Full Length Research Paper

The effect of hormonal contraceptives on platelet count of women in Sokoto State North Western Nigeria

[1]Isaac I. Z, [2]John R.T, [1]Suleiman A.S., [1*]Erhabor O. and [2]Ahmed Yakubu

[1]Department of Haematology and Blood Transfusion Science, Faculty of Medical Laboratory Science, Usmanu Danfodiyo University, Sokoto, Sokoto State, Nigeria.

[2]Department of Obstetrics and Gynecology Usmanu Danfodiyo University Teaching Hospital, Sokoto.

*Corresponding Author's E-mail: n_osaro@yahoo.com

Abstract

It has been figured that sometime this fall, the world's population will reach 7 billion people. Experts now forecast that by 2050, the population could be 10 billion. The need to control the increasing world population has triggered the implementation of policy to make family planning including the use of hormonal contraceptives much more widely available in the developing world. Forty three women on hormonal contraceptive for three months and above duration constituted the subjects for this case-control study. Twenty age- matched women who were not on any contraceptives were monitored as controls. The mean age and range of the subjects and was 28 ± 1.76 years and 18-45 years respectively. EDTA anticoagulated blood samples were collected from subjects and control participants and analysed using the SWELAB 3-part-differential haematology analyzer (Medonic, Sweden) for platelet count. Although the mean platelet count was marginally higher among subjects on hormonal contraceptives compared to controls, this difference however was not statistically significant (t = 190.0, p = 0.851). The mean and standard deviation of platelet count was 300.50 ± 63.60; 258.00 ± 94.10; 247.60 ± 61.20 and 244.00 ± 49.90 respectively among the age groups 20 – 24; 25 – 29; 30 – 34 and 35 – 40 years respectively. We observed a negative correlation between age of HCs users and platelet count (r=-0.56, p=0.03). The mean platelet count was significantly lower among long-term (>1 year) hormonal contraceptives users compared to short-term users (297.50 ± 56.40 versus 268.10 ± 89.00, p=0.05). This study indicates that early introduction of third generation hormonal contraception can produce an initial increase in the platelet count and that long-term use of hormonal contraceptives is associated with a reduction in platelets count.

Keywords: Hormonal contraception, Platelet count, Sokoto, Nigeria.

INTRODUCTION

As of December 28, 2013 the world's human population is estimated to be 7.134 billion by the United States Census Bureau (U.S. Census Bureau, 2010). The rapid increase in human population is causing great concern on the challenge of sustaining associated increased demand for resources such as fresh water, food natural resources and living conditions. Contraception has been identified as one of the ways to mitigate adverse effects associated with the overpopulation (Shirmeen et al., 2007,Silies, 2010). At the turn of the millennium, all over the world, contraceptive use have grown among married and unmarried women particularly with unsustainable growth in world population. More than 600 million married women are using contraception, with nearly 500 million in developing countries (Benagiano et al., *2006).* Family planning entails the use of family planning methods/contraception. Contraception is the use of various devices, drug agents, sexual practices or surgical

procedures to prevent conception and help women plan when they want to have a baby. Hormonal contraception containing different doses of estrogen and different types of progestogen is one method that is widely used, and can potentially help control the rising world population (Benagiano et al., *2004).*

Family planning is one of the pillars of the Safe Motherhood Initiatives (SMI) and a pivotal way to reduce maternal morbidity and mortality and one of the important indices for assessing universal access to reproductive health in the Millennium Development Goals (Abiodun and Balogun, 2009). The use of hormonal contraceptive has been associated with increased risk for thrombosis (Lidegaard et al., 2011, Vlieg et al., 2009). The first available preparation contained a high dose of the estrogen EE2, the dose of estrogen was reduced stepwise. The initial lowering of the estrogen dose from > 50 μg to 30μg was indeed shown to be associated with a clear decrease in the risk of venous thrombosis (Lidegaard et al., 2012, Pretorius et al., 2010).

There is report of increasing contraceptive use and awareness among Nigerian women of all age groups despite the several barriers including lack of access, socio-cultural and religious factors, partner's opposition and fear of side effects of contraceptives (Oye-Adeniran et al., 2005, Oyedokun, 2007). However there paucity of data on the effect of these agents on the platelet count of women on these agents in the area. The aim of this present study was to investigate the effect on hormonal contraceptives on the platelet count of women on long-term hormonal contraceptives in area and to determine the relationship with sociodemograhic characteristics.

Study area

The study area is Usmanu Danfodiyo Teaching Hospital Sokoto (UDUTH) established in the year 1975 in Sokoto metropolis. It is committed to the provision of continually improving tertiary health care services to the entire North-Western region and our neighboring border country - Niger Republic. The metropolitan city of Sokoto lies between longitude 11º 30" to 13º 50" east and latitude 4º to 6º north and covers an area of 28,232.37sq kilometer. It is bordered in the North by Niger Republic, in the East by Zamfara State and Kebbi State to the South and West. Sokoto is one of the hottest cities in the world with an annual average temperature of 28.3C. The warmest months are February to April (temperatures exceed 45^{0}C) while the rainy season lasts from June to October and Harmmattan season starts from late October to February. There are two main seasons in Sokoto, the wet (October to April) and dry (May to September). The main occupation of the people is grain production and animal husbandry. More than 80 percent of its indigenes practice agriculture. Crops produced include millet, beans, onions, tomatoes, rice, maize, guinea corn, wheat and cotton.

Other occupations commonly practiced are dyeing, blacksmithing, weaving, carving, trading and cobbling. Sokoto state had a population of 4.2million as at the 2006 census. The metropolis is estimated to have a population of 427,760 people (NPC/FRN, 2006). The population is made up of Hausa and Fulani majority and a minority of Zabarmawa and Tuareg. The major language in this state is Hausa and Fulfulde among the Fulanis. Socio cultural characteristics is homogenous as majority of its indigenes are Muslims, therefore the Muslim religion provides them the code of conduct and behavioral characteristics. Common practices are child marriage, polygamy, consanguity, multiple births, and male dominance.

Study design

This is a case -control study involving all consenting family planning clients on hormonal contraceptives attending the family planning clinic in Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria. Control group comprised of age-matched women who were not on any hormonal contraceptives.

Inclusion criteria

All adult and consenting women attending the family planning clients on hormonal contraceptives for at least three months were included in the study. Control group include non- pregnant and non-users of hormonal contraceptives.

Exclusion criteria

All new clients, non –consenting, clients on hormonal contraceptives for less than three months, those on other non-hormonal contraceptives and women with underlying disease conditions that might affect the clotting system were excluded from this study.

Data analysis

Data obtained was entered into computer software, Statistical Package for Social Science (SPSS) version 15.0 and analysed. The Medicalc was used to calculate the Odds Ratio. Data was presented using tables, frequency and percentages. Chi square test of significant was carried out to determine association between the categorical variables. The student t-test was carried out to compare the mean difference of age of the respondents in the two groups. The mean and standard deviation was determined for the continuous variables.

Table 1. Mean platelet count (PLC) of subjects on hormonal contraceptives and controls

Participant Groups	Number	Mean Platelet count (x 10^9/L)	t-value	P-value
Subjects	43	275.80 ± 85.40	190.0	0.851
Controls	20	270.80 ± 79.09		

Table 2. Mean platelet count of hormonal contraceptives users based on age groups

Age Groups	N (%)	Mean platelet count (x 10^9/L)	p-value
20-24	8 (18.6%)	300.50±63.60	0.03
25-29	22 (51.2%)	258.00±94.10	
30-34	9 (20.9%)	247.60±61.20	
35-40	4 (9.3%)	244.00±49.90	

Table 3. Mean platelet count among subjects based duration of hormonal contraceptives user.

Duration contraceptive use	Number (%)	Mean platelet count (x 10^9/L)	p-value
< 1 year	34 (79.1)	297.50 ± 56.40	0.0125
> 1 year	9 (20.9)	268.10 ± 89.00	

Ethical consideration

The ethical clearance and permission to conduct the study was obtained from Ethics Committee of Usmanu Danfodiyo University Teaching Hospital Sokoto. The laboratory testing and demographic data was collected after obtaining oral informed consent from the study participants.

RESULTS

Although the mean platelet count was marginally higher among subjects on hormonal contraceptives compared to controls, this difference however was not statistically significant (t = 190.0, p = 0.851). Table 1 shows the mean platelet count of subjects on hormonal contraceptives and controls. The mean and standard deviation of platelet count was 300.50 ± 63.60; 258.00 ± 94.10; 247.60 ± 61.20 and 244.00 ± 49.90 respectively among the age groups 20 – 24; 25 – 29; 30 – 34 and 35 – 40 years respectively. Table 2 shows the mean platelet count of hormonal contraceptives users based on age groups. We observed a negative correlation between age of hormonal contraceptives users and platelet count (r=-0.56, p=0.03). The mean platelet count was significantly lower among long-term (>1 year) hormonal contraceptives users compared to short-term users (297.50 ± 56.40 versus 268.10 ± 89.00, p=0.0125).

DISCUSSION

In this present study, we had investigated the platelet count of 43 women on hormonal contraceptives for three months and above. The mean platelet count was marginally higher among hormonal contraceptives users compared to controls. This difference was however not statistically significant. Our finding is consistent with previous report (Babatunde and Olatunji , 2004) among a cohort of women on oral contraceptives in Ilorin, Nigeria which indicated that the mean values of platelet count and fibrinogen were significantly increased while the PT and TT reduced significantly after three months of contraceptive use. Similarly, Joseph and colleagues (Joseph et al., 2008) in Jos investigated their cohort of women on oral contraceptives and observed that the mean platelet count, mean prothrombin time and mean activated partial thomboplastin time recorded for the users of the hormonal contraceptives showed no significant difference from that of non-user. Also Bulur and colleagues (Bulur et al., 2012) investigated ninety-five women using oral contraceptives in Turkey and observed that there was no difference between the platelet count and mean platelet volume at application and at the sixth month post- treatment. Similarly, Aisen and colleagues (Aisen et al., 2005) investigated a cohort of 55 non-breastfeeding women on hormonal contraceptives at 3, 6 and 12 months follow-up and observed that the mean values of the platelet count

showed no significant change at 3, 6 and 12 months follow-up. David and colleagues (David et al., 1990) investigated the effects of oral contraceptive treatment among their cohort of thirty-six young, healthy, non-smoking women and observed that the platelet number, platelet aggregating ratio, and plasma beta-thromboglobulin level were not significantly altered. Our finding is also consistent with previous report (Norris and Bonnar, 1997) which indicated that hormonal contraceptive use was associated with increase in platelet activity and platelet aggregation but not increased platelet count.

The effects of postmenopausal hormone replacement therapy on thrombosis remain controversial. Findings from this study does indicate that the increased thrombotic risk associated with long-term use of hormonal contraceptive may not be related to increase in platelet count but rather platelet changes and effect on other coagulation factors (Pretorius et al., 2010). Furthermore, the possible danger of intravascular coagulation resulting from the use of oral contraceptive pill had been extensively studied among the Caucasian women by laboratory measurements of coagulation and platelet changes in women taking the combined oestrogen-progestogen oral contraceptive pill (Parkin et al., 2000). Oral contraceptives have been reported to shorten the prothrombin time, the partial thromboplastin time and the thromboplastin generation test, increased levels of factors VII, VIII, IX, X and fibrinogen (Rosing et al., 2001). Platelet adhesiveness and aggregation are said to be increased (Zahavi et al., 1973) as well as reduction in venous flow velocity by increasing venous distensibility and whole-blood viscosity (Babatunde and Olatunji, 2004). A previous report (Saleh et al., 1993) investigated the hypothesis that estrogen or progesterone has no significant effect on thrombosis by means of newly developed markers of blood clotting, specifically prothrombin fragment 1 + 2, a marker of factor Xa generation, and thrombin-antithrombin III complex, a marker of thrombin generation and observed that thromboembolic complications among postmenopausal women receiving hormone replacement therapy may therefore be secondary to congenital or other acquired coagulation defects. Hormonal replacement therapy may increase the risk of thrombosis in women with congenital or acquired thrombophilia (Bonduki et al., 2007).

We observed a significantly lower platelet count among long-term hormonal contraceptives users compared to short-term users. There are several postulations to explain the normal or reduction in platelet count in women of hormonal contraceptives. Firstly is the use of formulation containing low dose of estrogen (Sumino et al., 2005). Secondly, platelets have estrogen beta receptors (ER β) (Gopal et al., 2000). Thirdly, it has been reported that platelet function may be modulated by sex hormone levels (Tarantino et al., 1994) and that estrogens have a week anabolic effect which can potentially suppresses the actions of other reproductive hormones and platelets count (Petra and Areyh, 2012).

We observed a significant negative correlation between platelet count and age of hormonal contraceptives users. Platelet counts were shown to decrease progressively with age. Previous report suggest that thrombocytopenia was more common among the elderly, while thrombocytosis was more frequent among younger people (Biino et al., 2011). It has been suggested that the decrease may be due to reduced hematopoietic stem cell reserve in aging individuals (Segal and Moliterno, 2006). It is also possible that the age-dependent decline in platelet number may be a reflection of epigenetic changes in the megakaryocyte genome, such as hypomethylation of genes that determine platelet count or changes in histone acetylation, which lead to differences in gene expression as we get older (Biino et al., 2011).

CONCLUSION

This study indicates that early introduction of third generation hormonal contraception in women can produce an increase in the platelet count and that long-term use of hormonal contraceptives produces a reduction in the number of platelets.

REFERENCES

Abiodun OM, Balogun OR (2009). Sexual activity and contraceptive use among young female students of tertiary educational institution in Ilorin. Nigeria. Contraception; 79(2):146–149.

Aisien AO, Enosolease ME, Shobowale MO (2005). Evaluation of haemostatic function in Nigerian Norplant acceptors after 12 months of use. J Obstet Gynaecol ; 25(4):377-381.

Babatunde AS, Olatunji PO (2004). Short-term effect of oral contraceptive pills on some haemostatic parameters in healthy Nigerian women. Niger Postgrad Med J; 11(4):246-250.

Benagiano G, Bastianelli C, Farris M (2006). Contraception today. *Ann N Y Acad Sci.; 1092:1-32.*

Benagiano G, Testa G, Cocuzzi L (2004). The meaning of fertility control in an integrated world. Minerva Ginecol*; 56(3):271-281.*

Biino G, Balduini C, Casula L, Cavallo P, Vaccargiu S, Parracciani D (2011). Analysis of 12,517 inhabitants of a Sardinian geographic isolate reveals that predispositions to thrombocytopenia and thrombocytosis are inherited traits. Haematologica. ; 96 (1):96–101.

Bonduki CE, Lourenço DM, Motta EL, Soares Jr JM, Haidar MA, Baracat EC (2007). Effect of estrogen-progestin hormonal replacement therapy on blood coagulation and fibrinolysis in postmenopausal women. Clinics (Sao Paulo); 62(5):553-560.

Bulur S, Albayrak M, Bulur S, Keskin F, Köse SA, Aslantaş Y, Türker Y, Ozhan H (2012). Effect of combined oral contraceptive use on platelet volume in women at reproductive age. Clin Exp Obstet Gynecol; 39(3):314-316.

David JL, Gaspard UJ, Gillain D, Raskinet R, Lepot MR (1990). Hemostasis profile in women taking low-dose oral contraceptives. Am J Obstet Gynecol; 163(1 Pt 2):420-423.

Gopal Khetawat, Nauder Faraday, Michele L. Nealen, K. Vinod Vijayan, Everlie Bolton, Stephen J. Noga, Paul F. Bray (2000). Human megakaryocytes and platelets contain the estrogen receptor β and androgen receptor (AR): testosterone regulates AR expression. Blood; 95(7):2289-2296.

Joseph JT, Abdulazeez AA, Obisesan OA (2008). Effect of hormonal contraceptives on some haemostatics parameters in women attending family planning clinics in Jos, Nigeria. Nigerian Journal of Health and Biomedical Sciences; 7 (1): 15-18.

Lidegaard Ø, Milsom I, Geirsson RT, Skjeldestad FE (2012). Hormonal contraception and venous thromboembolism. *Acta Obstet Gynecol Scand; 91(7):769-778.*

Lidegaard Ø, Nielsen LH, Skovlund CW, Skjeldestad FE, Løkkegaard E (2011). Risk of venous thromboembolism from use of oral contraceptives containing different progestogens and oestrogen doses: Danish cohort study, 2001-9. *BMJ; 343:d6423.*

Norris LA, Bonnar J. (1997). Haemostatic change and oral contraceptive. C*lin Obstet Gynaecol*; 11(3):545-564.

NPC/FRN (2006). Nigeria Population Commission, Federal Republic of Nigeria. Special FGN. Gazette number 23 on the 2006 Population Census.

Oye-Adeniran BA, Adewole IF, Odeyemi KA, Ekanem EE, Umoh AV (2005). Contraceptive prevalence among young women in Nigeria. J Obstet Gynaecol; 25(2):182–185.

Oyedokun AO (2007). Determinants of Contraceptive Usage: Lessons from Women in Osun State. Nigeria J Humanities Soc Sci; 1(2):1–14.

Parkin L, Skegg DC, Wilson M, Herbison GP, Paul C (2000). Oral contraceptives and fatal pulmonary embolism. Lancet; 355(9221):2133-2134.

Petra S, Areyh S (2012). Basics of blood management. Biomed Khim. 2012; 58(4):429-437.

Pretorius E, Oberholzer HM, van der Spuy WJ, Meiring JH (2010). The changed ultrastructure of fibrin networks during use of oral contraception and hormone replacement. Journal of thrombosis and thrombolysis; 30(4):502-506.

Pretorius E, Oberholzer HM, van der Spuy WJ, Meiring JH (2010). The changed ultrastructure of fibrin networks during use of oral contraception and hormone replacement. Journal of Thrombosis and Thrombolysis; 30(4):502-506.

Rosing J, Curvers J, Tans G (2001). Oral contraceptives, thrombosis and haemostasis. European Journal of Obstetrics, Gynecology, and Reproductive Biology; 95(2):193-197.

Saleh AA, Dorey LG, Dombrowski MP, Ginsburg KA, Hirokawa S, Kowalczyk C, Hirata J, Bottoms S, Cotton DB, Mammen EF (1993). Thrombosis and hormone replacement therapy in postmenopausal women. Am J Obstet Gynecol; 169(6):1554-1557.

Segal JB, Moliterno AR (2006). Platelet counts differ by sex, ethnicity, and age in the United States. Ann Epidemiol; 16(2):123–30.

Shirmeen A, Khan MF, Khan KH, Khan KH (2007). Assessment of fertility control efforts in a selected area of Karachi, Pakistan. Ulster Med J.; 76(3):144-145.

Silies EM (2010). Contraception as an instrument against population growth: expert discussions and the public sphere in 1960s West Germany. Ber Wiss; 33(3):246-262.

Sumino H, Ichikawa S, Sawada Y, Sakamoto H, Kumakura H, Takayama Y, Sakamaki T, Kurabayashi M (2005). Effects of hormone replacement therapy on blood coagulation and fibrinolysis in hypertensive and normotensive postmenopausal women. Thromb Res; 115(5):359-366.

Tarantino MD, Kunicki TJ, Nugent DJ (1994). The estrogen receptor is present in human megakaryocytes. Ann N Y Acad Sci; 714:293.

U.S. Census Bureau (2011). World POPClock Projection. Retrieved 2011-10-27.

Vlieg AVH, Helmerhorst FM, Vandenbroucke JP, Doggen CJ, Rosendaal FR (2009). The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study. BMJ; 339: b2921.

Zahavi J, Dreyfuss F, Kalef M, Soferman N (1973). Adenosine diphosphate induced platelet aggregation in healthy women with and without a combined and sequential contraceptive pill. Am J Obstet Gynecol; 117:107-113.