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Evaluation of reproductive health functions in administration of coffee and caffeine to female wistar rats

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Abstract
In recent times, the increasing worldwide resort to coffee and caffeine consumption may not be unconnected with recent findings that it contains ingredients that promote male and female reproductive health. In view of this, current study investigated female reproductive health functions due to coffee administration to female wistar rats. Seventy (70) rats were procured and acclimatized (in two weeks) for the study. The rats were then grouped into seven (7) with experimental group 1 receiving standard rat diet and water *ad libitum*. Groups 2, 3 and 4 were respectively given 40mg/kg, 60mg/kg and 80mg/kg doses of Coffee; whereas, groups 5, 6 and 7 received 30mg/kg, 45mg/kg and 60mg/kg doses of Caffeine respectively. Following period of administration, rats were euthanized by cervical dislocation. Blood samples were then obtained (via cardiac puncture) and assayed for various reproductive hormones [Follicle Stimulating Hormone – FSH and Luteinizing Hormone - LH]. In any case, body weight and selected organ weights [Liver and Kidney] were also obtained and compared between coffee and caffeine treated rats at variable doses. Following comparison with student t-test, study found a statistically significant decrease ($p < 0.05$) in serum FSH and LH levels following the administration of caffeine and coffee to wistar rats at all doses. Study also found a statistically significant increase ($p < 0.05$) in relative liver weight in medium dose and high doses of Caffeine but only in high dose of coffee treatment when compared to control and high dose respectively. We recommend routine addition of caffeine, coffee's active ingredient to dietary foods of females with low reproductive tendencies.

Keywords: reproduction, hormone, coffee and caffeine

Introduction

Infertility is an age-long world health concern. It affects approximately 15% of all couples with Male factor infertility contributing approximately half of these cases [1&2]. The drive for solutions to this problem has produced various causative findings including: environmental, dietary and genetic factors. While a host of these factors have been put forward as causes, a large number of scientists have implicated dietary life style as a main area of concern. Changes in physiological status probably due to dietary factors resulting in oxidative stress has been implicated as a potent predisposing factor in infertility [3].

In recent years, evidences have shown that oxidative stress may play a role in the pathogenesis of idiopathic male factor infertility [4] Oxidative stress results from free radicals, reactive oxygen species and imbalances in antioxidant and oxidants status but can be reduced by consumption of antioxidant supplementation such as honey tea, coffee, vegetables, wine, juice, sprouted grains and other food [5&6].

The increasing worldwide resort to coffee consumption may not be unconnected with recent findings that it contains ingredients that promote health in both male and female sexes. Coffee, a popular beverage consumed worldwide has been extensively studied as a protective food, able to produce physiological or metabolic effect in human organism [7]. This beverage is consumed by more than 75% of women of reproductive age in the U.S [8]. Caffeine is the active ingredient in coffee [9] and caffeine is widely consumed in different food drinks and drugs.

Like in every other system, coffee intake has been found to alter human reproductive functions; findings suggest that women are more at risk of coffee hazards than men. Coffee constituents cross the placenta to also affect the unborn baby suggesting that coffee may be contra-indicated in pregnancy [10]. The possible effect of coffee on disturbance in pregnancy may be due in part to imbalances in hormone levels caused by coffee [11].

Though reports abound on the effect of coffee on human subjects especially the negative effects of coffee on maternal health particularly in the temperate regions, however, not much investigation has been carried out on the effect of coffee on FSH and LH in females and Africans generally and whether the anti-oxidant status of coffee could boost the reproductive functions of male hormones [12, 13]. This study investigated the hormonal factors on different doses of Caffeine and Coffee on the reproductive system, tissue histology, hormone levels and reproductive health functions of wistar rats. There is a plethora of information on the dangers of coffee on the body systems however, there is little to conclude that coffee is good for reproductive health, this is much more intriguing with the increasing rate of infertility largely attributed to poor nutrition. The issue then is, will coffee consumption be beneficial or

detrimental to the consumer especially as it relates to reproduction?

Aim of Study

The aim of this study was to determine the effects of Coffee on the reproductive functions of Wistar rats. Specifically, study;

1. Investigated the effect of Coffee and Caffeine on general body and weights of selected organs [liver and kidney].
2. Determined the effect of Coffee and Caffeine on the histology of the Hypothalamus and Anterior Pituitary gland
3. Examined the effect of Coffee and Caffeine on the basal levels of selected female reproductive hormones (FSH and LH)

Materials and Methods

Study Design

Seventy (70) wistar rats were procured and acclimatized (in two weeks) for the study. The rats were then grouped into seven (7) with experimental group 1 receiving standard rat diet and water *ad libitum*. Groups 2, 3 and 4 were respectively given 40mg/kg, 60mg/kg and 80mg/kg doses of Coffee; whereas, groups 5, 6 and 7 received 30mg/kg, 45mg/kg and 60mg/kg doses of Caffeine respectively. All animals were fed with normal rat chow and water. All experimental rats were treated for four (4) weeks period. After administrations of test solutions, animals were sacrificed by cervical dislocation and serum samples collected for analysis.

Ethical Clearance

Ethical Approval for the use of animals was obtained from the Research and Ethics Committee of the College of Health Sciences, Delta State University, Abraka, Delta State, Nigeria.

Preparation of stock solution of Caffeine

High dose (60mg/kg)

1200mg (1.2g) of Caffeine was weighed with an electronic weighing balance and dissolved in 200ml of distilled water. This gave stock solutions of 1200mg/200ml (6mg/ml).

Medium dose (45mg/kg)

900mg (0.9g) of Caffeine was weighed with an electronic weighing balance and dissolved in 200ml of distilled water. This gave stock solutions of 900mg/200ml (4.5mg/ml).

Low dose (30mg/kg)

600mg (0.6g) of Caffeine was weighed with an electronic weighing balance and dissolved in 200ml of distilled water. This gave stock solutions of 600mg/200ml (3mg/ml).

3.7.2 Preparation of Stock Solutions of Coffee

Low dose (40mg/kg)

800mg (0.8g) of coffee was weighed with electronic weighing balance and constituted in 200ml of distilled water. This gave stock solutions of 800mg/200ml (4mg/ml).

Medium dose (60mg/kg)

1200mg (1.2g) 0f c0ffee was weighed with electronic weighing balance and constituted in 200ml of distilled water. This gave stock solutions of 1200mg/200ml (6mg/ml).

High dose (80mg/kg)

1600mg (1.6g) of coffee was weighed with electronic weighing balance and constituted in 200ml of distilled water. This gave stock solutions of 1600mg/200ml (8mg/ml).

Administration of Coffee Solution

High dose (80mg/kg), Medium dose (60mg/kg) and low dose (40mg/kg) were estimated from the lethal dose of coffee (192mg/kg). For high dose, medium and low dose of coffee, 1.6g, 1.2g and 0.8g were dissolved in 200ml of distilled water making the stock concentration to be (8mg/ml), (6mg/ml) and (4mg/ml) respectively. The body weight of male Wistar rats was taken and the dose of test drugs in millilitre to be administered was calculated.

Administration of Caffeine Solution

Caffeine was administered to experimental animals according to their body weight, such that animal weighing 200g, 150g, 170g received 2ml, 1.5ml and 1.7ml respectively. Caffeine was administered orally using orogastric canola.

Statistical Analysis

Evaluation of data for statistical significance was carried out with the Statistical Package for Social Sciences (SPSS, version 20), using the one-way Analysis of Variance (ANOVA). p-values < 0.05 was taken to be statistically significant.

Results

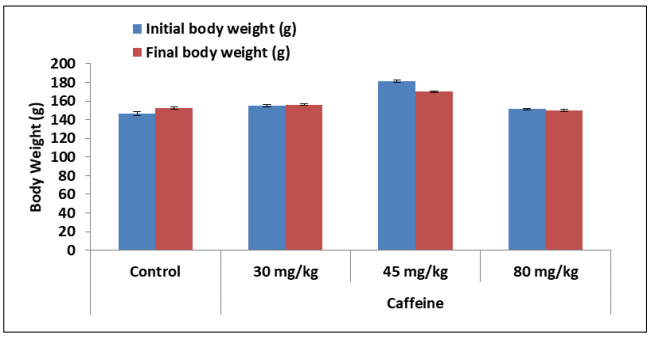

Fig 1: Comparative Effect of Caffeine on Initial and Final Body Weights

From above, administration of caffeine low dose caused weight gain of 4.10%. However, administration of caffeine high and medium dose caused weight reduction of -6.62% and -8.33% respectively when compared to control (with weight gain of 0.80%).

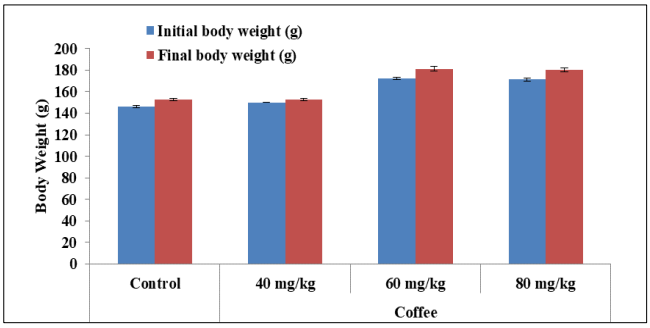

Fig 2: Comparative Effect of Coffee on Initial and Final Body Weights

From Figure II above, there was percentage weight gain of 4.83%, 1.48% and 4.86% in high dose, medium dose and low dose respectively when compared to control group (0.80%).

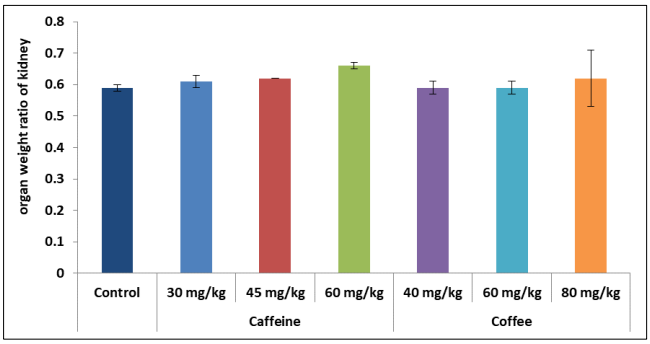

Fig 3: Comparative Effect of Coffee and Caffeine on Kidney Weight

From above figure, there was no significant difference (P>0.05) in relative kidney weight among groups (control, high dose, medium dose and high dose) in the caffeine group. there was also no significant difference (P>0.05) in relative kidney weight among groups (control, high dose, medium dose and low dose) means.

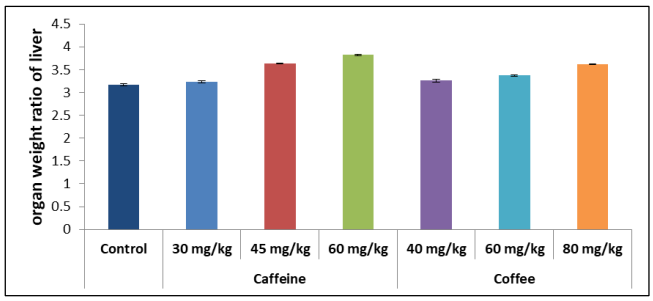

Fig 4: Comparative Effect of Coffee and Caffeine on Liver Weight

From Figure IV above, there was significant (P<0.05) increase in relative liver weight in medium dose and high doses of Caffeine but only in high dose of coffee treatment when compared to control and high dose respectively

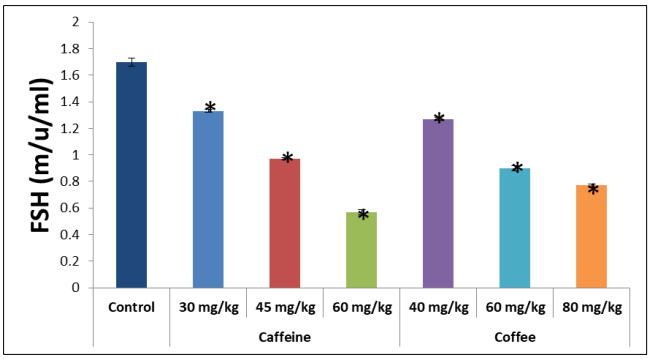

Fig 5: Comparative Effect of Coffee and Caffeine on FSH Levels

From Figure V above, There was significant decrease (P>0.05) in serum FSH levels following the administration of caffeine and coffee at all doses. FSH values in all doses significantly (P<0.05) decreased when compared to value in control group in a dose dependent manner, i.e. The highest values are seen in the lowest doses followed by medium and highest coffee, showing dose dependence.

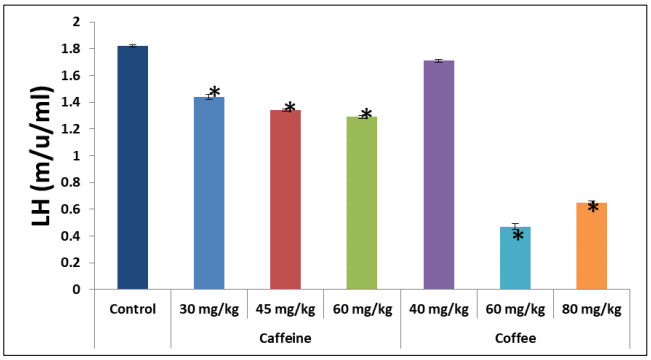

Fig VI: Comparative Effect of Coffee and Caffeine on LH Levels

There was significant decrease (P>0.05) in serum LH levels following the administration of caffeine at all doses except at low Coffee treatment. For coffee administration there was an anomalous dose effect on LH levels, though moderate and high doses were significantly decreased

Discussion

Caffeine is the most popular pharmacologically active substance consumed [14]. It is a stimulant and is often used to enhance mental alertness. Although there is no high quality evidence that a modest level of caffeine consumption has adverse effects on fertility or pregnancy outcome, putative beliefs about a relationship between caffeine intake and adverse reproductive outcomes are common and caffeine consumption is often perceived to be an unhealthy habit [15].

In this study, the effects of coffee consumption on female reproductive health state, specifically hormonal levels were studied. Serum levels of the follicle stimulating hormone (FSH) and Luteinizing hormone (LH) were evaluated.

Effect of Coffee on Body Weight

Findings from this study demonstrated that consumption of coffee may have the potentials of decreasing body weight. From the study (Figures I - IV), there was no significant change in weight ($p < 0.05$), indicative that weight decrease due to treatment must have been counterbalanced by weight gain due to growth and adequate feeding over the duration of experiment. This closely agrees with Greenberg *et al.*, (2005) [16] that reported that coffee reduces body weight and also with Lopez-Garcia *et al.*, (2006) [17] that reported that increase in the intakes of coffee were inversely associated with weight gain. More so this agreed with Lovallo *et al.*, 2005 [18] who opined that the significant loss in body weight could be attributed to the diuretic effect of Caffeine and its role in enhancing fat metabolism [19&20]. The findings observed may indicate that the effect of coffee could be due to compounds other than caffeine."Chlorogenic acid in coffee is able to attenuate glucose absorption in the digestive track, which could help control weight" as reported by Frary *et al.*, (2001) [21].

Effect on Female Reproductive Hormones

The results showed that coffee treatment on rats decreases both male and female hormones, though in varying proportion. In experiment to demonstrate the effects of chronic administration of caffeine and stress on feeding behaviour of rats. From the study carried out there was decrease in testosterone level. This decrease could be due to effects of caffeine, probably through acting on the hypothalamic-pituitary gonadal axis.

Also, administration of low caffeine caused significant reduction in serum FSH when compared to serum FSH in control group. It also shows reduction in serum FSH in medium dose and low dose caffeine when compared to serum FSH in high dose caffeine. The reduced level of serum LH, FSH could be as a result of the inhibitory effect of caffeine on the anterior pituitary gland [17]. The anterior pituitary gland secretes FSH and LH which are necessary for oogenesis. Inhibition of the pituitary gland could eventually lead to reduction in FSH and LH levels.

Again, the results from this study showed that there was significant difference in serum FSH among high dose, medium dose and low dose following administration of coffee to wistar rats. LH level in medium dose was significantly reduced when compared to serum LH level in control group and high dose. Serum LH in low dose was also significantly decreased when compared to serum LH level in medium dose. There is no previous literature to support this finding.

Conclusion

In the various investigations carried out in the study, Coffee was seen to rival the deleterious effects of caffeine in almost all parameters measured suggesting that caffeine content of coffee is up to the level at which pure caffeine exerts it effect. Both Caffeine and Coffee treatment showed a dose- dependent effect on most parameters measured.

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