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WEIGHT CHANGES AMONG DEPO-MEDROXYPROGESTERONE ACETATE ACCEPTORS IN SAGAMU, SOUTHWEST NIGERIA
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WEIGHT CHANGES AMONG DEPO-MEDROXYPROGESTERONE ACETATE ACCEPTORS IN SAGAMU, SOUTHWEST NIGERIA

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ABSTRACT

Background: **Depo-medroxyprogesterone acetate is a highly effective injectable contraceptive. Weight gain is a commonly reported side effect that makes women to discontinue the contraceptive method. Studies on weight changes among the users in Nigerian women are sparse. Hence, this study was aimed at determining the effect of Depo-medroxyprogesterone acetate on the weight and Body Mass Index of users at 6 months and 12 months.**

Methods: **This was a prospective longitudinal study conducted among sixty-eight new acceptors of Depo-medroxyprogesterone at the family planning clinic of Olabisi Onabanjo University Teaching Hospital Sagamu, Ogun State. Weight and Body Mass Index of acceptors were recorded. Women were followed up at 6months and 12 months. The data was analysed using SPSS version 24.**

Results: **The mean weight before starting Depo-medroxyprogesterone acetate was 62.9±10.5kg and at 6 months and 12 months the mean weights were 63.3±10.5kg and 63.8±9.8kg respectively. The increase in weight of the participants at 6 months was not significant (t=1.511, P=0.135), however after 12 months, there was significant weight gain (t=2.697, P=0.009). Similarly, Depo-medroxyprogesterone acetate was associated with a non-significant increase in Body Mass Index at 6 months (t=1.455, P=0.150) whereas users had statistically significant increase in Body Mass Index at 12 months post-commencement. Age, parity, educational status and pre-treatment Body Mass Index of study participants were not predictors of weight gain among Depo-medroxyprogesterone acetate users.**

Conclusion: **Depo-medroxyprogesterone acetate was associated with significant weight gain and Body Mass Index increase after 12 months of use. Appropriate counselling is important prior to initiation.**

INTRODUCTION

Depo-medroxyprogesterone acetate (DMPA) is a progesterone only contraceptive agent. It is one of the most commonly used long-acting reversible contraceptive.[1]About 90 million women in 106 countries use long-acting injectable contraceptives.[1,2] In Nigeria, injectable contraceptives account for three percent of the 17% total contraceptive prevalence.[3] The ease of administration in the clinic by community health workers with sufficient training under minimal supervision has made DMPA one of the most popular contraceptive method in the sub-Saharan African.[4] Apart from using DMPA for child spacing and to limit family size, there are some non-contraceptive benefits such as reduction in the risk of endometrial hyperplasia, endometrial cancer, endometriosis, pelvic inflammatory diseases and reduction in sickle cell crises in sickle cell disease.[5]

The mode of action of DMPA is primarily by inhibition ovulation.[6] This is achieved by suppression of pituitary gonadotrophin thereby inhibiting follicular maturation. Other mechanisms of DMPA include thickening of cervical mucus and atrophy of the endometrial lining of the uterus.[1,6] Depo-medroxyprogesterone is administered every three months thus obviating the compliance difficulty encountered with daily use of oral contraceptives and coitus-dependent barrier methods.[4] DMPA is highly effective with failure rate of 0.1-2 pregnancy per hundred women year and has a long-term good safety profile.[7] It is also the contraceptive of choice for lactating mothers, as it has no effect on the quality and quantity of milk.[7] Despite the numerous benefits of DMPA, there are some adverse effects which may be unacceptable to some women, and this is responsible for the high discontinuation rate.[8,9] These adverse effects include menstrual irregularity, weight gains, increase blood pressure, breast tenderness, ovarian cyst and decrease libido.[9]

Weight gain is a commonly reported side effect and was reported as second only to irregular menstrual bleeding.[10] This may cause women to avoid or discontinue the contraceptive method.[11] Reports from studies on the effect of DMPA use on the weight of users have been largely inconsistent. Some studies reported weight increase[11,12,13] while others find no weight changes unique to DMPA users.[14,15] Furthermore, the amount of weight gain associated with this method is unclear as the mean weight gain reported from the studies varies.[11-13] The only local study available in Nigeria was a retrospective study performed by Shittu et al[15] more than a decade ago and reported no significant change in weight among DMPA users. The aim of this study is to determine the effect of DMPA on the weight and body mass index of users

MATERIALS AND METHODS

The study was a prospective longitudinal study conducted at Olabisi Onabanjo University Teaching Hospital Sagamu, Ogun State. The study population was healthy women visiting family planning unit of the department of obstetrics and gynaecology of the hospital. The inclusion criteria are women aged 20-40 years, body mass index less than 30kg/m^2 and new acceptors of three-monthly depo-medroxyprogesterone acetate as methods of contraceptive. Women who were on hormonal contraceptive in the preceding 12 months, women who were breastfeeding in the preceding six months and women within six months postpartum, women with chronic medical disorder such as hypertension and diabetes mellitus, and women with risk factors

for coronary artery disease were excluded from the study.

The sample size was estimated using the formula for quantitative data.[16] Assuming 95% confidence interval and 80% power, and by using the standard deviation of the weight reported among DMPA users from previous study[17] which was (69.4±16.9kg), the minimum sample size calculated was 43. However, to improve the power of the study and allow for attrition a sample size of 68 was used for the study. The new acceptors of DMPA that met the criteria were recruited consecutively from July 2017 to August 2018, until sample size was reached. The study participants were adequately counselled, and a written informed consent was obtained.

At the baseline visit for the commencement of the contraceptive, the data capture sheet was used to collect information of subject. The client's family planning card was reviewed, medical history was obtained, and physical examination was done to ascertain the eligibility of the client for the study. Thereafter information on socio-demographic characteristics of the subject (age, marital status, religion, educational status, occupation, parity and ethnicity), the height, weight and body mass index were recorded on the data capture sheet.

All the participants were commenced on three monthly intramuscular injection of depot medroxyprogesterone acetate 150mg (Pharmacia, N.V/S.A. Puurs-Belgium). The study participants were followed for twelve months. The participants were followed-up via telephone conversations to ensure timely family planning clinic attendant, hence there was no attrition.

The body weight of the study participants was measured at 6 months and 12 months, using standardized digital weighing scale (MEDITIVE CHINA). The measurements were approximated to the nearest 0.1kg. The women wore light cloth and other accessories such as head gears, shoes and bangles were removed before weighing. The height was measured using wall mounted stadiometer (CHARDER HM 230m) to the nearest two decimal places in metres. The height was measured without shoe, head gears and bulky braided hair. Body mass index was calculated by dividing weight (kg) by square of height (m^2).

All the information obtained on the data capture sheet were entered into a personal computer and analysed using the statistical package for social science for window software version 24 (Armonk, NY:IBM Corp).Categorical variables were summarized using number and percentages while mean, standard deviation and range were used for continuous variables. The mean weight and mean body mass index at 6 months and 12 months were compared with pre-treatment values using paired t test. P value less than 0.05 and confidence interval of greater 95% was taken as statistically significant. Multivariate logistic regression was used to determine probable predictors of weight gain among study participants after 6 months and 12 months of DMPA use

Ethics

Ethical approval for the study was obtained from the Health Research Ethics Committee of Olabisi Onabanjo University Teaching Hospital, Sagamu (Reference number: OOUTH/HREC/174/2017). The research was conducted in accordance with the World Medical Association Declaration of Helsinki.

RESULTS

The sociodemographic characteristics of the subjects are depicted in table 1. The mean age was 32.7±5.1 years with age range of 21-39 years. The modal age group was 31-35 years

accounting for 31(45.6%) of the subjects. Sixty-seven (98.5%) of the women were married while majority of the subjects 52(76.5%) were of Yoruba ethnic tribe. The parity range was 1 to 5. Half of the clients (50.0%) were within parity group 3-4. The mean parity was 2.9±1.1. Twenty-four (35.8%) were traders. Majority 43(63.2%) were Christians, the educational status of the study population revealed that 7(10.4%) clients did not have any formal education, while 10(14.9%) completed primary school, 32(47.8%) completed secondary school while 18(26.9%) had tertiary education.

Table 1

Socio-demographic characteristics

Socio-demographics	Frequency	Percentage
Age (years)		
21-25	8	11.8
26-30	17	25.0
31-35	31	45.6
36-40	12	17.6
Mean±SD 32.7±5.1		
Marital Status		
Single	1	1.5
Married	67	98.5
Parity		
1-2	28	41.2
3-4	34	50.0
≥5	6	8.8
Mean±SD 2.9±1.1		
Ethnicity		
Yoruba	52	76.5
Igbo	10	14.7
Hausa	6	8.8
Occupation		
Unemployed	14	20.6
Artisan	12	17.6
Trader	24	35.3
Civil servant	10	14.7
Professional	8	11.8
Religion		
Christianity	43	63.2
Islam	24	35.3
Traditional	1	1.5
Educational status		
Informal	7	10.3
Primary	10	14.7
Secondary	32	47.1
Tertiary	19	27.9

Table 2 illustrates the mean weight changes at 6 months, and 12 months compared with pre-treatment value. Overall, 54.4% and 63.2% of the subjects experienced weight gain over the period of 6 months and 12 months respectively. Furthermore, about 32.4% and 27.9% of the participants had no change in the body weight after 6 months and 12 months of DMPA use whereas only 13.2% and 8.8% had reduction in weight at 6 months and 12 months respectively.

The range of weight change was -1.2kg to +2.6kg after 6 months and -1.5kg to +3.3kg after 12 months of using DMPA.

The mean weight before starting DMPA was 62.9±10.5kg and at 6 months and 12 months the mean weights were 63.3±10.5kg and 63.8±9.8kg respectively. The mean weight gain among DMPA users were 0.4±2.1kg and 0.9±2.7kg at 6months and 12 months respectively. Although, mean weight change after 6 months was not statistically significant (t=1.511, P=0.135), the mean weight gain was significant at 12 months. (t=2.697, P=0.009). Furthermore, the difference in the mean weight at 6 months (63.3±10.5kg) and that at 12months (63.8±9.8kg) was statistically significant.

Table 2

The mean weight of participants at commencement, and after 6 months and 12 months of using DMPA

Variable		Mean± SD	Mean Difference	% Mean Difference	t test value	p value
Weight (Kg)	Wt_0	62.91±10.53				
	Wt_6	63.31±10.50	0.40±2.14	0.639	1.511	0.135
	Wt_6	63.31±10.50				
	Wt_{12}	63.81±9.75	0.50±2.04	0.790	2.697	0.049
	Wt_0	62.91±10.53				
	Wt_{12}	63.81±9.75	0.90±2.72	1.430	2.005	0.009

Wt_0 Pre-treatment weight, wt_6 weight at 6 months, wt_{12} Weight at 12months

Table 3 shows that the pre-treatment Body Mass Index was 24.3± 3.8kg/m², while the mean Body Mass Index at 6 months and 12 months were 24.5±3.8kg/m² and 24.7±3.5kg/m² respectively. DMPA caused a non-significant increase in mean BMI at 6 months (t=1.455, P=0.150) whereas users had significant increase in mean Body Mass Index at 12 months when compared to pre-treatment values (t=2.706, P=0.009 respectively).

Table 3

The mean BMI among DMPA users at commencement, 6 months and 12 months

Variable		Mean±SD	Mean Difference	% Mean Difference	t test value	p value
BMI (Kg/m²)	BMI_0	24.32±3.78				
	BMI_6	24.48±3.77	0.15±0.86	0.616	1.455	0.150
	BMI_6	24.48±3.77				
	BMI_{12}	24.68±3.52	0.20±0.82	0.817	2.049	0.044
	BMI_0	24.32±3.78				
	BMI_{12}	24.68±3.86	0.36±1.08	1.480	2.706	0.009

BMI_0- Pre-treatment BMI, BMI_6- BMI at 6 months, BMI_{12}-BMI at 12 months

Table 4 and 5 show multivariate logistic regression of probable predictors of weight gain among DMPA users at 6 and 12 months respectively. There was no significant relationship between the age, parity, educational status, and pre-treatment body mass index, and weight gain at 6 and 12 months (P>0.05).

Table 4

Predictors of weight gain among study participants after 6 months of DMPA use

Variable	Weight gain at 6 months n=37	No weight gains n=31	P value	AOR	CI	P value
Age(years)						
≤30	11(52.4)	10(47.6)	0.822	0.9	0.3-3.5	0.915
>30	26(55.3)	21(44.7)				
Parity						
1-2	15(53.6)	13(46.4)	0.907	1.0	0.3-3.4	0.998
≥3	22(55.0)	18(45.0)				
Educational status						
No formal/Primary	8(21.6)	9(29.0)	0.482	0.7	0.2-2.8	0.547
Secondary/Tertiary	29(47.1)	22(52.9)				
Baseline Body Mass Index (Kg/m^2)						
<25	21(51.2)	20(48.8)	0.515	0.8	0.3-2.0	0.569
≥25	16(59.3)	11(40.7)				

Table 5

Predictors of weight gain among study participants after 12 months of DMPA use

Variable	Weight gain at 12months n=43	No weight gain n=25	P value	AOR	CI	P value
Age(years)						
≤30	13(61.9)	8(38.1)	0.879	1.3	0.3-5.2	0.705
>30	30(63.8)	17(36.2)				
Parity						
1-2	18(64.3)	10(35.7)	0.881	1.2	0.3-4.4	0.767
≥3	25(62.5)	15(37.5)				
Educational status						
No formal/Primary	12(70.6)	5(29.4)	0.468	1.5	0.5-5.1	0.512
Secondary/Tertiary	31(60.8)	20(39.2)				
Baseline Body Mass Index (Kg/m^2)						
<25	28(68.3)	13(31.7)	0.286	1.6	0.6-4.5	0.340
≥25	15(55.6)	12(44.4)				

DISCUSSION

Weight gain is one of the most common side effects encountered by women using progesterone only contraceptives and this may be responsible for discontinuation of the contraceptive agent.[10, 11] DMPA increases the percentage of body fat and in some situation causes truncal obesity which could increase the risk of cardiovascular disease.[18] This study assessed the weight and body mass index changes of acceptors of depo-medroxyprogesterone acetate over a period of 12 months

In this study, it was observed that DMPA users had significant weight gain and increase in body mass index after 12months compared to pre-treatment weight and BMI. The mean weight change after 12 months was noted to be 0.90±2.72kg and was statistically significant. This result is consistent with findings by Youzbaki et al[13] which revealed that use of DMPA was associated with significant weight increase after 12months of use compared to the pre-treatment weight. However, Sule et al[15] in Zaria stated that the effect of DMPA was not significantly different compared to control. The latter conducted a retrospective study as against prospective study performed in this study and by Youzbaki et al.[13]

Weight gain was not significant at 6 months but was significant at 12 months. Similar studies indicated that there was no significant weight gain in women who used DMPA for less than 12 months.[19] This is because the metabolic changes affecting the body composition such as increased body fat percentage and greater decrease in lean body mass among DMPA users requires a minimum time frame of 12 months.[19] Hence, women on DMPA should be advised to pay close attention to their weights after 12months of use and institute stricter mechanisms for prevention of weight gain. The differences in the degree of weight changes among DMPA users could also be attributed to varying levels of increased appetite associated with modification of satiety control centre in the hypothalamus.[20] The weight gain could also be as a result of increase in lipid profile parameter and subsequent deposition of excessive triglyceride in the subcutaneous tissue. Studies also suggest that physical activity, lifestyle, racial and ethnic differences influence variation in weight gain. Black women are likely to gain excessive weight overtime with continuous DMPA use than the Caucasian women.[21] This could be due to racial differences in fat distribution in the body.[22]

The other possible mechanism postulated by Guthrie et al[23] on the association of DMPA with weight gain, was its weak glucocorticoid activity that interferes with insulin action, and also the anabolic effect and fluid retention of the contraceptive. Some researchers have suggested that baseline risk factors such as BMI and parity were associated with early weight gain among DMPA users. Their findings indicated that women with BMI<30kg/m^2 were more likely to have significant early weight gain than obese women. In this study, only clients with BMI<30kg/m^2 were included; however, baseline BMI was not found to be predictive of weight gain. Contrary to reports from Le et al[20] which indicated that multiparous women experience early weight gain compared to nulliparous women on DMPA, this study did not show any relationship between parity and weight gain. Moreover, nulliparous women were not included in this study.

Another theory considered was the natural tendency of weight gain in human beings during aging, after 30 years.[24] This is due to the loss of muscle mass and replacement with adipose tissue associated with aging. In this

study, weight gain was commoner in women with age above 30 years when compared to those with age below 30 years;[24] however, this finding was not statistically significant. This suggests that age was not a significant predictor of weight gain among DMPA users.

This study found weight changes ranging from -1.5kg to 3.3kg. This variability in weight difference suggested that weight gain among DMPA users do not follow the same course. It is also imperative to closely monitor the clients' weight at every follow up clinic to determine those at risk of rapid weight gain from DMPA use.

This study has some limitations. Individual risk factors such as sedentary lifestyle, nutritional habits and genetic determinant that could potentially influence body weight were not controlled for in the study. Also, women older than 40 years and those with BMI above 30Kg/m^2 were excluded from the study, hence the pattern of weight change in this group of women could not be assessed. Overall, the findings from this study will assist in instituting appropriate and accurate counselling of prospective contraceptive users on this form of contraception. This will help reduce the discontinuation of the contraceptive due to perception of weight gain.

In conclusion, DMPA acceptors had a significantly higher weight increase after 12 months use when compared to the pre-treatment weight. Also, there was significant increase in the body mass index of the acceptors after 12 months. Appropriate counselling of prospective DMPA users is important prior to initiation. Larger prospective study with multivariate regression to control for confounding factors associated with weight gain is recommended.

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