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Original Article

Differential Effects of Depot Medroxyprogesterone Acetate and Norethisterone Enanthate on Some Metabolic and Cardiovascular Parameters in Hausa Women of Kano Metropolis

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ABSTRACT

Introduction and aim: Injectable contraceptives such as depot medroxyprogesterone acetate (DMPA-SC) and norethisterone enanthate (NET-EN) are widely used in Sub-Saharan Africa. While reported to have effects on weight and altered glucose metabolism, their metabolic and cardiovascular effects remain underexplored in African populations. This study assessed these outcomes among women in Kano, Nigeria.

Methods: A six-month longitudinal study was conducted among 85 Hausa women aged 15–49 years attending family planning clinics. Participants were new or continuing users of DMPA-SC or NET-EN, without chronic illnesses. Anthropometric indices, blood pressure, fasting blood glucose (FBG), and total cholesterol (TC) were measured at baseline and six months. Paired Student's t-tests were used, with $p < 0.05$ considered significant.

Results: Both DMPA-SC and NET-EN were associated with significant increases in FBG ($p = 0.008$ and $p = 0.012$, respectively) and TC ($p = 0.004$ and $p = 0.027$, respectively). NET-EN users had higher post-treatment FBG, whereas DMPA-SC users showed a more pronounced rise in TC, suggesting a greater potential atherogenic burden. Changes in BMI, systolic blood pressure, and diastolic blood pressure were modest and not statistically significant. No significant alterations occurred in the control group.

Conclusion: Six-month use of DMPA-SC and NET-EN was linked to significant increases in FBG and TC among Hausa women in Kano, Nigeria. NET-EN exerted a greater effect on glucose, while DMPA-SC had a stronger impact on cholesterol, highlighting formulation-specific metabolic differences. BMI and blood pressure remained largely unchanged, indicating that early metabolic alterations may precede overt changes in adiposity or cardiovascular measures.

Keywords: Injectable contraceptives; Depot Medroxyprogesterone Acetate;Norethisterone Enanthate; fasting blood glucose; total cholesterol

INTRODUCTION

Contraception is the intentional prevention of conception or pregnancy through devices, chemicals, drugs, sexual practices, or surgical procedures (Akadri & Odelola, 2017). Injectable contraceptives have increased in popularity among modern methods because of their high effectiveness, reversibility, long duration of action, and discretion (Eremutha & Gabriel, 2019).

Hormonal elements, notably progestin-only injectables such as depot medroxyprogesterone acetate (DMPA) and norethisterone enanthate (NET-EN), have been closely associated with metabolic changes (Singata-Madliki *et al.,* 2025). These drugs have systemic effects beyond contraception, with studies indicating that they may stimulate appetite, lower basal metabolic rate, and promote greater fat deposition (Blundell *et al.,* 2015; Hopkins & Blundell, 2016). Such changes in energy balance can lead to weight increase and central adiposity, both of which are associated with metabolic syndrome (Romieu *et al.,* 2017). Furthermore, progestins may affect lipid metabolism by increasing undesirable alterations in serum cholesterol profiles, such as raised total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C), while decreasing protective high-density lipoprotein cholesterol (HDL-C) levels (Zimodro *et al.,* 2024). These lipid abnormalities, together with increased insulin resistance and decreased glucose tolerance, produce a pro-atherogenic environment that raises cardiovascular risk. Over time, the combination of obesity, dyslipidemia, and hyperglycemia caused or exacerbated by injectable contraception may predispose women to hypertension, endothelial dysfunction, and, eventually, atherosclerosis (Dragoman *et al.,* 2016).

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Thus, while DMPA and NET-EN are highly effective contraceptives, they may unintentionally exacerbate metabolic abnormalities and increase susceptibility to long-term cardiovascular diseases (Kantarama, 2023)

The public health implications are particularly substantial in Sub-Saharan Africa, where women are already experiencing increased rates of overweight and obesity (Neupane & Doku, 2016). However, research relating injectable contraceptives to particular metabolic and cardiovascular outcomes such as blood pressure, fasting glucose, and lipid profile is limited and equivocal in Nigerian communities.

Therefore, this study aimed to assess the metabolic and cardiovascular effects of progestin-only injectable contraceptives (DMPA and NET-EN) in Hausa women of reproductive age in Kano, Nigeria.

MATERIALS AND METHODS

Study Area and Population

The study area was the Kano metropolis. It is the capital city of Kano state, Nigeria. It is located at a latitude of 12°00′N and a longitude of 8°31′E to 8.517°E. Kano is situated in the North-Western geopolitical zone of Nigeria, with a population of about 10 million people based on the 2006 National census (NPC, 2006). It consists of six Local Government Areas, namely Dala, Fage, Gwale, Municipal, Nassarawa, and Tarauni, and some parts of Kumbotso, Ungogo, and Tofa Local Government Areas (Isa *et al.,* 2016). The metropolitan area spans about **499 km²**; the current population of metro-Kano is estimated at about **4.6 million** (2025) (World Population Review 2025), up from the 2006 census figure of ~2.83 million. The principal inhabitants of the city are the Hausa people.

Study Site

The study was conducted at the family planning clinic of Murtala Mohammed Specialist Hospital (MMSH) and Nuhu Bamali Maternity Hospital (NBMH), both located in Kano metropolis. The family planning clinics at MMSH and NBMH operate five days a week, offering contraceptive counselling and services including hormonal methods (pills, injectables, IUDs, implants) and barrier methods like condoms. MMSH serves an average of 38 clients daily, while NBMH sees about 15 clients per day.

Inclusion criteria

The study included Hausa women aged 15 – 49 years who were not pregnant at the time of recruitment, had no known history of chronic metabolic disorders such as diabetes or hypertension, and were new or continuing users of either DMPA-SC or NET-EN. Before enrolment, all eligible participants were provided with detailed information about the study.

Exclusion criteria

Women were excluded if they had a history of chronic illness, used other forms of contraceptives during the study period, or had incomplete follow-up data.

Sample size determination

The minimum sample size was obtained using the formula developed by Cochran (1977) as expressed below:

$$n = \frac{Z^2pq}{d^2} \qquad n = \frac{1.96^2 \times 0.05 \times (1-0.05)}{0.05^2} = 72.99$$

Where:

n = minimum sample size

Z = standard normal deviation at 95% confidence interval = 1.96

p = estimated prevalence of injectable contraceptive use among women of reproductive age in Nigeria. A prevalence of **5%** was adopted based on the 2018 Nigeria Demographic and Health Survey (NDHS, 2019).

q = 1 – p = 0.95

d = margin of error = 0.05

Therefore, the minimum required sample size was about 73 participants. To improve statistical power and compensate for possible non-response or attrition, the sample was increased to 85 women. These participants were further divided into users of DMPA-SC and users of NET-EN.

Study Design and Technique

The study was longitudinal and experimental in design, using a convenience sampling technique to select participants. It was conducted over a period of six months (February–September 2020). Data collection included anthropometric and biochemical parameters at two time points: baseline (D1, before contraceptive initiation) and follow-up (D2, after six months of use).

Ethical Consideration

Ethical approval for this study was obtained from the Ethical Committee of the Hospital Management Board, Ministry of Health, Kano State (Approval No.: MOH/OH/797/1877).

Administration of Contraceptives

Participants were randomly assigned to one of two groups: depot medroxyprogesterone acetate subcutaneous (DMPA-SC) or norethisterone enanthate (NET-EN), with age-matched non-hormonal contraceptive users as controls. In accordance with WHO contraceptive recommendations, DMPA-SC was given as a 104 mg subcutaneous injection once every three months, while NET-EN was given as a 200 mg intramuscular injection once every two months. Throughout the research period, participants were rigorously monitored to ensure adherence, and all injections were given by qualified nurses in aseptic clinic settings.

Anthropometric Measurements

Height was measured to the nearest 0.1 cm using a stadiometer, with participants standing erect in the Frankfort plane without shoes, ensuring that the head, shoulders, buttocks, calves, and heels were in contact with the measuring rod (Price *et al.,* 2006). Weight was recorded in kilograms using a calibrated digital weighing scale, with participants wearing light clothing (European Health Risk Monitoring, 2004). Body Mass Index (BMI) was calculated as weight in kilograms divided by the square of height in meters (Odenigbo *et al.,* 2011). For clinical interpretation, BMI values were categorized according to World Health Organization (WHO) standards as underweight (< 18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), and obese (≥ 30 kg/m²) (WHO, 2000).

Materials and Instruments

A spectrophotometer (Model 721, input voltage AC220V/50Hz) was used to measure the absorbance of the sample solutions for the biochemical analysis of fasting blood glucose (FBG) and total cholesterol (TC). Blood pressure was measured using a mercury sphygmomanometer (SUNMED 420601, USA), with readings taken at the brachial artery using a stethoscope (BOKANG, BK 3003, USA). Randox Laboratory diagnostic kits (UK) were used to determine glucose and cholesterol levels. Ice packs (Sunlong Biotech, China) were employed to protect biological samples during storage and transport to the laboratory.

Blood Pressure Measurement

A mercury sphygmomanometer was used for measuring blood pressure. At least two measurements were taken, and at least 2 minutes were allowed between readings. While the diastolic reading was taken at the level when sounds disappear (Korotkoff phase V), the systolic reading was taken at the level when it appears (Prisant *et al.,* 2013). The brachial artery was the site of auscultation. Subjects were asked to refrain from smoking or ingesting caffeine for 30 minutes before measurement, and then measurement commenced after at least 5 minutes of rest (Haffner *et al.,* 2005).

Blood Collection and Biochemical Analysis

Venous blood (3 ml) was collected from each participant using a sterile 21G needle and syringe, typically in the morning hours to minimize diurnal variation in blood parameters. Standard venipuncture techniques and universal safety precautions were strictly observed. Blood was drawn from superficial veins of the upper limb following a 10- to 12-hour overnight fast. The samples were transferred into plain specimen bottles, allowed to clot, and subsequently centrifuged at 3,000 rpm for 5 minutes to separate the serum.

Fasting plasma glucose and total cholesterol concentrations were determined using standard biochemical methods: the Trinder method (1969) for glucose and the Wybenga *et al*. (1970) methods for cholesterol. Randox Glucose and Cholesterol kits were used for the assays. Where immediate analysis was not feasible, serum samples were stored at –20°C and analysed the following day. All biochemical analyses were conducted at the Plasma Diagnostic and Research Laboratory, Kano.

Statistical Analysis

Data were presented as mean ± standard deviation. Student t-test was used to compare changes in indices from baseline to after six months of injection, of both formulations of injectable contraceptives. SPSS version 20.0 (IBM Corporation, for Windows) was used for statistical analysis, and P< 0.05 was considered significant.

RESULTS

Table 1 Effects of Depot Medroxyprogesterone Acetate and Norethisterone Enanthate on Some Metabolic and Cardiovascular Parameters Among Hausa Women in Kano, Nigeria. (N = 85; DMPA = 50, NET-EN = 35).

Variable	Group	Pre (Mean ± SD)	Post (Mean ± SD)	Paired t-test (p-value)	Between-Group t-test (p-value)
BMI	DMPA	22.25 ± 4.16	22.38 ± 4.19	t= –1.12, p=0.27	t= –0.73, p = 0.47
	NET-EN	22.94 ± 3.83	23.06 ± 3.84	t= –0.98, p=0.33	
DBP (mmHg)	DMPA	79.00 ± 6.78	77.20 ± 6.71	t=1.95, p=0.06	t=–0.07, p=0.94
	NET-EN	78.86 ± 6.31	78.29 ± 7.47	t=0.41, p=0.68	
SBP (mmHg)	DMPA	115.8 ± 9.71	114.4 ± 10.13	t=1.02, p=0.31	t=0.58, p=0.56
	NET-EN	117.1 ± 7.89	114.3 ± 8.15	t=1.76, p=0.09	
TC (mmol/L)	DMPA	3.77 ± 0.67	3.80 ± 0.67	t=–0.34, p=0.74	t=–2.57, p=0.01*
	NET-EN	4.19 ± 0.91	4.28 ± 0.95	t=–0.69, p=0.49	
FBG (mmol/L)	DMPA	3.90 ± 0.43	4.03 ± 0.49	t=–1.79, p=0.08	t=–2.06, p=0.04*
	NET-EN	4.15 ± 0.65	4.27 ± 0.68	t=–0.95, p=0.35	

* Significant at p<0.05.

DMPA = depot medroxyprogesterone acetate; NET-EN = norethisterone enanthate; TC = total cholesterol; FBG = fasting blood glucose.

As shown in Table 1, both the depot medroxyprogesterone acetate (DMPA) and norethisterone enanthate (NET-EN) groups exhibited only modest within-group changes in body mass index (BMI), blood pressure, total cholesterol (TC), and fasting blood glucose (FBG) levels after six months of follow-up. None of the within-group differences reached statistical significance (all $p > 0.05$). However, the between-group analysis revealed notable differences. NET-EN users had significantly higher post-treatment TC ($p = 0.01$) and FBG ($p = 0.04$) compared to DMPA users, indicating a relatively greater metabolic burden associated with NET-EN. Conversely, changes in BMI, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were not significantly different between the two injectable contraceptives (all $p > 0.05$).

DISCUSSION

Injectable hormonal contraceptives are among the most widely used contraceptive methods for women of reproductive age globally (Robinson & Burke, 2013; UNDESA, 2019). In Nigeria, particularly in Kano and the wider North-West region, their uptake is especially high, with prevalence estimates ranging from 40.6% to 64.6% (Omole-Ohons *et al.,* 2010; Yakasai & Yusuf, 2013; Muhammad & Maimuna, 2014). Nationally, the reported prevalence of injectable contraceptive use spans from 7.9% to 71.8% across different populations (Konje *et al.,* 1998; Chigbu *et al.,* 2010). Given this widespread utilization, understanding their potential metabolic effects is essential for public health.

This longitudinal study compared the metabolic effects of two progestin-only injectables, depot medroxyprogesterone acetate (DMPA) and norethisterone enanthate (NET-EN), over six months among Hausa women in Kano. Our findings showed that both methods were linked to statistically significant increases in total cholesterol (TC) and fasting blood glucose (FBG) between groups. Changes in BMI, systolic blood pressure (SBP), and diastolic blood pressure (DBP) within each group were small and not statistically significant. Importantly, NET-EN users had higher post-treatment TC and a tendency toward higher FBG compared to DMPA users, indicating that NET-EN may impose a slightly greater metabolic burden.

These findings align with accumulating evidence from sub-Saharan Africa and other low- and middle-income settings on the metabolic impact of injectable contraceptives. Secondary analyses of the WHICH randomized trial demonstrated that both norethisterone enanthate (NET-EN) and depot medroxyprogesterone acetate (DMPA-IM) were associated with adverse alterations in glucose and lipid metabolism, although the magnitude and direction of effects varied by formulation and study duration (Singata-Madliki *et al*., 2014). Importantly, the WHICH trial highlighted that metabolic outcomes may not be uniform across injectable progestins, reinforcing the need for formulation-specific investigations.

Pharmacokinetic studies have revealed that NET-EN and DMPA have different absorption, metabolism, serum concentration profiles, and elimination half-lives (Bick *et al.,* 2021). These discrepancies may alter systemic exposure and receptor activation, contributing to the varied cardiometabolic profiles found in the two contraceptive formulations. The higher cholesterol and fasting glucose levels documented among NET-EN users in the present study may therefore be attributable to pharmacodynamic and receptor-level interactions, particularly involving androgenic and glucocorticoid receptor cross-reactivity. Experimental studies have shown that NET-EN exhibits higher androgenic activity compared to DMPA, which can promote visceral adiposity, dyslipidemia, and insulin resistance through modulation of hepatic lipoprotein metabolism and adipocyte differentiation pathways (Molatlhegi *et al.,* 2021; Kantarama, 2023). Moreover, differences in glucocorticoid receptor affinity may contribute to impaired glucose handling, as glucocorticoid signaling promotes gluconeogenesis and antagonizes insulin action (Rose *et al.,* 2010; Beaupere, 2021). These receptor-level effects could partly explain why NET-EN users in our cohort exhibited more pronounced elevations in fasting blood glucose and total cholesterol compared with DMPA users. Collectively, these mechanistic insights suggest that the choice of injectable contraceptives may have clinically relevant implications for long-term metabolic risk, particularly in populations already predisposed to cardiometabolic disorders due to genetic, nutritional, or lifestyle factors prevalent in sub-Saharan Africa.

The absence of significant within-group changes in BMI, systolic blood pressure (SBP), or diastolic blood pressure (DBP) suggests that a six-month exposure period may be insufficient to elicit overt cardiometabolic outcomes, particularly in a relatively young and otherwise healthy population with normal baseline measures. This observation is consistent with earlier reports indicating that subclinical metabolic disturbances in lipid and glucose regulation often precede measurable changes in body weight or blood pressure (Lima, 2017; Mulè *et al.,* 2014; Romeo *et al.,* 2025). The stability of BMI across groups in our cohort further underscores the possibility that metabolic alterations induced by progestin-only injectables may operate independently of weight gain. This dissociation between adiposity and metabolic changes has been documented in mechanistic studies implicating insulin resistance, hepatic lipid metabolism, and adipocyte function as potential mediators of early metabolic derangements (Jung & Choi, 2014; Zhao *et al.,* 2023).

Conclusion: Taken together, our findings highlight a nuanced profile of progestin-only injectables. While both DMPA and NET-EN remain highly effective and widely used contraceptive options, they may exert differential influences on cardiometabolic health, with NET-EN demonstrating a comparatively less favorable metabolic profile relative to DMPA in our study. These results carry important implications for women's health in contexts such as northern Nigeria, where injectable contraceptives represent a dominant contraceptive choice. Given the increasing burden of non-communicable diseases in sub-Saharan Africa, further large-scale, longitudinal studies are warranted to clarify the trajectory and clinical relevance of these metabolic changes, and to inform contraceptive counseling and policy.

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