100 woman years.

<u>Table 2</u> Side Effects Experienced by the Clients

Side-Effect	Frequency
Menstrual Disruptions	
Spotting or Inter-Menstrual Bleeding	302
Prolonged Menstrual Periods	117
Irregular Menstrual Periods	100
Secondary Amenorrhoea	829
Sub-Total	1348 (83.7%)
Specific Medical Disorders	
Hypertension	49
Diabetes Mellitus	7
Vulvovaginitis	15
Urinary Tract Infection	4
Varicose Veins	5
Injection Abscess	2
Sub-Total	82 (5.1%)
Psychological/Vasomotor Complaints	
Headache	36
Dizziness	6
Hot Flushes	4
Palpitations	4
Decreased Libido	2
Blurring of Vision	2
Sub-Total	54 (3.3%)
Weight-Related Complaints	
Weight Gain	27
Weight Loss	5
Sub-Total	32 (2.0%)
Miscellaneous	
Abdominal/Waist Pains	73
Chest/Joint Pains	6
Breast Lump/Pain/Discharge	6
Nausea and Vomiting	3
Muscle Cramps	3
Post Coital Vaginal Bleeding	2
Bodily Rashes/Acne	. 1
Decreased Milk Flow	1
Sub-Total	95 (5.9%)
Total Events	1611 (100%)
Total Number of Clients	1541

Discussion

This study has demonstrated that MPA is a very important contraceptive accepted by clients in Port Harcourt in recent years. It's convenience for our clients in being non-coitus related, with three month spacing of injections. Its efficacy, demonstrated by the low accidental pregnancy rates may have helped

in increasing its level of acceptance to the clients. Our results are similar to those from other Nigerian centres ^{18, 19, 20,21} and elsewhere ².

Table 3
Conditional Probabilities for Clients
Developing Secondary Amenorrhoea

Number of Injections	Number of Clients	Number With Amenorrhoea	Conditional Probability
1	387	50	0.13
2	244	84	0.34
3	155	79	0.51
4	166	75	0.65
5	99	67	0.67
6	58	42	0.72
7	65	49	0.75
8	61	55	0.90
9	64	56	0.87
10	38	35	0.92
11	36	33	0.92
12	29	23	0.79
13	21	17	0.81
14	21	20	0.95
15	19	18	0.95
≥ 16	128	126	0.98

The mean age of acceptors in this review is similar to that of a previous study from Lagos, Nigeria ¹⁹ suggesting popularity and use for terminal contraception in older Nigerian women of high parity who have passed the peak of their reproductive lives and therefore should aim for permanent contraception. Acceptance of bilateral tubal ligation in Nigeria is low even among women with formal education as seen in this study²². Also consistent with the findings of other studies in Nigeria and else where are the discontinuations of MPA injections in our study subjects ^{20,23}. There was however no corresponding high rate of method switches to other contraceptives as seen in those studies.

The longest users of Depo Provera® in this review had thirty-eight injections, corresponding to more than a hundred woman-months of contraceptive protection without any serious adverse clinical effects. This capacity of MPA injections for long-term use without any serious adverse effect is one that should be exploited by contraceptive practitioners during pre-contraceptive counselling.

Menstrual disorders have always been the commonest side effects of progestogen-only contraceptives, a finding confirmed in this study. About 10% of MPA users have normal menstrual periods in the first year of use while majority

experience irregular or prolonged bleeding in the first six months. Subsequently only about 1 to 2% experience heavy or prolonged bleeding ^{5,17,18,23}. In this study, secondary amenorrhoea was the commonest menstrual complaint reported in more than half of the subjects and was the commonest reason for discontinuation. Inability to exclude clients with lactational amenorrhoea, due to incomplete records and default from scheduled injections by many women, affected our reported onset and pattern of development of secondary amenorrhoea. Other menstrual abnormalities were also reported but were not associated with high discontinuation rates.

Non-menstrual side effects also occurred in our subjects. Some of these, especially psychological, vasomotor and weight-related ones, were predictable reactions to MPA while others were not. In some subjects, there was an apparent unmasking of pre-existing medical conditions like hypertension and diabetes mellitus, which then got worse. In other clients, such conditions developed for the first time. Though uncommon when compared to menstrual abnormalities, these conditions and the discovery of breast lumps were associated with relatively high discontinuation rates.

Weight gain as seen in some of our study subjects, is known to occur with MPA use. Even though the contraceptive induces appetite and is anabolic³, normal age-related weight gain may also have been contributory. In our study however, some subjects had no change in weight while others actually lost weight. Both weight gain and weight loss was responsible for discontinuations. The possibility of weight gain should always be discussed during counselling. Desire for pregnancy, objection, inconvenience of visits, non-availability of the contraceptive and preference for other methods of contraception (mainly oral pills and intrauterine contraceptive device) were less common reasons for discontinuation of MPA in this study. Our abscess rate was low compared to that following levonorgestrel (Norplant) insertion in a Nigerian study ²⁴. It did not lead to discontinuation.

Continued use of MPA depends largely on the ability of the client to accept and adapt to changes in her menstrual pattern, and to tolerate other side effects. A woman's attitude in this regard is complex and varied and reflects her knowledge and experience of the injectable and other contraceptive methods. Her partner's attitude and her cultural norms are also important. For many Nigerian women of reproductive age, secondary amenorrhoea is erroneously thought to have negative effects on

feminity and good health ²⁵. It accounted for just over a quarter of all discontinuations in this study.

Well-informed and supportive counselling during initiation of contraception and reinforcement during the follow-up visits can do much to promote satisfaction and hence continuation of contraception with medroxyprogesterone acetate injections.

References

- 1. Perez-Palacios G et al. On the mechanism of action of progestins. Acta Endocrinol. 1981, 79: 320-328
- Hatcher RS, Rinehart W, Blackburn R, Geller J. Depo medroxyprogesterone injectable contraceptive.
 In: The Essentials of Contraceptive Technology.
 Baltimore. Johns Hopkins School of Public Health.
 Population Information Program 1977: 7 21.
- Glassier A. Contraception. Sterilization and Abortion. In: Shaw RW. Soutter WP, Stanton SL (Eds). Gynaecology, 2nd Edition. London, Churchill Livingstone 1977: 393 – 409.
- Parveen L, Chowdhury AQ, Chowdhury Z. Injectable contraception (medroxy progesterone acetate) in rural Bangladesh. Lancet 1977; 2: 946-948
- 5. Panay N, Studd J. Problems with depot progestogens: a review. The Diplomate 1998; 5(2): 98-102.
- 6. Depot medroxyprogesterone acetate (DMPA) and cancer: Memorandum from a WHO Meeting. *Bull. WHO.* 1993; 71: 669-76.
- 7. Jordan A. Toxicology of depot medroxyprogesterone acetate. *Contraception* 1994; 49: 189-201.
- Chilvers C. Breast cancer and depot medroxyprogesterone acetate: a review Contraception 1994; 49: 211-222.
- La Vecchia C. Depot medroxyprogesterone acetate, other injectable contraceptives, and cervical neoplasia. Contraception 1994; 49: 223-230.
- 10. Lumbiganon P. Depot medroxyprogesterone acetate (DMPA) and cancer of the endometrium and ovary. *Contraception* 1994, 49: 203-209.
- Lumbiganon P, Rugpao S, Phandhufung S, Laopai boon M, Vudhikamraksa, Werawatakul Y. Protective effect of depot medroxyprogesterone acetate on surgical treated leiomyomas: a multicentre case controlled study. *Br J Obstet Gynaecol* 1995; 103: 909-914.
- 12. Enk L. Landgren BM; Linberg U.B., Silverstolpe G, Crona N.A. Prospective one year study on the effects of two long acting injectable contraceptives (depot medroxyprogesterone acetate and norethisterone oenanthate) on serum lipoprotein lipids. *Hormone Metabolic Research* 1992; 24: 185-189.
- 13. Garza-Flores J, De la Cruz DL, Valles de Bourges *et al.* Long term effects of depot medroxyprogesterone

- acetate on lipoprotein metabolism. Contraception 1991; 44: 61-71.
- Cundy T, Evans M, Robert H, Wattie D, Ames R, Reid I. Bone density in women receiving depot medroxyprogesterone acetate for contraception. BMJ. 1991: 303: 13-16.
- Cundy T, Cornish J, Evans MC, et al. Recovery of bone density in women who stopped using depot medroxyprogesterone acetate. BMJ, 1994; 308: 247-248.
- 16. Power MS, Schenkel L, Darkey PE, Good WR, Balestra JC, Place VA. Pharmacokinetics and pharmacodynamics of transdermal dosage form of 17β-Oestradiol: comparison with conventional oral oestrogen used for hormone replacement. Am J Obstet Gynecol, 1985; 152: 1099-1106.
- 17. Kirkman R, Williams E, Murby B. Bone density and use of depot medroxyprogesterone acetate D. MPA (Depo Provera) *Br J Fam Plan.* 1994; 20: 26-27.
- 18. Lakeru AA. Depot medroxyprogesterone acetate as an injectable contraceptive agent *Nig Med J.* 1972; 2: 24-27.
- 19. Ojo OA. International Forum: Acceptability and efficacy of Depo Provera. *Int J Gynecol Obstet* 1978; 16: 439-441.
- Fakeye OO. Contraception with Depo Provera and the unmet expectation for long term Use. Nig Med Pract, 1988; 16: 153-156.
- Fakeye OO. Depo Provera in Nigeria: geographical variation in acceptability and time trends in the development of amenorrhoea. Trop J Obstet Gynaecol, 1993; 10: 1-3.
- Emuveyan EE, Dixon RA. Family Planning Clinics in Lagos, Nigeria: clients, methods accepted and continuation rates. Nig Med. J. 1995; 28: 19-23
- Narkavonnakit T, Bennett T, Balakrishnan T.R, Continuation of injectable contraceptives in Thailand. Stud Fam Plan 1982; 13: 99-105.
- 24. Ogedengbe OK, Giwa-Osagie OF, Adeboye M, Usifoh C.A. The acceptability and role of Norplant as a Long Acting Contraceptive in Lagos, Nigeria. Trop J Obstet Gynaecol, 1997; 14: 28-33.
- Adeleye JA, Adeleye GI. Knowledge attitude and practice of family planning amongst women in Ibadan, Nigeria. Trop J Obstet Gynaecol, 1985; 5: 19-26.