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Original Article

Red Cell Parameters in Nigerian Women Using Oral Contraceptives (Lo-Femenal).

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ABSTRACT

The study was designed to assess the Red Blood Cell parameters in Nigerian women using oral contraceptives (Lo-Femenal). 50 women practicing the oral contraception method for varying length of time were recruited for the study. They comprise 22 women who had been on Lo-femenal for < 1 year 9 women who had been on Lo-femenal for 1 year and 19 women had been on Lo-femenal for > 1 year. Similarly 50 women not practicing contraception were recruited and served as control. Blood samples collected from all participants were used for the analysis of some haematological parameters using standard haematological techniques. The result showed that the Haematocrit, haemoglobin and red blood cell count dropped significantly in the Lo-femenal users compared with non-users ($p < 0.001$). The drop in blood levels of these parameters was much profound in users of < 1 year duration. On the other hand, red cell indices (MCHC, MCV and MCH) were significantly raised in users compared with non-users ($p<0.001$). These elevations were more in users of < 1 year duration. Blood films from Lo-Femenal users predominantly showed mild macrocytosis and anisocytosis. The reversibility of haemoglobin and packed cell volume with time in women who initiate Lo-Femenal warrants further study.

Keywords: Oral contraceptives, Lo-Femenal, Red cell parameters.

INTRODUCTION

The continuous growth of the world population and the recognition of gender equity, equality and women empowerment has necessitated the introduction of oral contraceptives (pills) as one of the family planning regimen for the prevention of unwanted pregnancies and abortions as well as to improve the timing of child birth in women of child bearing age [1, 2]. Oral contraceptives containing synthetic oestrogen and progestogen have been shown to be efficacious in preventing pregnancy with only about 0.34 pregnancies per 100 women occurring in OCs users[2]. In addition to prevention of pregnancies, oral contraceptive may affect many organ systems. For example, it has been found that OCs containing oestrogen decrease bile flow and bromosulphtalein excretion while progestin containing OCs have the propensity to cause intrahepatic cholestasis and decrease in bilirubin conjugation[3]. An increased risk of thromboembolic diseases [4], myocardial infarction[5], migraine[6] and circulatory disease and carcinogenicity[7] have been formally demonstrated in women taking oral contraceptive, although the risk tended to diminish with the use of low doses of hormonal steroids. It has been found that oral contraceptives alter some biochemical laboratory values [8] depending not only on the dose and choice of oestrogenic and progestional components but also on the interactions between the two. For instance, a review of nutritional aspect of OCs has shown that vitamin A is increased during oral contraceptive use in contrast to decreases in serum vitamins B_1, B_2, B_6 and B_{12}, ascorbic acid and zinc [9]. Available data on haemostatic studies in oral contraceptive

users, mostly from developed countries have produced divergent results [10-13]. There is paucity of information on the effect of oral contraceptives especially, Lo-Femenal, on the haematology of users in developing countries. The aim of the present study is to ascertain the changes, if there is any, in the red cell parameters in Nigerian women using Lo-Femenal brand of oral contraceptives.

MATERIALS AND METHODS

Our subjects were recruited from women (aged 21-38 years) attending Family Planning Clinic in the Department of Obstetrics and Gynaecology of the Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria. The Research Ethical Committee of Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife approved the protocol for this study. The purpose of the study was explained to the participants after which willing volunteers gave their consent to participate in the study. Women were included if they were on Lo-Femenal brand of oral contraceptives and were willing to participate in the study. Those excluded were smokers, users of other brands of oral contraceptives or have haematological disorders that may interfere with the outcome of the study. In all, a total of fifty (50) women comprising users of Lo-Femenal for < 1 year (n = 22), 1 year (n = 9) and > 1 year (n = 19) respectively were enlisted for participation. Sociodemographic data such as age, duration of Lo-Femenal use, level of education, occupation and parity of the participants were obtained by oral interview. Weight (in Kg using a standard hospital balance) and height (in m using a metal rule) were measured (in light clothing, without shoes). Fifty (50) apparently healthy non-pregnant, non-contraceptive users matched for age, weight, height and socioeconomic status and who do not smoke comprising staff of Obafemi Awolowo University Teaching hospital Complex, Ile-Ife served as controls. Two millilitres (2ml) of blood were collected at 08.00 hours from the antecubital veins of participants into EDTA bottles and thoroughly but gently mixed. Haematocrit, haemoglobin concentration and red cell indices were calculated [14]. Thin blood films made were stained by standard Leishman techniques, dried and viewed under oil immersion for the morphology of red blood cells. All samples were analysed within 2 hours of collection. Body mass index (BMI) was calculated using the formula: BMI = weight (Kg)/ height (m^2) [15] while level of education and occupation were used to assess the socio-economic status of the participants.

DATA ANALYSIS

Data were analysed for mean and standard deviation. Significant difference between groups was determined by students't-test at $p < 0.001$.

RESULTS

The baseline characteristics of the subjects and controls are shown in table 1. Twenty two (22) women had been on the pills for less than one year, 9 for one year, and 19 for more than one year. Although there was no significant age, parity and BMI differences between Lo-Femenal users and non-users, the users were heavier, older and had more deliveries than the non-users. Lo-Femenal users had significantly ($p < 0.001$) lower haematocrit, Hb and red cell count, which were much lower in those who had been on the pills for a period of less than one year than the non-users (table 2). However, the decreases in haematocrit and Hb concentration in users tend to normalise with increasing duration of Lo-Femenal use such that the mean haematocrit and Hb in women who had been on the pill for greater than one year were comparable to non-users (table 2). On the other hand, red cell indices (MCHC, MCV and MCH) were significantly ($p < 0.001$) higher in women who use Lo-Femenal than those who do not and this elevations were more in those who had used the pill fro less than one year (table 2). Blood films of Lo-Femenal users predominantly showed mild macrocytosis and anisocytosis (data not shown).

DISCUSSION

Most studies on the effects of hormonal oral contraceptives have concentrated on the biochemical and haemostatic parameters [11-13, 16]. In the present study, red cell indices among oral contraceptive (Lo-Femenal) users varied significantly from non-users. For instance, the mean haematocrit, Hb and red cell count were significantly depressed in users in corroboration with the study of Frassinelli-Gunderson *et. al.* [17]

Table 1: Baseline characteristics of Lo-Femenal users and non-users.

Duration	N	Mean age ± SD (yrs)	Mean parity ± SD	Mean BM (Kg/m^2)
Controls	50	27.9 ± 3.3	1.6 ± 1.8	25.7 ± 1.7
< 1	22	29.2 ± 3.4	2.7 ± 1.0	26. 2 ± 2. 4
1	9	31. 1 ± 4.5	3.2 ± 2.0	26.6 ± 2.6
>1	19	31.7 ± 2.1	4.1 ± 1.2	27. 1 ± 1.9

BMI (Body mass index); **SD** (Standard deviation).

Table 2: Red cell parameters in Lo-Femenal users and non-users.

Duration (yrs)	Hct (L/L)	Hb (g/dl)	Rbc x 10^{12}/L	MCHC(gHb/dl rbc	MCV (fl)	MCH (pg/cell)
Controls (n = 50)	0.39±0.02	13.1±0.68	5.3±0.43	32.5±0.54	75±4.40	24.8±1.88
<1(n =22)	0.36±0.02*	11.8±0.40*	3.6±0.40*	33.5±0.91*	102±10.34*	35.1±5.95*
1 (n = 9)	0.37±0.02*	12.3±0.36*	3.7±0.33*	33.1±0.93	99±6.98*	32.9±2.30*
>1(n= 19)	0.39± 0.02†	12.8±0.58†	3.9±0.52*†	32.9±0.31*	101±11.71*	33.1±3.9*

Legend: *p < 0.001 from controls; †p < 0.001 from < 1 year; **Hct** (Haematocrit); **Hb** (Haemoglobin); **Rbc** (Red blood cell count); **MCHC** (Mean corpuscular haemoglobin concentration); **MCV** (Mean corpuscular volume); **MCH** (Mean corpuscular haemoglobin).

except that in their study, the difference in Hb between the users and non-users was not statistically significant. It however contrasts the findings of Prasad *et. al.* [18] where no effect of oral contraceptive agents was seen on Hb, haematocrit and erythrocytes count. The discrepancies in the findings may be attributed to the study population. While Prasad and colleagues [18] conducted their study in America (developed country) the present study was done in developing country where sub-clinical anaemia is not uncommon probably due to latent micronutrient deficiencies [19]. Although the cause of decreases in Hct, Hb and red cell count in women who initiate Lo-Femenal is yet unknown, it may be related to haemostatic adjustment to the drug as study has shown that women initiating hormonal oral contraceptives reported more bleeding-spotting days [16]. On the other hand, investigation has shown decreased serum and red cell folate concentrations in women taking oral contraceptives, and cases of megaloblastic anaemia related to folate deficiency have been reported [10]. Additionally, OCs and other drugs have been shown to change the requirements for folic acid [20]. Interestingly however, the lower Hb and Hct observed in patients initiating Lo-Femenal

tended to normalise with increasing duration of OCs use as evidenced by lack of significant difference in Hct and Hb in women who had used the pill for greater than one year and non users. This finding suggests that the initial decreases in Hb and Hct may be partly attributed to maternal depletion syndrome.

Although, we could not establish the nutritional status of our subjects as this was not included in the original design of the present study, maternal depletion of iron, ferritin, folic acid and vitamin B_{12} may account for the initial decreases in Hb and Hct observed. This may probably be a consequence of inadequate child spacing as women in this group have had approximately 3 (2.7) deliveries before initiation of OCs. On the other hand, OCs use might have improved the haematological parameters in users as previous *in vitro* [21] and *in vivo* [22] studies showed evidence of inhibition of lipid peroxidation by oestrogen, suggesting that OCs may have antioxidant activity. This antioxidant protection may account for the higher values of Hb and Hct in women who had been on Lo-Femenal for greater than one year than those who had been on it for shorter duration in the present study thus reaffirming the safety of prolonged use of Lo-Femenal as a combined oral contraceptive [23]. The significantly raised levels of MCHC, MCV and MCH observed in the present study are in accord with earlier reports by Frassinelli-Gunderson *et. al.* [17] and may be due to difference in iron stores between the OCs users and non-users. We conclude that Lo-Femenal brand of combined oral contraceptive produces reversible depression of haemoglobin and haematocrit during initiation. Further study is needed to clarify the mechanism underlying these effects and to elucidate the effect of Lo-Fermenal in anaemic women.

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