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RESEARCH PAPER

THE EFFECT OF ORAL CONTRACEPTIVE PILLS (OCP) ON BODY WEIGHT: A CALL FOR FURTHER STUDIES

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ABSTRACT

The relationship between oral contraceptives pills (OCP) and body weight gain has long been established and remains one of the major setback of OCP. This study therefore, was designed to establish the effect of OCP in rabbits. It was a six weeks study involving 15 female rabbits that were divided into three groups (A, B, and C). Group A served as the control, while B and C served as the test groups involving rabbits with lower and higher weights respectively. Weight changes were determined in three phases: during 2 weeks of acclimatization; during 2 weeks post acclimatization (without OCP administration); and during 4 weeks post acclimatization (with OCP administration in the last 2 weeks). Throughout the period of the study, water, rabbit feed and grasses were given *ad libitum*. The results showed weight gain after acclimatization and after the next 2 weeks without OCP administration in all the groups. However, during OCP administration, weight gain (+0.06kg) was observed in group A, but weight loss (-0.06kg) in group C, while no weight change was observed in group B. The results of this study suggest therefore, that there is a need for further studies particularly on the dosing pattern of OCP.

Keywords: Oral contraceptive pill, Weight, Female, Rabbits.

INTRODUCTION

The increasing population no doubt puts strain on the world's resources such as land/space, water/food and clean air. In this regards, ESHRE Capri Workshop Group (2005) stated that "at a global level, contraception has played important role in helping to reduce overcrowding, pressures on resources, pollution, global warming, and a loss of animal species due to loss of habitat". Although the prevalence of contraceptive usage has increased worldwide, oral contraceptives are among the most extensively studied and used medications in the world (Hatcher et al., 1998) reason being that they are accessible, does not requires doctor's prescription, and/or can be gotten over the counter.

Since its introduction some 50 years ago, many studies have been conducted and there are numerous documentations on its efficacy and availability. The World Health Organization estimated in 1998, that over 100 million women worldwide are on oral contraceptive pills (OCP) (WHO, 1998) and this fact was corroborated by Trussell (2007). Despite that however, many women who require continuing contraception, stop using it primarily because of tolerability issues, including cycle control, weight gain, water retention, perimenstrual symptoms, and hypertension (Bagshaw, 1995; Fotherby and Caldwel, 1994), as well as venous and arterial cardiovascular complications (Burkman *et al.*, 2001; Kemmeran *et al.*, 2001; Baillargeon *et al.*, 2005). The minor side effects produced by OCP steroids, like nausea, breast tenderness, weight gain, irregular menstrual bleeding as well as thrombosis were common and occasionally severe enough to cause discontinuation of use (Avonts *et al*,, 1990; Henderson *et al.*, 1991; American College of Obstetricians and Gynecologists 1992; Endrikat et al., 1995). These side effects are of

great clinical importance and have over the years resulted in many important changes in the composition and use of these preparations to reduce the side effects. Amongst all the side effects, young women are especially concerned with issues of weight gain (Emans et al., 1987), as there is an established relationship between the use of OCP containing an estrogen and progestogen, with mean increases in body weight (Weir, 1978; Crane and Harris, 1978; WHO. 1989).

Of greater concern, is the fact that despite extensive clinical experience, many metabolic effects of OC treatment remains to be explored. In fact, there are only few studies evaluating body composition and OCP usage. Indeed, the questions about metabolic effects of OCPs and weight gain are of particular relevance to females during OCP treatment. This study therefore, is designed to determine the durational effect of OCP usage on the body weight changes in adult female rabbits.

MATERIALS AND METHODS

Experimental Animals: Fifteen adult female rabbits were obtained from Aduwawa market in Benin City, Nigeria, and transported to the experiment site where they were housed in a well-ventilated room under a 12/12 hours light/dark cycle and fed feed (Vital feed (Grower pellets produced by Grand Cereals Ltd, a subsidiary of UAO Nigeria PLC, Jos, Plateau State), grasses and water *ad libitum.*

Drug of study: OCP (AVA containing Levonorgestrel 0.15mg and Ethinylestradiol 0.03mg) was purchased from a Medical Pharmacy in Ekpoma, Nigeria. AVA 30 ED is a combined oral contraceptive consisting of 21 hormonal tablets and 7 non-hormonal tablets. Each white hormonal tablet contains a small amount of two different female hormones. These are levonorgestrel (a progestogen) and ethinylestradiol (an estrogen). Because of the small amount of hormones, it is considered as a combined low-dose oral contraceptive preparation.

Experimental grouping: The rabbits were divided into three groups (A, B and C) of 5 rabbits each; A served as the control, while B (low weight group) and C (high weight group) served as the test groups.

Drug administration: Each day a tablet is dissolved in 100ml distilled water and the appropriate dose per kg was measured out using a 2ml syringe for oral administration via an oro-gastric tube. Group B received 0.14mls while group C received 0.30ml of the prepared drug. These doses were determined based on comparative dosage per weight proportion akin to humans.

Body weight determination: Weight changes were determined in three phases: during 2 weeks of acclimatization (phase one); during 2 weeks post acclimatization without OCP administration (phase two); and during 4 weeks post acclimatization (with OCP administration in the last 2 weeks) (phase three). Descriptively, phase 1 weight-change determination represents body weight changes during acclimatization period that lasted for two weeks. Phase 2 represents body weight changes during the next 2 weeks after acclimatization without OCP administration, while phase 3 represents body weight changes during the actual experimental period (2 weeks after phase 2 weight-change determination) in which OCP was administered. These weight measurements were conducted weekly, using a goat meat weighting scale (China). The mean values were determined and recorded appropriately.

Data analysis: The mean ± standard deviation was determined and one-way ANOVA analyses of variance were performed using SPSS version 17 soft ware. The significance level was set at $p<0.05$. Results were presented in suitable tables and graphs.

RESULTS

Mean body weight in groups A, B and C, is presented in table 1, while figures 1 and 2 show graphical representations of the mean weight and pattern of weight changes between the groups. As shown in table 1 and Figure 1 and 2, mean body weight increased in group A (control). The weight differences in group A were significantly higher as the week progresses (Table 1). On the other hand, while weight gain were observed in phase 1 and 2 of group B and C, mean body weight loss was observed in phase 3, during which OCP was administered. These weight changes was significantly different ($P>0.05$) in group B but not in group C ($P>0.05$).

Also presented are the differences in weight gain during the three phases (Phase 1, 2 and 3). Group A (control) progressively gained weight throughout the study period. Unlike A, group B and C progressively gained weight during phase 1 and 2 but during phase 3 as group B showed no change in weight, while group C presented losses in

weight (see table 1 and figure 1). Specifically, after acclimatization (phase 1), a weight gain of 0.12kg, 0.20kg and 0.12kg occurred in group A, B and C respectively. During phase 2, a weight gain of 0.12kg, 0.10kg and 0.10kg occurred in group A, B and C respectively. But during phase 3, group A presented a weight gain of 0.06kg, while B and C presented an unchanged weight of 0.00kg and a reduction in weight by -0.06kg respectively.

Table 1: Mean body weight changes (kg) at the different phases of the experiment

Group	Weight (kg) Phase 1			Weight (kg) Phase 2			Weight (kg) Phase 3		
	Wk 1	Wk 2	D1	Wk 3	Wk 4	D2	Wk 5	Wk 6	D3
A	1.74 ±0.20^{a}	1.86 ±0.15^{ab}	+0.12	1.96 ±0.11^{bc}	2.08 ±0.80^{c}	+0.12	2.14 ±0.06^{c}	2.20 ±0.00^{c}	+0.06
B	0.82 ±0.13^{a}	1.02 ±0.08^{bd}	+0.20	1.12 ±0.11^{cd}	1.22 ±0.22^{c}	+0.10	0.88 ±0.16^{ab}	0.88 ±0.11^{ab}	0.0
C	1.60 ±0.31^{a}	1.72 ±0.26^{a}	+0.12	1.82 ±0.24^{a}	1.92 ±0.22^{a}	+0.10	1.60 ±0.46^{a}	1.54 ±0.39^{a}	- 0.06

Values are mean± Standard deviation and values with in the groups having different superscript are statistically significant at P<0.05.

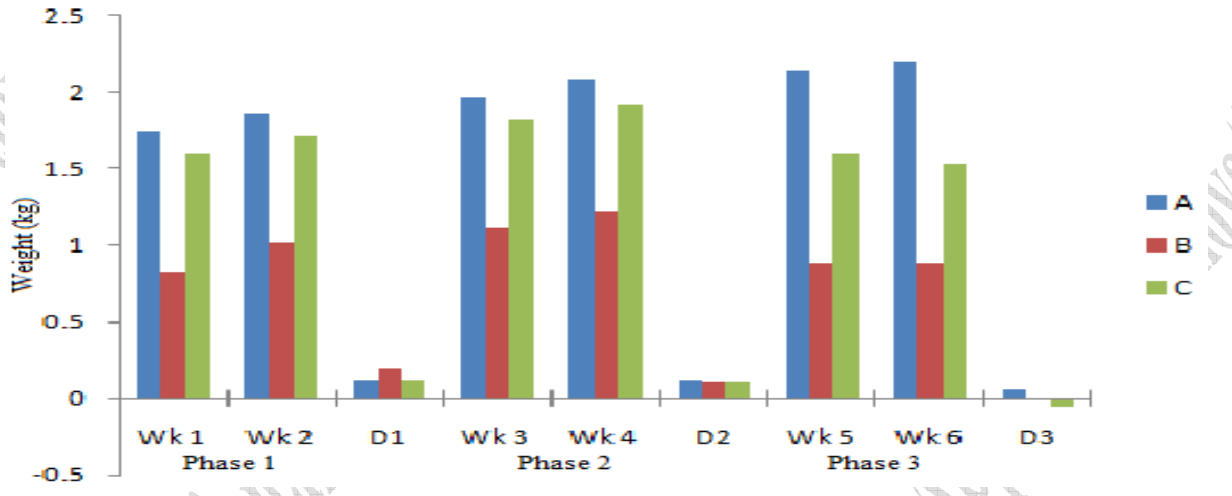

Figure 1: Bar chart showing means weight changes of rabbits fed oral contraceptive pill.

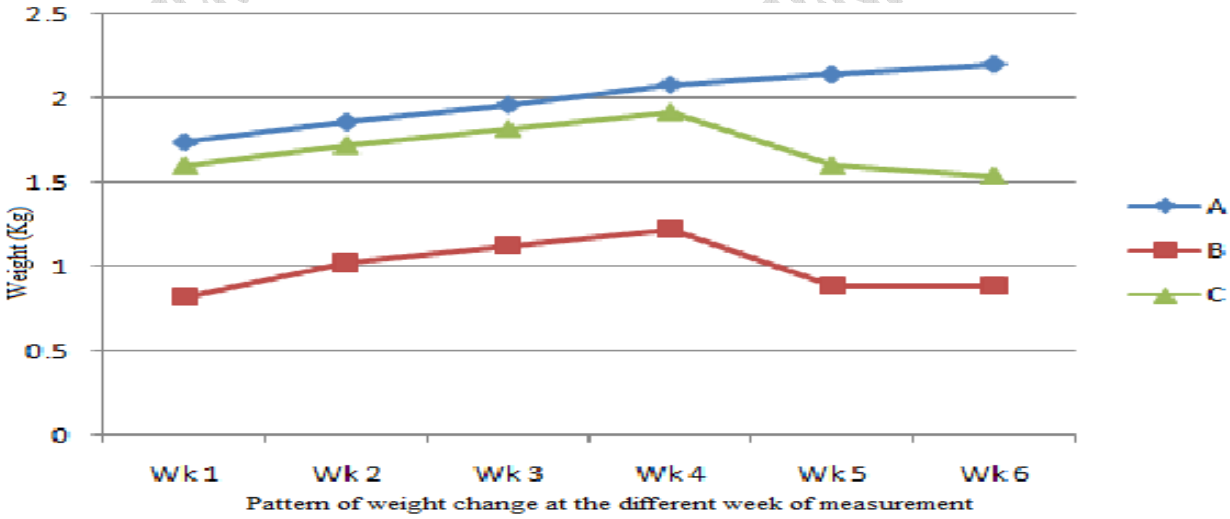

Figure 2: Line graph showing weekly weight changes pattern of rabbits fed oral contraceptive pill

DISCUSSION

Increase in the world's population if allowed at the present rate, will surely cause a burden on public health and world's resources. Unfortunately, contraception, which could have countered this phenomenal growth rate, remains inadequately utilized due to several known side effets. In fact, several studies have reported that many women stop using OCP primarily because of weight gain (Fotherby and Caldwel, 1994; Bagshaw, 1995), which undoubtedly, poses a major risk for chronic diseases, including type II diabetes, cardiovascular disease, hypertension, stroke and certain forms of cancer (WHO, 2009). Bhattacharya et al. (2011), argues however, that despite the controversies associated with the use OCPs, its health benefits still outweighs the risks.

Interestingly, the results of this study has shown that OCP may reduce total weight in women who are already on weight management therapies, as well as the overweight, who are considering reducing their weight. In line with the present finding, some studies evaluating body composition during oral contraceptive treatment have also shown that no significant body weight change is associated with OCP usage (Reubinoff et al., 1995; Franchini et al., 1995, Lloyd et al., 2002). More recently a Swedish study concluded that a combined oral contraceptive use cannot be a predictor for weight increase in the long term (Lindh et al., 2011) as there is also no evidence that modern low-dose pills cause weight gain, but yet, the fear of weight gain contributes to the poor drug compliance to OCP, which often results in unintended pregnancies, especially among adolescents (Gupta, 2000).

Specifically, a randomized trial confirmed that OCP usage does not cause weight or fat mass gain, at least among young female runners (Procter-Gray et al., 2008). Similarly, a Hungarian study comparing two high-dose estrogen (both 50 µg ethinyl estradiol) pills, found that women using a lower-dose biphasic levonorgestrel formulation (50 µg levonorgestrel x 10 days + 125 µg levonorgestrel x 11 days) showed a significantly lower incidence of weight gain as compared to women using a higher-dose monophasic levonorgestrel formulation (250 µg levonorgestrel x 21 days) (Balogh, 1986). Procter-Gray et al. (2008) however, dichotomizes the argument, stating that OCP usage is associated with lean mass gain in eumenorrheic runners but not in those with irregular menses.

Although sex steroids have been shown to interfere with appetite, metabolic functions, and weight, in some women using oral contraceptive, the association with OCP treatment however, is unclear (Rickenlund et al., 2004). The cause of weight gain as regards increase in hips size, breast, or thigh has been reported to be estrogen, while progesterone causes increase in appetite and permanent weight gain **(**Crystal, 2005). The oral contraceptive pill used in this study contains both estrogen (Ethinylestradiol 0.03mg) and progesterone (Levonorgestrel 0.15mg), but yet, a weight loss outcome was recorded. Nevertheless, while endogenous androgens are related to abdominal obesity (Leenen et al., 1994), exogenous androgen treatment has been shown to reduce body fat and weight in postmenopausal women (Gruber et al., 1998).

However, oral administration of estrogen has been found to reduce postprandial lipid oxidation and increase fat mass (O'Sullivan et al., 1998). In this regards, Rickenlund et al. (2004), reports that the precise mechanisms responsible for the increases in weight and body fat remain to be elucidated, but that increase in weight and fat mass is associated with the decline in androgen levels unlike the other hormone where no association was observed with hormonal changes

On the other hand, estradiol has been reported to inhibits feeding in animals (Geary, 2001) while high dose progestins are appetite stimulating (Maltoni et al., 2001). This fact may support the finding of this study considering the low dose progestins (Levonorgestrel 0.15mg) in the OCP used as compared to other OCPs. While Rickenlund et al. (2004) reported that sex steroids may exert metabolic effects in adipose tissue, OCPs has been said to also decrease insulin sensitivity and the effect on carbohydrate metabolism has been attributed to the progestin component (Krauss and Burkman, 1992). Hence, lower doses of estrogen and progesterone in combination (as that used in the present study) may elicit anti-obesity properties.

Judging by the findings of this study therefore, one can conclude that OCP, mainly used for birth control, may also have potentials for weight management in both the obese and non-obese individuals. Our findings suggest also, that there is a need for further studies on the effect of OCP on body weight, and the dosing pattern in particular.

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AUTHOR(S) CONTRIBUTION

This study was supervised by Dr Ekhator CN with assistant from Dr. Osifo UC. The materials search, statistical analysis and interpretation, technical criticism, initial draft and Final correction that resulted into this article were performed by both authors.