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COMPARISON OF CARDIOVASCULAR DISEASE RISK ASSOCIATED WITH THE USE OF IMPLANON AND JADELLE CONTRACEPTIVES IMPLANTS AT A TERTIARY HEALTH INSTITUTION OF NORTH WESTERN NIGERIA

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ABSTRACT

Background: Cardiovascular diseases are the leading cause of adult mortality. Abnormal lipid profiles have been associated with a major risk factor for cardiovascular disease (CVD) which is one of the most dominant causes of death in the world. Dyslipidemia contributes to the development of arthrosclerosis. **Objectives:** The purpose of this study is to determine baseline Castelli index in women who use Implanon and those who use Jadelle contraceptive implants. Compare the extent of cardiovascular atherosclerotic risk associated with the lipid metabolism in women using Implanon and Jadelle subdermal implants over 3 and 6 month of use and evaluate changes in Castelli 1 and 2 indices over 3 and 6 months of use in each group. **Methodology:** This was a prospective study of clients who desired contraception and chose any of the two subdermal implants (Implanon and Jadelle) as the method of contraception from 1st November 2015 to 30th June 2016. Venous blood samples (fasting) were taken before insertion of the implant (baseline) and at third and sixth month of insertion from each participant. The serum was analysed for lipid profile. Castelli indices I & II were calculated to determine the CVD risk. All the results were entered in to SPSS version 20 and analysed. **Results:** A total of 100 clients were enrolled for this study. Eighty-seven clients completed the study, 42 for Implanon and 45 for Jadelle with an overall response rate of 87%. The baseline Castelli1 indices were 4.1 mg/dl ±1.0 and 3.8 mg/dl ±0.9, Castelli2 indices were 2.6.1 mg/dl ±1.0 and 2.4 mg/dl ±0.8 for Implanon and Jadelle respectively. These values did not change to a statistically significant level over 3 and 6 months of use when compared between the two implants except in the value of castelli 2 index at 6 month of use $p = 0.038$. There was statistically significant increase in Castelli 2 index among the Jadelle group at 3 month of use and also at sixth month when compared with baseline ($p<0.05$). The other indices were not statistically significant ($p>0.05$). **Conclusion:** The cardiovascular risk associated with the use of Implanon and Jadelle appears low, however clients on long term contraceptive implants may require close monitoring of serum lipid profile to checkmate possible occurance of cardiovascular disease risk.

KEYWORDS: Castelli, sokoto, jadelle, implanon, contraception.

INTRODUCTION

Dyslipidemia has been identified as one of the most important risk factors associated with coronary artery disease (CAD).[1,2] Low HDL-cholesterol (HDL-C), high triglycerides (TG) and high LDL-cholesterol (LDL-C) levels have been associated with increased incidence of CAD. Low HDL-cholesterol (HDL-C), high triglycerides (TG) and high LDL-cholesterol (LDL-C) levels have been associated with increased incidence of CAD.[2] Castelli Risk Index-I (CRI-I) is defined as calculated value of Total Cholesterol /High Density Lipoprotein (HDL) and Castelli Risk Index-II (CRI-II) as Low density Lipo protein (LDL)/HDL.[1] Contraceptive implants are progesterone only contraception that are inserted sub dermally. They are highly effective, suitable for nearly all women and it is gaining popularity.[3] Subdermal contraceptive implants release low amounts of synthetic progestogens from polymer capsules placed under the skin providing effective (but readily reversible) contraception. Abnormal lipid profiles have been associated with major risk for cardiovascular disease.[4] Contraceptive implant use has been linked to abnormalities in lipid metabolism. This could be due to arthrosclerosis.[5] Hormonal contraceptives (HCs) have

been shown to alter lipid profile among various population groups with different patterns of dyslipidemia and cardiovascular risk.[6] The cardiovascular effects of long term use of hormonal contraception have continued to generate interest. Studies on the cardiovascular effects of Implants depend largely on the evaluation of changes in serum lipids.[7]

Consideration of implants as a contraceptive option depends on the mode of counselling as well as positive perceptions among the general public. Studies in women using implants have indicated that perceptions of implants among users are favourable and that acceptance is high.[6] Women who use implants have identified ease of use (79%) and high effectiveness (30%) as the most desirable features.[6] The majority of users (54%) reported that difficulty or dissatisfaction with other methods of contraception was a primary reason for choosing implants, with most women reporting previous use of three or more methods of birth control.[7] These women also considered convenience and ease of use important in their decision to use implants, even though use of the device requires a minor surgical procedure for insertion and removal. The advantage of the one or two rod implant system is the ease of placement and removal.

In the Usmanu Danfodiyo University Teaching Hospital family planning clinic the implants available for clients to choose from are the single rod (Implanon) and the two rod (Jadelle) subdermal implants. The Castelli index profile of these two implants in healthy non diabetic non hypertensive Nigerian women was determined in this study.

OBJECTIVES

The purpose of this study is to determine baseline Castelli index in the group of women who use Implanon and those who use Jadelle. Compare the extent of cardiovascular atherosclerotic risk associated with the lipid metabolism in women using Implanon and Jadelle subdermal implants over 3 and 6 month of use and evaluate changes in Castelli 1 and 2 indices over 3 and 6 months of use in each group.

METHODOLOGY

Usmanu Danfodiyo university teaching hospital is the tertiary hospital in Sokoto. It has all the major clinical departments and provides all levels of care. The Department of Obstetrics and Gynaecology has four units which operate the antenatal, postnatal and gynaecological clinics on all weekdays. The average annualnds delivery rate was 3000. The Fertility Research unit is the family planning unit of the Department of Obstetrics and Gynaecology (O&G) of UDUTH Sokoto. The clinic runs from 8 am to 4 pm on Mondays to Fridays. Services provided include counselling on the various modern methods of family planning, administration of such services following informed choice as well as periodic follow-up after a choice has been made. Contraceptive methods available at the unit include hormonal agents like the contraceptive pills, injectables and implants. This was a prospective longitudinal study of clients who desired contraception and chose any of the two subdermal implants (Implanon and Jadelle) as the method of contraception from 1st November 2015 to 30th June 2016. Patients were counselled and those who consented were consecutively recruited till the desired sample size was reached, Venous blood samples (fasting) were taken before insertion of the implant (baseline) and at the third and sixth month of insertion from each participant. The serum was analysed for lipid profile. Castelli indices I & II were calculated to determine the CVD risk. All the results were entered in to SPSS version 20 and analyzed. Level of significance was set at $p<0.05$. ethical approval was obtained from the health research and ethics committee of the hospital and each client provided informed consent.

RESULTS

A total of 100 clients were enrolled for this study. Eighty-seven clients completed the study, 42 for Implanon and 45 for Jadelle with an overall response rate of 87%. Further analyses were limited to these women.

Table 1: Socio-demographic characteristics of clients.

Sociodemographic characteristics	Jadelle	Implanon	statistics
Age (years)	**frequency (%)**	**Frequency (%)**	
15 -19	1 (2.2)	4 (9.5)	
20 – 24	8 (17.8)	23 (54.7)	χ^2= 22.03
25 - 29	14 (31.1)	11 (26.2)	df = 5
30 - 34	13 (28.9)	3 (7.2)	p = 0.001*
35 – 39	8 (17.8)	1 (2.4)	
40 – 44	1 (2.2)	0 (0.0)	
Tribe			
Hausa/Fulani	33 (73.3)	35 (83.3)	χ^2= 8.17
Yoruba	3 (6.7)	3 (7.1)	df = 3
Igbo	3 (6.7)	2 (4.8)	p = 0.613
Others	6 (13.3)	2 (4.8)	
Religion			χ^2= 1.621

Islam	35 (77.8)	35 (88.1)	df = 1
Christianity	10 (22.2)	7 (11.9)	p = 0.203
Address			χ^2= 0.278
Urban	43 (95.6)	41 (97.6)	df = 1
Rural	2 (4.4)	1 (2.4)	p = 0.598
Occupation of clients			
House wife	26 (57.8)	30 (71.4)	χ^2= 14.91
Civil servant	13 (28.9)	3 (7.1)	df = 3
Trader	4 (8.9)	0 (0.0)	p = 0.02*
Student	2 (4.4)	9 (21.5)	
Husbands' occupation			
Civil servant	33 (73.4)	32 (76.2)	χ^2= 3.16
Trader	11 (24.4)	9 (21.4)	df = 2
Private firm employee	1 (2.2)	1 (2.4)	p = 0.531
Educational status of clients			
Not formally educated	2 (4.4)	3 (7.1)	χ^2= 0.631
Primary	2 (4.4)	1 (2.4)	df = 3
Secondary	17 (37.8)	17 (40.5)	p = 0.889
Tertiary	24 (53.4)	21 (50.0)	
Husbands' educational status			
Not formally educated	2 (4.4)	1 (2.4)	χ^2= 1.55
Primary	0 (0.0)	1 (2.4)	df = 3
Secondary	5 (11.1)	6 (14.3)	p = 0.672
Tertiary	38 (84.5)	34 (80.9)	
Parity			
0	0 (0.0)	2 (4.8)	χ^2= 28.78
1-4	36 (80.0)	38 (90.4)	df = 2
≥ 5	9 (20.0)	2 (4.8)	p = 0.000*
Last pregnancy			
< 6 weeks	12 (26.7)	21 (50.0)	χ^2= 8.13
≥ 6weeks - one year	33 (73.3)	19 (45.2)	df = 3
> One year	0 (0.0)	1 (2.4)	p = 0.045*
No pregnancy	0 (0.0)	1 (2.4)	

*** Statistically significant**

Apart from the fact that he women who chose Implanon were younger and of lower parity than those who chose Jadelle, the women were mostly Hausa Fulani Muslims who resided in the urban areas.

Table 2: Serum lipid profile of subdermal implants (Implanon and Jadelle) at baseline, third month and sixth month with comparison between the two implants.

Serum lipid (mg/dl)	Subdermal implant		statistics			
	Jadelle	Implanon	Df	T-test	p-value	CI
Cholesterol-1 (Baseline)	185.73±35.21	181.79±39.35	85	0.494	0.623	11.95-19.85
Cholesterol-2 (Third month)	186.11±58.34	206.04±77.53	85	1.360	0.177	49.05-9.20
Cholesterol-3 (Sixth month)	194.38±72.08	226.89±80.21	85	1.991	0,005*	64.98 -0.05
TG-1 (Baseline)	77.85±37.02	94.88±39.56	85	2.021	0.046*	33.79-0.28
TG-2 (Third month)	76.90±31.16	97.12±56.16	85	2.095	0.039*	39.41-1.034
TG-3 (Sixth month)	170.14±62.40	87.82±51.93	85	0.803	0.424	121.56-286.21
HDL-1 (Baseline)	50.16±9.26	45.07±6.22	85	2.984	0.004*	1.696-8.472
HDL-2 (Third month)	56.75±20.82	58.62±20.38	85	0.422	0.674	10.66-6.92
HDL-3 (Sixth month)	65.07±26.08	72.82±30.15	85	1.284	0.203	19.74-4.25
LDL-1 (Baseline)	117.16±34.55	116.74±38.97	85	0.053	0.958	15.26-16.09
LDL-2 (Third month)	146.14±61.32	161.61±69.58	85	1.102	0.274	43.39-12.44
LDL-3 (Sixth month)	151.10±60.82	173.16±91.07	85	1.337	0.185	54.86-10.75

The mean baseline triglyceride (TG) was significantly higher in implanon group (p=0.046) while that of high density lipoprotein (HDL) was significantly higher in jadelle group (p=0.004). At 3 months, the triglyceride value was significantly higher in implanon group (p=0.039). Similarly at 6 months, the cholesterol value

was significantly higher in implanon group (p=0.005). There were no significant differences in the other values.

LDL; Low density lipoprotein

Table 3: Anthropometric measurements of subdermal implants (Implanon andJjadelle) users at baseline, third month and sixth month.

Measurements	Subdermal implant		Statistics			
	Jadelle	Implanon	Df	t-test	p-value	CI
WEIGHT-1 **(Baseline)**	70.39±14.16	67.90±19.17	85	0.693	0.490	4.66-9.64
WEIGHT-2 **(Third month)**	71.06±14.23	67.98±19.66	85	0.842	0.402	420-10.36
WEIGHT-3 **(Sixth month)**	70.90±14.28	67.94±20.04	85	0.798	0.427	4.42-10.34
BMI-1 **(Baseline)**	27.34±4.73	26.14±7.62	85	0.891	0.375	1.48-3.89
BMI-2 **(Third month)**	27.51±4.80	26.20±7.96	85	0.932	0.354	1.49-4.08
BMI-3 **(Sixth month)**	27.41±4.95	26.15±7.96	85	0.889	0.376	1.55-4.06
WAIST Circumference-1 **(Baseline)**	89.73±13.18	87.12±13.39	85	0.917	0.3614	3.05-8.28
WAIST Circumference-2 **(Third month)**	89.87±12.83	87.19±13.50	85	0.948	0.346	2.94-8.290
WAIST Circumference-3 **(Sixth month)**	90.48±12.30	86.43±14.67	85	1.398	0.166	1.71-9.81
HIP Circumference-1 **(Baseline)**	102.3±11.63	99.95±13.45	85	1.033	0.304	2.57-8.132
HIP Circumference-2 **(Third month)**	103.48±11.05	100.74±12.84	85	1.069	0.288	2.36-7.84
HIP Circumference-3 **(Sixth month)**	103.91±10.30	101.76±13.53	85	0.837	0.405	2.956-7.254

Table 4: Base line Castelli index.

Group Statistics					
	Implantchoosen	n	Mean	Std. Deviation	Std. Error Mean
Castelli1a	Jadelle	45	3.7855	.88675	.13219
	Implanon	42	4.0939	.98808	.15246
Castelli2a	Jadelle	45	2.4063	.82934	.12363
	Implanon	42	2.6441	.96582	.14903

The baseline Castelli1 indices were 4.1 mg/dl ±1.0 and 3.8 mg/dl ±0.9, Castelli2 indices were 2.6mg/dl ±1.0 and 2.4mg/dl ±0.8 for Implanon and Jadelle respectively. These values did not change to a statistically significant level over 3 and 6 months of use when compared between the two implants except in the value of castelli 2 index at 6 month of use p = 0.038. There was statistically significant increase in Castelli 2 index among the Jadelle group at 3 month of use and also at sixth month when compared with baseline ($p<0.05$). The other indices were not statistically significant ($p>0.05$).

Table 5: Castelli index at 3 and 6 months of implant use.

Group Statistics					
	Implantchoosen	N	Mean	Std. Deviation	Std. Error Mean
CASTELLI1B	JADELLE	45	3.6673	1.60431	.23916
	IMPLANON	42	3.8172	1.82937	.28228
CASTELLI1C	JADELLE	45	3.2117	1.12365	.16750
	IMPLANON	42	3.5690	2.29015	.35338
CASTELLI2B	JADELLE	45	2.9192	1.65589	.24685
	IMPLANON	42	2.9942	1.69733	.26190
CASTELLI2C	JADELLE	45	2.4766	.90160	.13440
	IMPLANON	42	2.6713	2.08563	.32182

DISCUSSION

In this study it was found that there was a difference regarding the ages of the clients. The younger clients chose the single rod Implanon subdermal implant (mean age 23.98±4.10) while the older clients chose the 2 rod Jadelle subdermal implant (mean age 29.36±5.48). The mean age in the Jadelle group was closer to the mean age finding in Ibadan Nigeria (27.5±6 5.2). Regarding Parity, majority of clients of low parity chose the single rod Implanon subdermal implant while majority of those with higher parity chose the 2 rod Jadelle subdermal implant. There was no statistically significant difference in other socio demographic characteristics. It appears the those with higher parity preferred the longer spacing period of 5 years that Jadelle provides compared with the shorter three use for Implanon.

The baseline serum lipid profile values in this study were normally distributed except for triglycerides and HDL. A consistent rise in the serum cholesterol level was noted from the baseline through the third month up to the sixth month of use in both Jadelle and Implanon group. This

increase in serum cholesterol level was only significant at six months among Implanon users (p=0.005). This finding was similar to that of Affandi et al in Indonesia.[8] and Adekunle et al in Ibadan South western Nigeria.[9] These similarities likely occurred due to the similarities in socio demography of the clients studied especially the study population in Ibadan Nigeria. Inal and colleagues in Turkey[10] also reported increase in cholesterol to a statistically significant level when used for three years. The study by Inal and colleagues therefore suggested that the changes might have long occurred even before the third year. The decrease in triglycerides (TG) in the Jadelle group was observed at third month of the implant insertion but a rise was noted at six months of use. However, in the Implanon group there was a rise in TG at third month followed by a decrease in the mean TG value at sixth month of use. These changes were however not statistically significant (p>0.05). The only significant difference was noted when TG was compared at baseline and third month between Jadelle and Implanon. This was different from the findings in Turkey.[10] and Ibadan.[9] where there was consistent rise to a statistically significant level. There was also persistent rise in the values of high-density lipoprotein (HDL) in both groups from baseline through third month to sixth month after Implanon insertion and these reached a statistically significant level (p=0.00). This may have a beneficial effect for the affected individual as HDL is protective against cardiovascular diseases and no significant increase in Castelli index. Suharti et al in Indonesia showed no clear pattern in the change of HDL in the population studied over the three-year period. A different finding of decrease in HDL was noted in Netherlands population in a study conducted by Biswas et al. [11] There was an increase in the values of low-density lipoprotein (LDL) in both Jadelle and Implanon group, but these changes were not statistically significant when compared between the two groups. However, when these changes were compared over the duration of use a significant difference was observed at third month (p=0.002) and sixth month (p=0.003). The mean serum lipid profile changes when compared between Jadelle and Implanon showed significant changes even at pre-insertion period with an increase in the mean serum cholesterol level at sixth month (p=0.005), increase TG at baseline (p=0.046), increase TG at third month (p=0.039) and decrease HDL at baseline (p=0.004). All these changes are in favour of Implanon (p<0.05). The differences in the socio-demographic characteristics in the clients may be responsible in the baseline changes. The constituents of the individual implants may have accounted for the observed changes during the study period.

The anthropometric measurements in this study were not significantly affected by the subdermal implants Implanon and Jadelle except mean weight in the Jadelle group at third month of use (p=0.025) and mean hip circumference at third month (p=0.002) and sixth month (p=0.021) of use for Implanon users where some little increase were noted during the study period.

CONCLUSION

The cardiovascular risk associated with the use of Implanon and Jadelle appears low, however clients on long term contraceptive implants may require close monitoring of serum lipid profile to checkmate possible occurance of cardiovascular disease risk.

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