

Experience with Norethisterone Enanthate (Noristerat) at the University of Port Harcourt Teaching Hospital, Port Harcourt, Southern Nigeria

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Authors' contributions

This work was carried out in collaboration between both authors. Author CEE designed the study, wrote the study protocol and first draft of the manuscript, literature search and discussion. Author MJ performed the collation of data and statistical analysis. Both authors read and approved the manuscript.

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ABSTRACT

Aim: To evaluate the experience with Norethisterone enanthate at the university of Port Harcourt Teaching hospital, Southern Nigeria.

Study Design: Retrospective study.

Place and Duration of Study: Department of the obstetrics and gynaecology, family planning unit (FPU) between January 1st 2006 and December 31st 2015.

Methods: Six thousand, five hundred and eighteen clients were seen in the FPU; out of which three hundred and thirty –three accepted Noristerat. Information retrieved from their case records included socio-demographic characteristics, side effects, discontinuation and sources of information. These were entered into Microsoft excel and analysed using Statistical Package for Social Sciences (SPSS) for windows 15.0.

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Results: Norethisterone enanthate users formed 5.11% of contraceptive acceptors during the study period. The mean age of acceptors was 31.5 ± 5.13 years, while most clients (69.37%) had tertiary level of education and multiparous (79.58%); majority of them got their information from health clinics (75.07%). Secondary amenorrhea was the most common side effect (63.66%); and desire for pregnancy was the foremost reason for discontinuation. There was no accidental pregnancy.

Conclusion: This study suggests that Norethisterone enanthate is a safe, effective and acceptable method of contraception in our centre. The print and electronic media should be involved in the propagation of accurate information about contraceptives, especially to the rural and non-literate population.

Keywords: Experience; norethisterone enanthate; Port Harcourt; Southern Nigeria.

1. INTRODUCTION

Different contraceptive methods have been used throughout the years; with the goal to prevent unwanted pregnancies. Achieving this objective will prevent maternal morbidity and mortality, resulting from abortion, which account for 13% of pregnancy related deaths globally [1], and about 40% in Nigeria [2]. Despite the introduction of modern contraceptives, the unintended pregnancy continues to be a major problem. Nigeria has a fertility rate of 5.7% but an overall contraceptive prevalence among women of 16.0% [3]. This is lower than other African countries such as South Africa with a rate of about 64.3% [4].

Norethisterone Enanthate (Noristerat, NET-EN) is a progestin, with anti-gonadotropic properties [5]. It is along acting contraceptive administered by intramuscular injection that is effective, convenient, reversible and increasingly popular family planning method. Recognition of these benefits accompanied by approval by the International Planned Parenthood Federation in 1983 and eventual US Food and Drug administration catalysed a global doubling of injectable contraceptive use between 1995 and 2005, a trend that was particularly prevalent among low income countries [6]. Long acting reversible contraceptives (LARCS) are those that are administered less frequently than once a month [6].

Norethisterone enanthate is an oil suspension and given at a dose of 200 mg. The injection should be given in the first five days of a normal menstrual cycle but, it can also be given at any other time in the menstrual cycle if pregnancy is ruled out. Once injected, Norethisterone Enanthate is converted into its pharmacologically active compound Norethisterone. Serum levels of Norethisterone reach a peak one week after

injection with a value of 13.4 ± 5.4 ng/ml [7]. Serum levels decline steadily thereafter and generally are no longer detectable from two and a half ($2\frac{1}{2}$) to three (3) months. It is metabolized completely. Norethisterone enanthate is split mainly in the liver by enzymatic hydrolysis into norethisterone and hepatonic acid [8]. Its primary mechanism of action is inhibition of follicular development thereby inhibiting ovulation [9,10]. Norethisterone enanthate decreases the pulse frequency of gonadotropin releasing hormone (GnRH) release by the hypothalamus, which decreases the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH) by the anterior pituitary. Decreased levels of FSH inhibit follicular development, preventing an increase in estradiol levels. Its negative feedback on LH release prevent LH surge. Inhibition of follicular development and the absence of LH surge prevent ovulation [11]. Its secondary mechanism of action is inhibition of sperm penetration by changes in the cervical mucus [8].

Inhibition of ovarian function during NET-EN use causes the endometrium to become thin and atrophic. These changes in the endometrium could theoretically, prevent implantation. However, because NET-EN is highly effective in inhibiting ovulation and sperm penetration, the possibility of fertilization is negligible. No available data support prevention of implantation as a mechanism of action of NET-EN [11].

It is common in Europe, Africa and Central America [12,13], and popular with a variety of women especially those whose partners had vasectomy and want to protect pregnancy while the procedure takes effect, and also those who are being immunised against rubella and did not want to get pregnant while the virus is still active [7]. Norethisterone enanthate is associated with small loss of bone mineral density and possibly a

subsequent increased fracture risk which reverses after stopping [14]. Potential benefits include, no increased risk of deep vein thrombosis, pulmonary embolism, stroke or myocardial infarction. It reduces the risk of endometrial cancer by 80% as well as symptoms of endometriosis [15]. Unlike most other hormonal contraceptives, its effectiveness is not affected by enzyme – inducing antiepileptic drugs; as such there is decrease incidence of seizures in women with epilepsy. It also causes decreased incidence and severity of sickle cell crises in women with sickle cell disease [16].

Common side effects associated with Norethisterone enanthate include changes in menstrual bleeding pattern, breast discomfort, headache, dizziness, nausea, depressed mood and weight gain [17]. Its use is contraindicated in women with abnormal vaginal bleeding of which the cause of vaginal bleeding has not been diagnosed; women with breast or cervical cancers, liver tumours, depression, high blood pressure, diabetes mellitus, hereditary blood disorders (acute porphyrias) and those who had surgery within twelve (12) weeks [18]. The reported cumulative pregnancy rate is 0.4% at 1 year and 0.4% at 2 years [19].

Despite the side effects, it is commonly used in Nigeria, hence the need for this retrospective study in our centre. This aims to evaluate the experience with Norethisterone enanthate at the University of Port Harcourt Teaching Hospital with the aim of documenting the acceptability, efficacy, side effects and compare with the experience elsewhere.

Port Harcourt, capital of Rivers state in southern Nigeria is cosmopolitan, oil rich and has people from all parts of the country. The population of Port Harcourt was estimated at 1.5 million in 2013 [20]. University of Port Harcourt Teaching Hospital is the apex tertiary hospital in the state. It has 800 beds and offers general and specialist care to the citizenry of Rivers state and neighbouring states.

2. METHODOLOGY

A retrospective study conducted at the family planning clinic of University of Port Harcourt Teaching Hospital. This involved selecting the records or files of all clients who accepted Norethisterone enanthate from January 1, 2006 to December 31, 2015. Ethical approval for the

study was given by University of Port Harcourt Teaching Hospital, Rivers State, Nigeria.

The protocol used at the family planning clinic was; the clients (who came from Port Harcourt and neighbouring towns and villages) were counselled by trained family planning nurse practitioners and physicians; and thereafter allowed to make informed choice based on their needs and available contraceptive for which they are suitable.

Following this, a full medical history and clinical examination were performed. In the absence of complication(s), follow up visits were at the first four weeks and then every two months subsequently. Clients were encouraged to come to the clinic if complications arose and all complaints / complications were documented. At each follow up visit, the client weight and blood pressure were recorded and complications managed as appropriate. Clients who do not report two or more consecutive scheduled visits were usually regarded as lost to follow up.

The information retrieved from the client's case records was collected in a data form which included: the client's socio- demographic characteristics, sources of information, side effects, discontinuation and accidental pregnancies. The data was coded and entered into a Microsoft excel and analysed using SPSS 15.0.

3. RESULTS

A total of six thousand, five hundred and eighteen (6,518) clients were seen at the family planning clinic of University of Port Harcourt Teaching Hospital within the period under review.

Table 1; shows the contraceptive method chosen by clients during the period under review. Norethisterone enanthate was the fifth, followed closely by oral contraceptive pills. It formed 5.11% of contraceptive acceptors during this period.

3.1 Ages of Clients

The age range of the clients who accepted Noristerat was 19 – 45 years with a mean age of 31.5 ± 5.13 years. Ages 35 and above made up 26.71%. The modal acceptor age group was 30-34 years (33.33% of the clients). More than three quarter (86.18%) of the clients were between 25 and 39 years (Table 2).

3.2 Educational Status

Majority of clients had tertiary education 231(69.37%); 75(22.52%) had secondary education while 27(8.11%) had primary education / koranic education. All the clients had formal education.

3.3 Occupation

Public / civil servants contributed to the highest number of acceptors 121(36.34%) followed by housewives 83(24.92%), traders 69(20.72%), students 36(10.81%), artisans 24(7.21%).

3.4 Parity

The parity distribution of the clients was as follows; nulliparous 2(0.60%), multiparous 265(79.58%), while grand multiparous was 68(19.82%). The mean parity was 2.09±0.35.

3.5 Religion

Most of the clients were Christians 308(92.50%); followed by Muslims 19(5.70%) and traditional / non specified 6(1.80%).

3.6 Marital Status

Most of the clients were married 325(97.60%) followed by single 5(1.50%), the divorced/ widow were 3(0.90%).

3.7 Side Effects

Fig. 1 shows the side effects that were encountered by clients that used noristerat. Common side effects include secondary amenorrhoea 212(63.66%), scanty menstruation 50(15.01%), weight gain 32(9.61%), heavy menstrual bleeding 22(6.61%) and intermenstrual bleeding 17(5.11%).

3.8 Discontinuation of Noristerat

Table 3 shows the reasons for discontinuing of noristerat injectable contraceptive. The common reasons were desire for pregnancy 38(57.58%) and change to other methods 13(19.70%). This is because some of the clients had completed their family size and desire a long lasting contraceptive method. Others include secondary amenorrhoea 8(12.12%), weight gain 5(7.57%) and non-compliance 2(3.03%). The total discontinuation rate in the study was 19.82%.

3.9 Sources of Information

Fig. 2 shows the distribution of clients on the basis of their source of information on Noristerat. Health clinic was the leading source of information 250(75.07%), followed by friends and relations 35(10.51%) amongst others.

3.10 Accidental Pregnancy

There was no accidental pregnancy seen among the clients using Noristerat. Those who desired pregnancy discontinued the use of Noristerat and planned for pregnancy. Seven clients were lost to follow up.

Table 1. Contraceptive choices of clients at the UPTH FPC between 1st January 2006-31st December 2015

Contraceptive method	No of clients	Percentage (%)
Barrier	3194	49.00
Implants	888	13.63
IUD	886	13.59
Dmpa	682	10.46
Noristerat	333	5.11
OCP	327	5.02
Norigynon	208	3.19
Total	6518	100.00

4. DISCUSSION

Norethisterone enanthate was accepted by 5.11% of the attendants, but from them, only 4.5% discontinued the use for side effects and 3.9% for other methods. In as much as it is not among the preferable in the centre; may be because of lack of knowledge, it is well accepted by the users. This finding is in keeping with other studies done in Port Harcourt, Aba, Ilorin, Europe and central America [12,13,21,22,23].

Contraceptive prevalence is related to the range of methods available, patient choice, health /clinic personnel bias, prevailing cultural and religious beliefs, perception of method effectiveness, side effects and spouse influence. [22,24]. Our women considered the convenience of not having to take pills every single day, spouse not detecting any foreign body in them, and having to take a single injection every two months and accepted Norethisterone enanthate injectable contraceptive.

The socio-demographic characteristic of acceptors of NET-EN is consistent with what has been shown in other population. The result shows that the modal age group was 30-34 years

with the mean age of 31.51 ± 5.13 years; which represents peak obstetric carrier age. This result agrees with other findings in the other centres in the country and elsewhere [13,21,22,23]. All the clients in this study had formal education, with 231 (69.37%) having tertiary level education. This means that the cohorts were highly literate. This finding is similar to studies in Nigeria and developed world [18,21,23].

Table 2. Socio-demographic characteristics of acceptors

Characteristics	Number (N)	Percentage (%)
Age (Years)		
≤19	2	0.60
20-24	23	6.91
25-29	108	32.43
30-34	111	33.33
35-39	68	20.42
≥40	21	6.31
Total	333	100.00
Educational level		
Primary/Koranic	27	8.11
Secondary	75	22.52
Tertiary	231	69.37
Total	333	100.00
Occupation		
Public/Civil servants	121	36.34
Housewives	83	24.92
Traders	69	20.72
Students	36	10.81
Artisans	24	7.21
Total	333	100.00
Parity		
0	2	0.60
1-4	265	79.58
≥5	66	19.82
Total	333	100.00
Religion		
Christianity	308	92.50
Islam	19	5.70
Others	6	1.80
Total	333	100.00
Marital status		
Single	5	1.50
Married	325	97.60
Widow/Divorced	3	0.90
Total	333	100.00

The parity profile of the clients showed that majority of the subjects were multiparous with only one-fifth being grand-multiparous, only two clients were nulliparous. This confirms that the clients were either limiters or spacers. This is similar to the study at Ilorin Nigeria [23].

The predominance of Christians in this index study is not surprising because of the Christian background of the population in Port Harcourt as shown by earlier studies [25].

Table 3. Reasons for discontinuation of method

Reasons	Number of subjects	Percentage
Desire for pregnancy	38	57.58
Change to other methods	13	19.70
Secondary amenorrhoea	8	12.12
Weight gain	5	7.57
Non compliance	2	3.03
total	66	100.00

Menstrual disturbance were the most frequent side effects reported by users of Norethisterone enanthate in our study. This is due to the endogenous ovarian steroid secretion and endometrial angiogenesis [26].

Weight gain as seen in our clients is known to occur with NET-EN use [27]. Even though it increases appetite and is anabolic, normal age related weight gain may also have been contributory. The possibility of weight gain should always be discussed during counselling.

Continued use of NET-EN depends largely on the ability of the user 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 as well as reflects her knowledge and experience of NET-EN and other contraceptive methods. Her partner's attitude and her cultural norms are also important. In many Nigerians of reproductive age, secondary amenorrhoea is erroneously thought to have a negative effect on femininity and good health [28]. It accounted for one-eighth of the reasons for the discontinuation of Norethisterone enanthate in our study. With proper counselling, majority of the acceptors of NET-EN will endeavour to tolerate such side effects.

The clients had more than one source of information on Norethisterone enanthate, however health clinic was the main source of information (75.07%), followed by family and friends (10.51%). This might be explained by the numerous health centres in the state and the involvement of the community health extension workers in the propagation of information on family planning. It also brings to the fore, the contribution by family members and friends in disseminating information on family planning. This finding while agreeing with other studies in Uyo [29] and Enugu [30] is in contrast with findings by Ezeugwu where family / friends were the leading source of information [31].

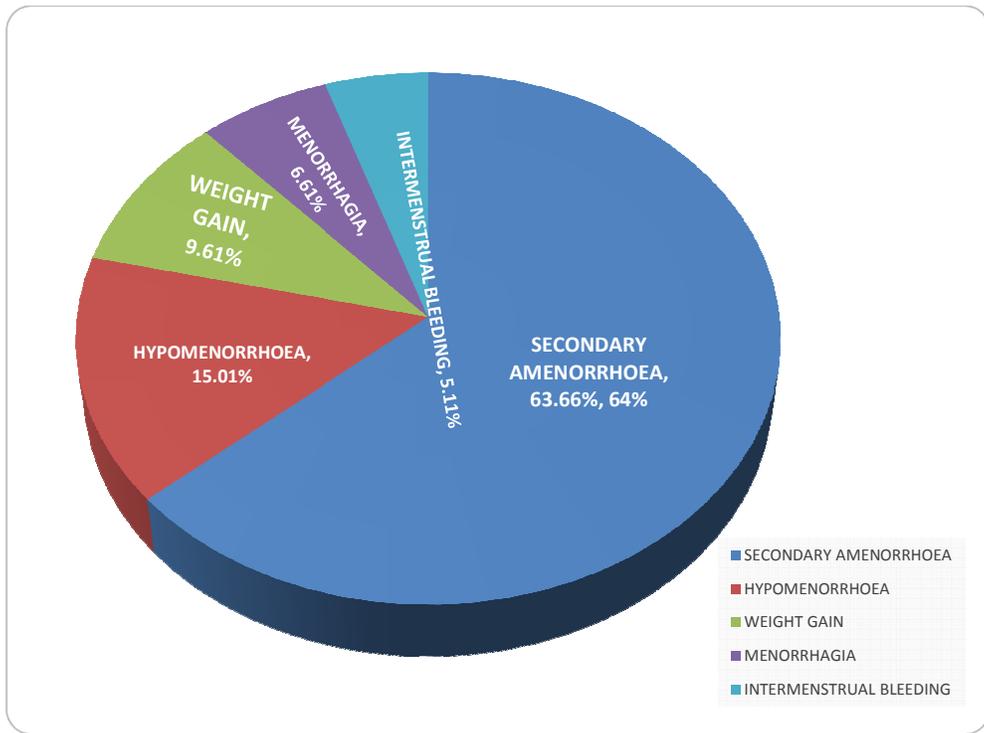


Fig. 1. Frequency of side effects

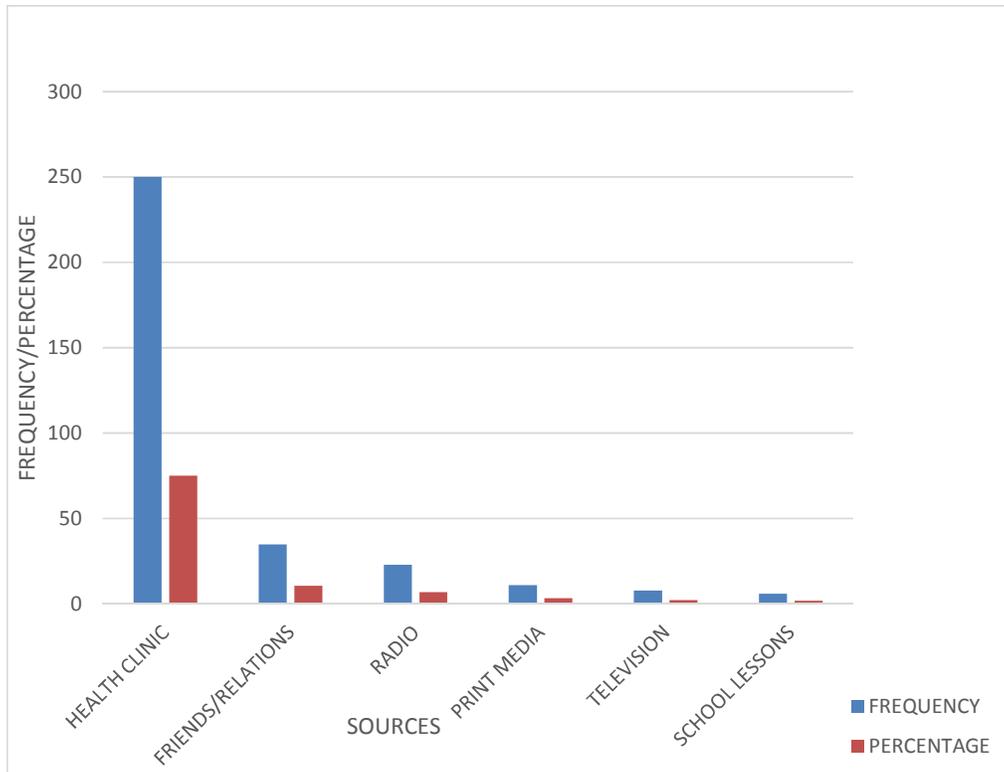


Fig. 2. Sources of information

There were no accidental pregnancies recorded during the period under review.

5. CONCLUSION

Norethisterone enanthate is a safe, effective and acceptable method of contraception for women who desire a relatively long term reversible contraceptive method in our population. It was mostly used by primiparous / multiparous women and those in the late twenties / earlier thirties; it should be available to all who wish to make informed choice about a reversible method of contraception. The print and electronic media should be more involved in the propagation of accurate information about contraceptives including NET-EN to members of the community, especially the rural/non literate population so they can make informed choice on contraception.

CONSENT

Client consent was not applicable in this study; no personal identifying data was given on any client.

ETHICAL APPROVAL

All authors hereby declare that all evaluations have been examined and approved by the appropriate ethics committee and have therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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