

Effects of Postinor use on Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Prolactin and Progesterone Serum Levels

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Abstract

Postinor-2, also known as the 'morning after pill', is used as an emergency contraceptive. The aim of the study is to evaluate the effects of Postinor on FSH, LH, prolactin and progesterone serum levels on female albino rats. The experimental animals were separated into five groups (A - E). Each group contains ten rats each (n = 10) using 5 big cages to house them. Group A served as the control, while groups B - E served as the test groups. The administration of postinor was given orally as follows: Group A (Control) received only normal feed (growers' mash) and distilled water daily for four weeks. Group B were administered with 1ml of 1.5mg/100ml of postinor, Group C were administered with 2ml of 1.5mg/100ml of postinor, Group D were administered with 3ml of 1.5mg/100ml of postinor, Group E were administered with 4ml of 1.5mg/100ml of postinor. Determination of serum progesterone, prolactin, FSH and LH was done using ELISA TECO kit. The result, Mean and SD of FSH, LH, prolactin and progesterone serum levels on female albino rats on Postinor, in which FSH for control was 6.733 ± 2.3485 while that of the test was 2.3485 ± 7.7746 . For LH, the control was 11.5667 ± 7.7746 while that of the test was 1.3939 ± 7.4075 . For the prolactin, the control was 8.2778 ± 4.2426 while the test group was 15.7455 ± 4.23896 . For the Progesterone, the control was 0.8167 ± 4.2426 while the test was 1.5109 ± 3.6281 . However, a statistically significant ($P < 0.05$) decrease was observed for the FSH and LH of test group administered with postinor while an increase was observed for the Prolactin and Progesterone levels of the test group when compared with the control. In conclusion, this present study concludes that no significant changes was observed in the body weight of all groups and Group B to E were administered with small and large doses of postinor showed significant variations.

Keywords: Postinor; Postinor; Follicle Stimulating Hormone (FSH); Luteinizing Hormone (LH); Prolactin and Progesterone

Introduction

Postinor-2, also known as the 'morning after pill', is used as an emergency contraceptive. It is a morning pill taken after unprotected intimate intercourse to prevent pregnancy. Postinor is a brand name of levonogestrel, contraceptive tablet manufactured by a Hungarian firm (Adelaide, 2007). Postinor is marketed in Nigeria as a post-coital drug for the prevention of conception. It has not been shown to be safe or effective for the prevention of conception. It has been proposed that postinor should be marketed as an emergency contraceptive, the only indication for which has been shown to be effective, but its uses may not change unless the reasons why women use it are addressed. When excess postinor-2 is being administered orally, some of the components such as silica colloidal anhydrous, give rise to deleterious effect on the liver which include inflammatory disorders and sarcoidosis (Newman, Rose & Bresnitz, 2004). In a research work, Loss of weight and dullness was observed in all the groups treated with various doses of Postinor-2 drug.

Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are called gonadotropins because stimulate the gonads - in males, the testes, and in females, the ovaries. They are not necessary for life, but are essential for reproduction. These two hormones are secreted from cells in the anterior pituitary called gonadotrophs. Most gonadotrophs secrete only LH or FSH, but some appear to secrete both hormones.

Progesterone (P4) is an endogenous steroid and progestogen sex hormone involved in the menstrual cycle, pregnancy, and embryogenesis of humans and other species (Crabbé et al., 1983). It belongs to a group of steroid hormones called the progestogens and is the major progestogen in the body. Progesterone has a variety of important functions in the body. It is also a crucial metabolic intermediate in the production of other endogenous steroids, including the sex hormones and the corticosteroids, and plays an important role in brain function as a neurosteroid (Szejtli & Szente, 2012).

As a form of progesterone, levonorgestrel exerts its actions on the hypothalamus through a negative feedback mechanism, which causes a decrease in the secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Both LH and FSH normally stimulate ovulation. Thus, by reducing their secretion, levonorgestrel serves to inhibit ovulation. The drug also inhibits implantation, the point when a fertilized egg embeds in the uterine wall, where it will grow and develop into an embryo. The aim of the study is to evaluate the effects of Postinor on FSH, LH, prolactin and progesterone serum levels on female albino rats.

Materials and Methods

This study was carried out in the experimental site of Histopathology Laboratory Department of Ambrose Alli University, Ekpoma, Edo State. Fifty (50) Adult albino rats of comparable sizes and weights ranging from 90g to 130g (age of rats is five (5) weeks) were procured from the animal farm, Histopathology Laboratory Department of Ambrose Alli University, Ekpoma, Edo State and transferred to the experimental Histopathology Laboratory Department, Ekpoma, where they were allowed two (2) weeks of acclimatization. They were kept in wire mesh cages with tripod that separates the animal from its faeces to prevent contamination. During this period of acclimatization, the rats was fed with Growers' mash and water *ad libitum*. The animals were maintained and utilized in accordance with the standard guide for the care and use of Laboratory animals.

Grouping of Animal Model

The experimental animals were separated into five groups (A - E). Each group contains ten rats each (n = 10) using 5 big cages to house them. Group A served as the control, while groups B - E served as the test groups.

Substance of Study

The drug (postinor) was purchased from a government approved pharmacy in Ekpoma, Edo state and diluted to appropriate concentrations using commercially produced distilled water. The drugs were administered orally using 1.0ml standard syringe for four weeks. Each of the animals in group B to E were picked at a time with a hand towel and appropriate volumes of the drugs were administered to the animals orally.

Substance Administration

The administration of postinor was given orally as follows:

- i. Group A (Control) received only normal feed (growers' mash) and distilled water daily for four weeks.
- ii. Group B were administered with 1ml of 1.5mg/100ml of postinor.
- iii. Group C were administered with 2ml of 1.5mg/100ml of postinor.
- iv. Group D were administered with 3ml of 1.5mg/100ml of postinor.
- v. Group E were administered with 4ml of 1.5mg/100ml of postinor.

Sample Collection and Analysis

The weights of the animals were measured before and after acclimatization and similar weight measurements were done at the end of each phase and the average weight recorded accordingly.

Analytical Methods

Determination of serum progesterone, prolactin, FSH and LH

Testosterone hormone level was determined according to the method of Tiez and Andresen, (1986) using ELISA TECO kit for testosterone.

Assay procedure

All samples and reagents were allowed to reach at room temperature (~25°C). Reagents mixed by gentle inversion before use. Standards, controls and samples assayed in duplicate.

1. Microtitration Strip was marked to be used.
2. 25µL of the standards, controls and samples were added into each appropriate well.
3. 200µL of Conjugate Reagent were added into each well using a precision pipette.
4. The wells were mixed for 10 seconds.
5. The wells were incubated for 60 minutes at room temperature (~25°C).
6. Each well was aspirated and washed 3 times by added 400 µL of working Wash Solution.
7. 200 µL of substrate solution were added into each well using a precision pipette and gently mixed for 10 seconds.
8. The wells were incubated in the dark for 15 minutes at room temperature (~25°C).
9. 100 µL of Stop Solution were added into each well using a precision pipette and mixed for 10-20 seconds.
10. The absorbances of the solution in each well were read at 450 nm.

Calculation

The absorbance for each standard, control, or samples were obtained, and then the stander curve prepared by plotted the absorbance readings for each of the standards along the Y-axis versus standard concentrations in ng/mL along the X-axis, the mean absorbance values for each sample were determined the corresponding concentration of testosterone in ng/mL from the standard curve.

Statistical Analysis

Analysis of variance (ANOVA) at $P \leq 0.05$ level of significance was used to compare results in both the control and the test groups (all results shall be reported as mean \pm standard deviation); using a computer program named SPSS for windows release 20.0. Confidence interval values $P \pm 0.05$ shall be considered significant.

Result

Table 1 shows a comparison of Mean \pm S.E of different stages of weight measurement in groups and control group using ANOVA in which the weight (gram) before acclimatization of the control to group 5 increased sequentially, 132.10 \pm 4.12g to 150.0 \pm 4.84g. However, this increase was not significant. The weight (gram) after acclimatization, shows that it increases 135.0 \pm 2.20g to 160.0 \pm 5.40g, also this was not significant.

Table 2 shows the Mean and SD FSH, LH, prolactin and progesterone serum levels on female albino rats on Postinor, in which FSH for control was 6.733 \pm 2.3485 while that of the test was 2.3485 \pm .77746. For LH, the control was 11.5667 \pm .77746 while that of the 1.3939 \pm 74075. For the prolactin, the control was 8.2778 \pm .42426 while the test group was 15.7455 \pm 4.23896. For the Progesterone, the control was 0.8167 \pm .42426 while the test was 1.5109 \pm .36281. However, a statistically significant ($P<0.05$) decrease was observed for the FSH and LH of test group administered with Postinor while an increase was observed for the Prolactin and Progesterone levels of the test group when compared with the control.

Table 3 shows the of FSH, LH, prolactin and progesterone serum levels on female albino rats of different groups administered with Postinor in which group A serum FSH, LH, Prolactin and progesterone levels was 6.73 \pm 2.133, 11.56 \pm 12.95, 8.27 \pm 2.759 and 0.8167 \pm .424 respectively. For group B, the serum FSH, LH, Prolactin and progesterone levels was 2.01 \pm 1.09, 0.7250 \pm 0.55, 19.48 \pm 4.90 and 1.76 \pm 0.433 respectively. For group C the serum FSH, LH, Prolactin and progesterone levels was 2.42 \pm .68, 1.55 \pm 0.62, 16.58 \pm 3.86 and 1.67 \pm .349 respectively. For the group D, the serum FSH, LH, Prolactin and progesterone levels was 2.51 \pm 0.821, 1.81 \pm .727, 13.71 \pm 2.07, 1.40 \pm .205 respectively. For group E the serum FSH, LH, Prolactin and progesterone levels was 2.51 \pm 0.82, 1.43 \pm 0.661, 13.45 \pm 3.16 and 1.21 \pm 0.16 respectively. However, a statistically ($P<0.05$) significance was observed across all the groups and also when each group was compared to the control a statistically ($P<0.05$) significance variation was observed.

	Control or Group 1 (N=10)	Test Groups				F-Value	P value
		Group 2 (N=10)	Group 3 (N=10)	Group 4 (N=10)	Group 5 (N=10)		
Weight (gram) before acclimatization	132.10 \pm 4.12	141.7 \pm 2.20	143.0 \pm 3.10	147.2 \pm 4.13	150.0 \pm 4.84	0.07	0.232
Weight (gram) after acclimatization	135.0 \pm 2.20	142.5 \pm 3.10	144.0 \pm 3.00	148.0 \pm 3.40	160.0 \pm 5.40	0.30	0.242

Key: * Means statistically significant ($p<0.05$).

Table 1: Comparison of Mean \pm S.E of different stages of weight measurement in groups and control group using ANOVA.

Variables	Control Mean\pmSD	Test Mean\pmSD	T-Test	P-value
FSH (ng/L)	6.733 \pm 2.3485	2.3485 \pm .77746	6.057	0.000**
LH (ng/L)	11.5667 \pm .77746	1.3939 \pm 74075	2.355	0.046*
Prolactin (ng/L)	8.2778 \pm .42426	15.7455 \pm 4.23896	-6.332	0.000**
Progesterone (ng/L)	0.8167 \pm .42426	1.5109 \pm .36281	-4.482	0.001**

Key *. The mean difference is significant at the 0.05 level.

** : statistically significant at $p<0.000$.

Table 2: Mean and SD of FSH, LH, prolactin and progesterone serum levels on female albino rats on Postinor.

Variables	Group A Mean±SD	Group B Mean±SD	Group C Mean±SD	Group D Mean±SD	Group E Mean±SD	F-value	P-value
FSH (ng/L)	6.73±2.133 ^{abcd}	2.01±1.09 ^a	2.42±.681 ^b	2.51±0.821 ^c	2.51±0.82 ^d	23.271	0.000
LH (ng/L)	11.56±12.95 ^{abcd}	0.7250±0.55 ^a	1.55±0.62 ^b	1.81±.727 ^c	1.43±0.661 ^d	5.035	0.002
Prolactin (ng/L)	8.27±2.759 ^{abcd}	19.48±4.90 ^a	16.58±3.86 ^b	13.71±2.07 ^c	13.45±3.16 ^d	12.467	0.000
Progesterone (ng/L)	0.8167±.424 ^{abcd}	1.76±0.433 ^a	1.67±.349 ^a	1.40±.205 ^c	1.21±0.16 ^d	11.021	0.000

Key: * The mean difference is significant at the 0.05 level.

Same Superscript a, b, c, d, shows statistical significance when compared with control.

Table 3: Mean and SD of FSH, LH, prolactin and progesterone serum levels on female albino rats of different groups administered with Postinor.

Discussion

It is a speculated fact that postinor amongst other birth control pills possess economical and societal benefits, however, it is pertinent to note that extensive studies are still on-going on the effects of postinor on the uterus and even generally on the female reproductive system (Conz et al., 2020).

In this research work, weight gain was observed though not significant. This was however in contrast the studies of Adigun et al., (2016), who carried out research on histo-toxic effects of the drug postinor®-2 on the liver of female wistar rats” and observed Loss of weight and dullness was observed in all the groups treated with various doses of Postinor-2 drug. Group A (control) received only normal feed (growers’ mash) and distilled water daily.

The result for hormonal profile showed a statistically significant ($P<0.05$) decrease was observed for the FSH and LH of test group administered with Postinor while an increase was observed for the Prolactin and Progesterone levels of the test group when compared with the control. These changes could be due to the fact that the Postinor drugs initially stimulate secretory changes in the hormonal glands, followed by glandular regression resulting in small, inactive glands. The result from this study was in similarity with studies of Maqueo et al. (1964).

This result also showed a statistically ($P<0.05$) significance was observed across all the groups and also when each group was compared to the control a statistically ($P<0.05$) significance variation was observed. This could be due to a slight rise in the concentration of sex-hormone-binding globulin (SHBG), which amplifies the fall in free testosterone concentrations. Norgestrel-containing oral contraceptives, being androgenic, block the oestrogen-stimulated increase in SHBG (van derVange et al., 2000). The result from this study was in close relation with the studies of Chiaffarino et al. (2008) which reported the ovarian cysts in women who are current or recent oral contraceptive users.

The report from our study was also in similarity with the studies of Tz, Iglesias, & Salinas, (2002) who reported that the changes could be due to consistent with the well-recognized negative feedback effect of the sex steroids on gonadotropin production. Decrease in gonadotropin levels results in inhibition of follicle maturation and luteinization as well as consequent reduction in ovarian size. Some works suggest the hypothesis that fertility drugs do not significantly contribute to ovarian cancer risk (Schüler et al, 2013). Other studies have reported an increased risk of ovarian cancer in women treated with fertility drugs (Russo et al., 2013).

The last hypothesis is the “Gonadotropin theory”. It suggests that an increase in FSH and LH lead to an overstimulation of the ovarian epithelium by increasing local levels of estrogen. This plays an important role in ovarian cancer development. A support to this theory arises from the observation that ovarian cancer incidence increases considerably during menopause, when gonadotropin levels grow (Risch et al., 2014). According to these three theories, fertility drugs should be related to an increase in ovarian cancer risk, because

they can cause a gain in LH and FSH levels, and stimulate ovulation. But women who assume fertility drugs have per se a high risk because of their infertility (Althuis et al., 2005). It is clear that one of the main difficulties in this field is to separate these risk factors, presenting together in infertile women treated with fertility drugs. Three large meta-analyses have been conducted about our issue (Ness et al., 2002).

Conclusion

The present study concluded that no significant changes was observed in the body weight of all groups and group B to E were administered with small and large doses of postinor showed significant variations.

From this study it is recommended that over use of this postinor toxicity could result in uterine carcinoma.

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