ORIGINAL ARTICLE

A -Five Year Review of the Complications of Progestogen only Injectable Contraceptive at the University of Port-Harcourt Teaching Hospital

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Abstract

Background: *The injectable progestogen only contraceptive is a widely accepted method of contraception in our environment and very little has been reported on its complications in our environment. The aim of the study was to highlight the complications associated with use of Injectable Medroxyprogesterone Acetate and Norethisterone Enanthate in clients at the University of Port-Harcourt Teaching Hospital, Port-Harcourt, South-South Nigeria*

Methods: *It was a - 5 year retrospective study of the clients who accepted and used progestogen only injectable contraceptives (depot medroxyprogesterone acetate and noerthistherone enantate) at the family planning units of the University of Port Harcourt Teaching Hospital between 1st January 2000 and 31st December 2004. The case files of these clients were retrieved their data extracted. The information included the clients sociodemographic characteristics, the types doses of of injectable contraceptives received and the side effects reported at the follow up visits. The data was coded and entered into a data bank and analysed using SPSS for windows 11.0 version.*

Results: *Seven hundred and seventy seven (777) injectable contraceptive acceptors out of the 1720 contraceptive acceptors during the study period. This accounted for 45.17% of the new acceptors over the 5 years period, making the injectable contraceptives the most commonly used method of birth control in UPTH. Five hundred and five (505) clients took depot medroxyprogesterone acetate (DMPA) while 272 used norethesterone enanthate (NE-ET). The mean age of the injectable contraceptive users was 31.31±5.5 years and the mean parity was 5.5±2.5 deliveries. The users reported multiple side effects with 579 episodes. Secondary amenorrhea was the commonest side effect occurring in 350 (45.34%) clients. Others were hypertension in 17 (2.94%) and metabolic disturbances in 14 (2.41%).*

Conclusion: *Injectable progestogen only contraceptive is associated with multiple side effects, with secondary amenorrhoea being the most common. The contraceptive failure rate of this method in our women is low.*

Keywords: *progestogen injectable contraceptive, medroxyprogesterone acetate, norethisterone enanthate, complications, secondary amenorrhoea.*

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Introduction

From a global perspective, many countries currently face the crises of a rapid growth of human population that has begun to threaten human survival. To stem this, the voluntary control of fertility therefore became of paramount importance to the modern society. About 50% of all couples in the world are now using a modern method of contraception.[1,2]

Though the contribution of these contraceptives to the betterment of health and life in general has been simply tremendous, none of these including the injectable progestins is without side effects/ complications.[1]

These steroids acting primarily by inhibition of ovulation, thickening of cervical mucus or induction of endometrial atrophy, extensive clinical experience accumulated over recent years indicate that the available progestin-only formulations: depo-medroxyprogesterone acetate and norethisterone enanthate are highly effective, long lasting and reversible agent of fertility control, used by over 10million persons globally.[1-10]

However the use of some of these agents is not without adverse effects and complications which may be unacceptable to the women therefore

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resulting high discontinuation rates in some studies[7,11,12,13,14].

Major concerns have also been raised over the long term safety of these agents including the possibility of induction of carcinogenesis, adverse metabolic effects, cardiovascular diseases and osteoporosis.[10] But interestingly and contrary to the fears expressed, no studies to date have demonstrated increased incidence of any type of cancers, ischaemic heart disease or cerebrovascular accidents.[9,15,16,17] Notable complications are menstrual disorders including secondary amenorrhea with its strong negative socio-cultural perception in our environment[18], irregular vaginal bleeding, menorrhagia and metrorrhagia.[12,13,14,19,20] Other reported complications include accidental pregnancies, weight changes, decreased libido, abdominal and chest pains. Less reported side effects are psychological and vaso motor disturbances[2,4,7,10,21].

Port Harcourt, the Rivers state capital has been the nerve center for oil and gas prospecting and refining activities in Nigeria for over 50 years. The UPTH draws its patients from a cross section of multi ethnic and indigenous population who reside in Port Harcourt and from its extended catchement areas that traverse the difficult terrain of the Niger Delta areas of Nigeria.

Materials and Methods

This was a – 5 retrospective study between 1st January 2000 and 31st December 2004 evaluating the complications of the two forms of progestogen only injectable contraceptives (noerthisterone enanthate and medroxyprogesterone acetate) in clients at the family planning clinic of the University of Port Harcourt Teaching Hospital. The case notes of all the 777 clients who accepted and used injectable medroxyprogesterone acetate and norethisterone enanthate within this period were identified and analyzed. The information extracted were clients' age, parity, educational status, type and doses of injections received, number of discontinuations, side effects and complications. The data was coded and entered into a data bank and analyzed using SPSS for windows 11.0 version and presented as frequency tables, means standard deviations, median values and percentages.

After counselling by family planning nurse practitioners and physicians, a full medical history was taken and clinical examination performed. Those who were pregnant or had contraindications to progestogen hormonal contraception were excluded.

A dose of 200mg norethisterone enanthate (NET-EN) or 150mg medroxyprogesterone acetate (MPA) was injected into the gluteal /deltoid muscle within the first seven days of a normal menstrual period where menstrual dates were known. It was also given after abortion and six weeks after delivery in breastfeeding mothers who were yet to resume menstruation. Repeat injections and observation were done after every 60 days for those receiving NET-EN and every 90 days for clients on MPA. At each visit, all the complaints volunteered by the patient were documented. The weight, blood pressure and result of urinalysis were recorded. A patient was considered lost to follow up if she defaulted more than twice from scheduled injections.

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

Pearl Index = Ax 100/B/12

Where A is the number of accidental pregnancies during the use of the injectable contraceptives and B is the number of woman-months of contraceptive protection.

Results

During the five year period under review, there were 1720 new contraceptive acceptors. A total of 777 (45.17%) of the acceptors used progestogen only injectatable contraceptive.

Of these, 505 clients accepted depot medroxyprogesterone acetate, while 272 clients accepted norethisterone enanthate. This confirms progestogen only injectable contraceptive as the most accepted method of family planning in our centre. Over 38.22% of the clients used it for 'permanent' contraception in place of sterilization, while 58.81% used it for child spacing. The rest were undecided as to the size of family they wanted but still used it for contraception.

Age distribution: The age range of the clients was 17-43 years, with a mean ±SD of 31.31 ±5.5 years.

Educational status: Seventy-five (0.96%) of the clients did not have formal education, 167 (21.49%) had primary education while 535 (68.85%) had secondary to post secondary education as shown in table II.

Parity: Table III shows the parity distribution of clients. The parity ranged between 0-11 deliveries with a mean parity ± SD parity of 5.5± 2.5 deliveries. Five (0.6%) clients were nulliparous women, while 226 (29.1%) clients were grand multiparous women.

Dose of injection received: Table IV shows the distribution of doses of injection received. The number of injections received by clients ranged from one to twenty- three. Only four clients received 20 doses of the injections and above, corresponding to 168 woman-months. Two hundred and eleven (27.15%) did not return for a second injection, either because they discontinued voluntarily, lost to follow up or were not yet due. Two hundred and fifty four (32.69%) discontinued after 2 to 4 injections. One hundred and eighty one (23.29%) received between 5 to 9 injections.

Seventy three (9.34%) received 10 -19 while 4 clients received 20 injections and above. At the end of the study period 177 clients had received at least two doses of the injections and were still attending the clinic, excluding those who had just received one injection and were not yet due for a subsequent dose (30 clients). Discontinuations were common (600), giving a cumulative discontinuation rate of 77.22%.

Complications : The most common complications were menstrual disorders occurring in 510(65.64%) of the clients. Secondary amenorrhea was the commonest menstrual disturbance reported in 60.05% of the study population. The conditional probabilities of developing secondary amenorrhea increased with the doses of injections received, 27% at the 1st dose and 86% at the 9th dose.

The other menstrual disturbances encountered in the study were menorrhagia (3.12%), irregular menstruation (2.25%) and metrorrhagia and intermenstrual bleeding occurred in 22.23%. Seventeen (17) clients had blood pressure elevation/ hypertension accounting for 2.95% of the complications. They were subsequently referred to the physicians and discontinued the injections. Two (0.35%) had diabetes mellitus and were also referred to the physicians and discontinued. Injection abscess occurred in two (0.35%) subjects.

Two (2) accidental pregnancies occurred, giving a Pearl pregnancy index of 0.26 per woman years.

Miscellaneous disorders include chest/ joint pain reported in 4 (0.69%) clients, mastodynia in another 4 (0.69%), and abdominal/waist pain in 5 (0.86%) subjects as shown in table VI.

Table I. Yearly distribution of clients receiving progestogen only injectable contraceptives

Year	DMPA	NET-EN	Total	Percentage
2000	100	82	182	23.4%
2001	89	49	138	17.8%
2002	139	21	160	20.6%
2003	106	50	156	20.1%
2004	71	70	141	18.1%
Grand total	**505**	**272**	**777**	**100%**

Table II: Educational status

Level of education	DMPA	NET-EN	Total	Percentage
none	61	14	75	9.7%
Primary	125	42	167	21.4%
Secondary/tertiary	319	216	535	68.9%
Grand total	**505**	**272**	**777**	**100.%**

Table III. Parity distribution

Parity	DMPA	NET-EN	Total	Percentage
0	2	3	5	0.6%
1-4	329	217	546	70.3%
5-9	168	52	220	28.3%
=10	6	0	6	0.8%
Grand total	**505**	**272**	**777**	**100%**

Table IV. Distribution of doses of injection received

Dose	DMPA	NET-EN	Total
1	131	80	211
2-4	148	105	253
5-9	118	63	181
10-14	0	14	14
15-19	54	19	73
20	0	4	4
Grand total	**451**	**285**	**736**

Table V: Conditional probabilities of developing secondary amenorrhea

No. of injections	No. of clients	Clients with secondary amenorrhea	Conditional probability of developing 2^0 amenorrhea
1	113	30	0.265
2	91	40	0.439
3	82	49	0.597
4	47	31	0.659
5	42	32	0.769
6	28	22	0.786
7	20	16	0.80
8	23	19	0.826
9	16	14	0.875
10	17	15	0.882
11	8	7	0.875
12	14	13	0.920
=13	21	20	0.950

Table VI. Complications of injectable contraceptives

Complication	Frequency	Percentage (%)
2^0 Amenorrhea	350	60.05
Spotting	129	22.23
Menorrhagia	18	3.12
Irregular periods	13	2.25
Hypertension	17	2.95
Diabetes	2	0.35
Injection abscess	2	0.35
Weight gain	10	1.73
Weight loss	2	0.35
Headache	10	1.73
Palpitation	5	0.86
Decreased libido	4	0.69
Dizziness	2	0.35
Accidental pregnancy	2	0.35
Chest/joint pain	4	0.69
Mastodynia	4	0.69
Abdominal/waist pain	5	0.86
Total events	**579**	**100**

Discussion

Menstrual disorders were the commonest complications experienced by the study subjects, occurring in 510 (65.64%) of the clients. This is in keeping with results of previous studies. [10,18-24] The aetiology of this disturbance have been linked to the endogenous ovarian steroid secretion.[25]

Secondary amenorrhea was the most common menstrual disturbance reported by over 60.05% of the clients which was higher than the figure reported in a previous Nigerian study[7], and elsewhere[4,26,27,28]. Also the conditional probabilities of developing secondary amenorrhea corresponding to[1,6,9] injections received were 0.27, 0.79, 0.86, also significantly higher than reported in previous studies.[10,18]

The comparatively higher rate of secondary amenorrhea could be entirely due to chance in this series. It could also be as a result of endometrial atrophy or very rarely accidental pregnancy.[9,21, 23]

Two (2) accidental pregnancies occurred in this series. The 0.05% discontinuation rate due to secondary amenorrhea and the cumulative discontinuation rate of 77.22% is inconsistent with result of earlier findings elsewhere.[1,6,12,14]Five hundred and forty-five (70.14%) either discontinued voluntarily or were lost to follow up. Majority of clients in this group may have discontinued voluntarily due to secondary amenorrhea.

The other disturbances of menstruation encountered in this study include menorrhagia (3.12%), irregular vaginal bleeding (2.25%) and metrorrhagia/intermenstrual bleeding in 22.23%. Gulati etal14 reported irregular vaginal bleeding in 16% while Chaudhuri etal[27] reported same in 57% of their study subjects. These figures are relatively higher than observed in this study. The reason for this wide disparity is not exactly known, but environmental factors may be partly responsible. However, 3.12% 0f the clients had menorrhagia/prolonged bleeding. This is in keeping with result of previous findings.[9, 29]

Inability to exclude clients with lactational amenorrhea due to incomplete records and defaults from scheduled injections by many women affected the reported onset and pattern of development of secondary amenorrhea.

Two accidental pregnancies occurred, giving a pearl index of 0.26 per woman years, comparable to rates reported by other workers.[10,23]The first pregnancy occurred in September 2002 in a 29 year old lady after receiving eleven doses of depot medroxyprogesterone acetate injections. The second pregnancy occurred in September 2004 in a 32 year old lady, para 2, after five doses of depo-provera injections. Both pregnancies were uneventful and carried to term. Outcomes were live male babies with good Apgar scores and average birth weights.

Although no ectopic pregnancies were observed in this study, their occurrence have been reported by other authors.[9,23]Though not a desirable outcome in this circumstance, it goes to reinforce earlier observation by Gebbie etal,[29] that injectable contraceptive have no permanent impact on fertility. This is particularly worrisome when viewed against the backdrop that a good proportion of women in our environment use injectable contraceptives for terminal contraception,[10] due to fear and aversion to surgical sterilization, even among women with formal education.[30] This was corroborated by the finding in this study where 38.22% of the clients accepted injectable contraceptives for terminal contraception majority of this had formal education.

The other major medical complication were hypertension and diabetes mellitus observed in 2.95 and 0.35% of the clients respectively. Their occurrence in previous studies have been reported,[7,10] but could be probably due to apparent unmasking of pre-existing medical condition which then got worse. Hypertension had earlier been reported in 0.7% of acceptors of hormonal implants in this center and a decrease in glucose tolerance reported in studies elsewhere.[31] The19 clients with complicating hypertension and diabetes mellitus in this series subsequently discontinued with the injectables and switched to intra uterine contraceptive devices.

Injection abscess occurred in 2 of the clients. This was lower than the figure reported following levonorgesterol insertion in Lagos Nigeria.[32]

The other non-menstrual side effects include weight related changes. One point seventy-three (1.73%) of the study group reported increase in their weight. These were confirmed with our weighing scale. Weight gain is known to occur with use of progestins .[2,7,23, 24,33] as they are anabolic and tend to induce appetite.[34] Normal age related weight gain may have also been contributory in these patients.

Two clients had significant weight loss necessitating discontinuation. Similar weight loss had been reported in this center and elsewhere,[10] though it could be due to other confounding factors including nutritional and immunodeficiency states.
Vasomotor and psychological changes were also reported by the subjects in this series. Another 1.73% had persistent headache, 0.86% had palpitation, 0.69% had decreased libido while 0.35% reported dizziness. These disturbances have also been reported by other authors.[7, 10, 23] Other miscellaneous disturbances reported elsewhere and noted in less than 2% of the study group include mastodynia, chest pain, abdominal pain, waist pain and joint pain.[9, 10, 23]
Other complications noted by previous authors but not reported in this study include blurring of vision, hot flushes, muscle cramps, acne, bloatedness, decreased milk flow, varicose veins, astenia, depression, urinary tract infection and vulvovaginitis.[9,10,23,]

It has also been noted that short lasting reactions: urge to cough, coughing fits, respiratory distress occur in rare cases during or immediately after injection of these drugs. These were not noted in our patients. Possible long term consequencies include risk of neoplasia, osteoporosis, cerebrovascular accidents, thromboembolic phenomenom, ischaemic heart disease and decrease in low density lipoproteins.[9 10, 23]

It was not possible to identify these either because the facilities were not available or they require long term follow up which is particularly difficult in our setting for obvious reasons, but it is reassuring to note that parallel studies elsewhere did not show any increased incidence of any type of cancers, ischemic heart disease or cerebrovascular accidents,[15,16, 17] and infact the protective effect of these injectables against endometrial carcinoma and uterine fibroids have been reported.[35,36]

In conclusion, since menstrual disorders remain the major complications of progestogen only injectable contraceptive and whereas a good proportion of our contracepting women use them for permanent contraception in preference to surgical sterilization, adequate counselling at the first visit about the possible menstrual disturbances especially in the initial period, as these tend to resolve or ameliorate later with continued patronage. This is particularly important when viewed against the backdrop that the continued use of these agents depend on their ability to accept and adapt to changes in their menstrual pattern, and to tolerate other side effects. Well informed and wholesome pre-commencement counselling and re-enforcement during follow up visit can do much to promote satisfaction and hence continuous use of the agents.
Alternatively, the one monthly combined injectable containing 25mg medroxyprogesterone acetate and 5mg of estradiol cypionate per dose, with higher efficacy and with bleeding pattern resembling those of normal menstrual cycles,[1,29,37,38] should be introduced in our centers, since for many Nigerian women of reproductive age, secondary amenorrhea is erroneously thought to have negative effects on feminity and good health.[39]

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