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SAFETY, EFFICACY AND ACCEPTABILITY OF IMPLANON A SINGLE ROD IMPLANTABLE CONTRACEPTIVE (ETONOGESTREL) IN UNIVERSITY OF BENIN TEACHING HOSPITAL

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ABSTRACT

Objective: The study evaluated the safety, efficacy and acceptability of Implanon (etonogestrel) subdermal implant contraceptive amongst its acceptors.

Study Design: This was part of an on going prospective longitudinal study that involved 32 women out of 46 sexually active healthy informed volunteers recruited from our family planning clinic between February and March 2007. All the subjects received the single rod subdermal implant Implanon which contains 68mg etonogestrel. Data on socio-demographic characteristics, menstrual pattern, haematological indices, weight, blood pressure, side effects and user's satisfaction were collected and analysed. The subjects served as their own control.

Results: The mean age and parity were 33.9 ± 5.2 years and 3.1 ± 1.7 respectively. The mean weight was 71.4 ± 12.0kg at pre-insertion. At 6 months the weight reduced to a non significant ($p < 0.13$) mean value of 70.0 ± 10.5kg and increased to a non significant ($p < 0.88$) mean value of 71.5 ± 11.6kg at 12 months. The mean systolic and diastolic blood pressures did not show statistical significant changes at 6 months follow up ($p<0.17/0.64$). However at 12 months there were significant but within normal reductions ($p < 0.003/0.05$) in the systolic and diastolic blood pressures. The side effects were menstrual abnormalities. Eighteen (56.3%), 1 (3.1%) and 13 (40.6%) reported reduced, increased and combinations of bleeding patterns respectively. No participant had normal cycle. Other experiences were headache, 4 (12.5%) and reduced libido 3 (9.4%). The mean packed and white blood cell concentrations did not show statistical significant changes at 6 and 12 months follow up. At 12 months there was statistical significant increase ($p<0.04$) in the mean ± SD platelet count (205312.5 ± 75694.8per ul) when compared with the pre-insertion mean value (176343.8 ±52945.3per ul). One acceptor had thrombocytopenia without any untoward effect.
Two subjects discontinued method on account of menorrhagia and headache. The efficacy and continuation rate were 100% and 93.8% respectively. All the clients received adequate information about the method and most of them were satisfied with it at follow up.

Conclusion: Implanon was an effective, safe and acceptable method of contraception amongst its acceptors. Menstrual abnormalities were the major side effects which most of the subjects found tolerable with adequate counseling. The reduced platelet concentration of the one acceptor would require follow up to ascertain the trend.

Key Words: Implanon implant, safety, efficacy and acceptability *(Accepted 28 August 2009)*

INTRODUCTION

Implanon subdermal progestogen (etonogestrel) is a second generation implant developed as a need to reduce some of the problems associated with the six implant system, Norplant[1,2]. It is an effective long term reversible method of contraception[3,4], suitable for many women across different reproductive ages[5-7]. Even though it has been in use for some time[8,9], it was only introduced into Nigeria in 2006.

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The most common side effect of Implanon is disruption of menstrual cycle[3,6,8,10-21]which has led to discontinuation amongst its acceptors in various studies[3,8,10,12,15-21]. In spite of these, no patient had been reported to have anaemia with its use[12-14]. This is relevant in developing countries where many women already have nutritional deficiencies coupled with anaemia[22]. Other common drug related adverse events reported include headache, weight gain, acne and depression[3,5,10,12,14,16,20,23]. The contraceptive action of Implanon is mainly by inhibition of ovulation that lasts for 3 years[5,24,25]. The contraceptive efficacy

before 2004 was 100%[26]. It has been found to have satisfactory profile with quick return to fertility[6,8,9,11,14].

At this initial stage of Implanon introduction into our contraceptive method mix, it is important to document its safety, efficacy and acceptability amongst the users.

MATERIALS AND METHODS

Forty six sexually active, healthy informed volunteers aged between 24-45 years were recruited from our Family Planning Clinic of the University of Benin Teaching Hospital, Benin-City, Edo State, Nigeria between February and March 2007. One hundred and ninety clients accepted family planning methods during the period out of which fifty clients chose Implanon. The forty six who consented to participate in the study had not received any injectable contraceptive within 6 months preceding recruitment and they were all having regular normal menstrual cycles. All the acceptors were given a calendar each, to keep daily record of menstrual bleeding events. The coding used for bleeding events were zero "0" for no bleeding 'S' for spotting (defined as scanty vaginal bleeding that did not require sanitary protection) and "X" for vaginal bleeding that required sanitary protection. Data analysis for the bleeding patterns was based on completed 90 day interval for reference period[27,28].

Venous blood (5mls) was collected from each subject from the contra lateral arm and placed in a tube containing EDTA anticoagulant for the estimation of packed cell volume (PCV), platelets and white blood cells (WBC) concentrations. Blood samples were collected at pre-insertion and at 6 and 12 months follow up. Each participant served as her own control.

Data on socio demographic characteristics, weight, blood pressure, side effects, and user's satisfaction were also collected and analysed.

Each subject received Implanon, a single rod subdermal implant, containing 68mg of etonogestrel.

Methodology

The haematological indices were evaluated using Abacus junior (Diatron Ltd 2003) haematology analyzer. It uses the impedance method (also known as coulter method) to count.

Analysis

Thirty two (32) subjects who had complete records at 12 months were analysed. Paired t-test was used for statistical analysis. The level of significance was set at $p<0.05$. The remaining clients even though were followed up, they were not consistent at blood sampling.

RESULTS

Socio demographic characteristics

The age range and mean of the subjects were 24-45 years and 33.9 ± 5.2 years. Parity range and mean were 0-6 and 3.1 ± 1.7 respectively. 31 (96.9%) of the subjects were married and had formal education, with 15 (46.9%), 15 (46.9%) and 1 (6.2%) having tertiary, secondary and primary levels of education respectively. One client was unmarried and had secondary level of education.

Weight changes

The mean weight was 71.4 ± 12.0 kg at pre-insertion. There were no statistical significant changes in mean weight at six (70.0 ± 10.5kg) and twelve months (71.5 ± 11.6kg) when compared with pre-insertion mean value. (Table 1). Fifteen 46.9% subjects had increased weight, 14 (43.7%) had a weight reduction while 3 (9.4%) had no weight changes.

Blood pressure

The systolic and diastolic blood pressures did not show any statistical significant changes at 6 months of study ($p< 0.17/0.64$). However at 12 months follow up there were statistical significant reductions (0.003/0.05) in the mean values of the systolic and diastolic blood pressure which were within normal limits (Table 1).

Menstrual analysis

The main adverse events reported were menstrual abnormalities where 18 (56.3%), 1 (3.1%) and 13 (40.6%) subjects reported reduced, increased and combinations of bleeding patterns respectively. There was no subject with normal menstrual cycle in the reference periods (Tables 2 and 3).

Packed cell volume (PCV)

At the time of admission into the study the mean value of the PCV was 37.3 ± 2.5%. There were no statistical significant changes at six and twelve months of study ($p<0.83$ and $p< 0.22$ respectively (Table 4).

White blood cell concentration (WBC)

The mean concentration of white blood cells at pre-insertion was 5275 ± 1124.5per µl. There were no statistical significant changes at six and twelve months of study ($p<0.06$ and $p<0.43$) respectively (Table 4).

Platelets concentration

The mean concentration of the platelets at pre-insertion was 176343.8 ± 52945.3per µl at insertion. This rose to a non significant mean normal concentration at 6 months of 203875 ± 73603.0 per µl ($p<0.1$) and a significant increase $p<0.04$) at 12 months of study (Table 4). One subject had platelet concentrations of <100000 at 12 months with concentrations of 89000per µl.

Continuation rate, efficacy, acceptability

Two subjects discontinued use at 6months because of menorrhagia and headache giving a continuation rate

of the 32 acceptors as 93.8%. Other adverse events reported were headache 5 (12.2%), reduced libido 3 (7.3%). The efficacy was 100% as no subject became pregnant during the 12 months period. The users were satisfied with the method (Table 5).

Table1: **Mean weight (mean ±SD) kg and Mean Blood Pressure (mean ± SD) mmHg of Implanon Acceptors at 6 and 12 months of Study.**

….	Pre-insertion	6 months	12 months
Weight	71.4 ± 12.0	70.0 ± 10.5	71.5 ±11.6
P-value	-	0.13	0.88
Blood pressure	118.4 ±14.4/76.6 ± 9.7mmHg	121.6 ± 14.2/75.9 ±8.4mmHg	109.7±12.6 /72.2±8.7m mHg
P-value	-	0.17/0.64	0.003/0.05

Table 2: **Reduced Bleeding Irregularities of 32 Subjects during the Reference Periods (1st period 1-90 days, 2nd period 91-180 days, 3rd period 181-270 days and 4th period 271-360 days).**

Bleeding irregularities	Reference period	Number (n) Percentage
Infrequent bleeding (less than two episodes)	1	(11) 34.4
	2	(8) 25
	3	(11) 34.4
	4	(6) 18.8
Few bleeding days (less than 5 days)	1	(12) 37.5
	2	(12) 37.5
	3	(8) 25
	4	(12) 37.5
Amenorrhoea (60 days without bleeding or spotting)	1	(11) 34.4
	2	(7) 21.9
	3	(7) 21.9
	4	(15) 46.9
Amenorrhoea (90 days without bleeding or spotting)	1	(6) 18.8
	2	(16) 50
	3	(8) 25
	4	(10) 31.3

Table 4: **Haematological Parameters of Subjects (mean ± SD): Pre-insertion 6 and 12 months of follow up.**

Parameter	Pre-insertion	6 months	12 months
Packed cell volume (PCV) %	37.3 ± 2.5	37.4 ± 2.3	36.6 ±3.4
P value		0.83	0.22
White cell concentration (WBC)per µl	5275±112 4.5	5700±1358.4	4765.6±3803.5
P value			0.43
Platelets per µl	176343.8 ± 52945.3	0.06 203875±736 03.0	205312.5±75694.8
P value		0.10	0.04

Table 3: **Increased Bleeding Irregularities in 32 Subjects during the Reference Periods (1st period 1-90 days, 2nd period 91-180 days, 3rd period 181-270 days and 4th period 271-360 days).**

Bleeding irregularities	Reference period	Number (n) Percentage
Frequent bleeding (5+episodes)	1	(2) 6.3
	2	(2) 6.3
	3	(1) 3.1
	4	(1) 3.1
Prolonged bleeding (8+days per episode)	1	(10) 31.3
	2	(6) 18.8
	3	(7) 21.9
	4	(7) 21.9
Numerous bleeding and spotting days (21+days)	1	(4) 12.5
	2	(4)12.5
	3	(2) 6.3
	4	(1) 3.1
Numerous bleeding and spotting days (31+days)	1	(1) 3.1
	2	(1) 3.1
	3	(0) 0
	4	(0) 0

Table 5: **User's Satisfaction.**

Features		Number	%
1.	Liked Features:		
	a. Convenience	32	100
	b. Low risk of pregnancy	32	100
	c. Long duration of action	32	100
2.	Least liked Feature:		
	a. Bleeding irregularities	10	31.3
3	Discomfort during insertion	0	0
4	No negative feelings about the method	28	87.5
5	Recommendation of the method to a friend	32	100
6	Usage of a second set of implant for contraception	25	78.1
7	Satisfaction about the choice of method	32	100
8	Received enough information about implant for decision making	32	100

DISCUSSION

The study has shown that the mean age of the subjects as well as the parity distribution were within those reported in the literature[6,8,15,17,20]. The women in the study had either reduction, increase or no weight change without any statistical significant difference when compared to the pre-insertion mean weight. Other studies had documented either no change in weight[6] or increase in weight[3,10,12,13,20,23]. Implanon is a derivative of 19 nortestosterone which actions are anti oestrogenic and androgenic. The weight gain observed may have been a consequence of the anabolic effect of the method in addition to a normal increase in weight over time[29].

Experiences from studies have shown no changes in blood pressure[12,14,23] while one study[6] found a normal diastolic blood pressure followed by a decline in systolic blood pressure after 6 months of study. This study showed statistical significant reduction but within normal limits in the systolic and the diastolic blood pressure at 12 months follow up. This trend is advantageous as the women are not predisposed to hypertensive disease.

The most common adverse experience reported by acceptors of Implanon was menstrual disruption[3,6,8,10-21] which had led to discontinuation of use[3,8,10,13,15-21]. In this current study the subjects reported reduced, increased and combination of both reduced and increased bleeding patterns. Similar observation has also been reported in the literature[29,30].

Hormonal contraceptive methods interfere with the pituitary ovarian axis that controls the menstrual cycle. The combined oral contraceptive pill is able to regulate and simulate normal menstruation because of its oestrogen content unlike the progestogen only contraceptives hence the bleeding irregularities associated with them. One subject discontinued Implanon at 6months because of frequent bleeding and spotting episodes. No participant discontinued because of reduced bleeding. The analysis of bleeding patterns in those who discontinued the use of Implanon showed that they had experienced more prolonged and frequent bleeding. However women who had amenorrhoea were unlikely to discontinue Implanon use[29]. The apparent tolerance of irregularities of the menstrual cycle by our clients may be due to effective counseling at the time of insertion. The importance of counseling has been highlighted in implant users[22,31-33] where the overall acceptability of the method improved.

Inspite of the irregular menstrual abnormalities experienced, the packed cell volume of the acceptors were normal. Other reports have found similar changes[12,13,14]. The white blood cell concentration did not show statistical significant changes over the months of follow up. Studies[29,34,35] conducted had shown that the effects of Implanon on haemostatic system are not only small, but also not indicative of a change towards either coagulation or fibrinolysis. In this study the mean platelet concentration rose to significant but normal mean normal value at 12 months. There was one participant that had thrombocytopenia without associated bleeding abnormalities.

Other side effects reported were headache and reduction in libido which are method related and have also been reported[3,10,14,16,29]. One patient discontinued because of persistent headache.

The continuation rate at 12 months was 93.8%. Similar high continuation rate has also been reported[15,21,36]. The efficacy was 100%. Many other studies had reported a Pearl Index of 0.0. However no contraceptive method is 100% efficacious and very small number of pregnancies even after correct insertion of Implanon had been reported[29].

In conclusion Implanon subdermal implant produced bleeding irregularities amongst the acceptors which was well tolerated and no participant became anaemic. Implanon was an acceptable and effective method of contraceptive with satisfactory safety profile amongst the users. The thrombocytopenia experienced by one of the participants is however worrisome and needs follow up to establish the trend.

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