# Effect of some anesthesia drugs on rabbit ovarian activity and some physiological responses

Kishk W.

Suez Canal University, Faculty of Agriculture, Animal Production Dept., Ismailia, Egypt

**Summary**

16 female rabbit does (White New Zealand) were used in this experiment to be subjected for control treatment versus anesthesia condition for four successive hours before 4 hrs. of expected time of ovulation. Ovarian activity criteria were measured in which right and left ovary were observed for number of large Graffian follicles and number of formed corpora lutea. The obtained results showed that, there were no significant differences between control group and anesthetized does in their ability to ovulation after 8 hrs. of copulation (number of ovulated does was 7 for control versus 6 for anesthetized group). While, there were significant differences between control and anesthetized does group in the number of formed corpora lutea (8.5 for control vs. 6.5 for anesthetized does group). The physiological responses as regards respiration rate and pulse rate differed significantly between two groups and within anesthesia period. It could be noticed that anesthesia could adversely affect rabbit ovarian functions, physiological responses as well.

**Keywords:** Rabbit, anesthesia, ovary, ovulation, corpus luteum, Graffian follicle.

## Introduction

General anesthesia mechanism is seemed to be very complicated. The aim of anesthesia is to render rabbit to insensitive state. General anesthesia can be divided into four stages. These stages are, analgesia, excitement, surgical anesthesia and respiratory arrest (Kaplan and Timmons, 1979). Recent evidences indicate that most of anesthesia drugs act on ion channel receptors and specially on $GABA_B$ (Gamma-aminobutyric acid is the major inhibitory mediator in the brain) and glycine receptors to increase $Cl^-$ conductance. The effects of GABA on $Cl^-$ conductance lead to marked antianxiety activity, effective muscle relaxants, anticonvulsants and sedatives. In addition, metabolites of the steroid hormones progesterone and deoxycorticosterone bind to $GABA_A$ receptors and increase $Cl^-$ conductance. It is known that, progesterone and deoxycorticosterone are sleep-inducing and anesthetic in large doses and these effects are due to their action on $GABA_A$ receptor (Ganong, 1999).

Hypothalamic gonadotropin-releasing hormone (GnRH) is believed to be the final neurohumoral link between the brain and pituitary in the regulation of gonadotropin release. The rabbit is an excellent species in which to probe these issues since the major ovarian steroids in estrous does have been identified (Pau and Spies, 1986). Steroids can act at both central and pituitary sites (Pau and Spies 1984). One of the most beliefs is that gonadal steroids namely, estradiol-17 beta acts in the central nervous system (CNS) to restrain secretion of luteinizing hormone-releasing hormone

(GnRH) and that peaks and valleys in the levels of luteinizing hormone (LH) (Kalra and Kalra, 1989).

Thermoregulation of body heat of rabbits is dependent mainly on respiration. Respiration is considered to be the dominant way for evacuation of latent heat, since most sweat glands in rabbits are not functional and perspiration is not great due to the fur (Marai and Habeeb, 1994). The most prevalent cause of respiratory depression and respiratory arrest is over dosage of anesthesia drugs or narcotics (Guyton and Hall, 1996).

The aim of the present study is to find out the effect of anesthesia drugs during preovulatory stage on ovarian activities and body physiological responses.

## Materials and Methods

Experimental animals and treatment:

16 White New Zealand rabbit does were allocated into two groups for control and anesthesia group. Does average age was 18 months (multiparous does) and average body weight was 3.650 Kg Does were reared in metal wire separated boxes and provided with pelleted feeding (16% crude protein, 12% crude fibre, 2.9 crude fat, 6.5 ash and 2700 Kcal DE / Kg diet) and free access of fresh water through metal nipples. All does were subjected to natural mating after examination estrous manifestation to buck mating and receptivity ability. After doe copulation with double mating with the same buck, does were put under observation for control group in which respiration rate (RR), pulse rate (PR), and rectal temperature (RT) were measured during last four hours before the ending of entire preovulatory period (12-hours after mating). Whereas, the anesthetized group was subjected to general anesthesia by deep muscular injection of a mixture containing xylazine (5 mg/ kg), kitamine (40mg/ kg) and acepromazine (0.5 mg/ kg) according to Pau and Spies (1986). Anesthesia was applied for two times during four hours which started after 8 hours of natural mating. The same physiological parameters were measured (RR, PR and RT) for anesthesia group. After that, all does were subjected to general anesthesia for a surgery to cut (3-5 cm) in the midline of the abdominal region to examine both right and left ovary for each doe. Number of large Graffian follicles and ovulation rate were counted for each group of does.

Statistical analysis:

Data were subjected to test significant differences between two groups as regards physiological responses (RR, PR and RT) during four-hour period by using ANOVA test according to SPSS program. Also, mean of ovulation points and mean of large Graffian follicles were tested for significant differences using Duncan multiple range test according to Steel and Torrie, (1984).

## Results and Discussion

Data which presented in Table 1 showed that there were significant differences ($P<0.05$) between control group and does which treated with anesthesia as regards pulse rate (PR). Where, PR values were $100.25 \pm 2.25$, $138.67 \pm 10.41$, $149.67 \pm 1.20$, $153.33 \pm 4.81$ and $160.00 \pm 2.31$ for control, first, second, third and fourth hour of anesthesia period, respectively. There was a liner increase in PR during anesthesia period. While, there were no significant differences as regards respiration rate (RR) and rectal temperature (RT) between control anesthetized does as shown in Table 1. In which, control group was slightly higher in RR and RT but without significant

differences than treated does with anesthesia. These differences in physiological responses can declare the influences of anesthesia on physiological functions during different four stages of anesthesia (Kaplan and Timmons, 1979). Hence, there is a degree of inhibition for higher centers of central nervous system (CNS) for sympathetic nerve fibers which leads to a general depression of most physiological functions (Guyton and Hall, 1996). Anesthesia stages could overlap and become very interacted reaching abdominal breathing instead of chest breathing (Kaplan and Timmons, 1979). From these observations, it is very clear that there were highly significant differences ($P< 0.05$) between control group and anesthesia group as respect PR criteria as shown in Table 1. This is may be due to highly stress condition as a sequence of prolonged anesthesia (4-hour anesthesia).

Ovary functions could be affected as a consequence of prolonged anesthesia period (four-hour). As shown in Table 2, number of ovulated does was higher than that of anesthetized does (7 for control and 6 for treated group, respectively) but did not differed significantly. This indicates that anesthesia did not affect surges of LH secretion which are responsible for ovulation. This is in agreement with Tsou, *et al.*, (1977). Where they stated that, copper salts initiate pituitary luteinizing hormone (LH) release since systemic injection of copper acetate (CuAc) increases GnRH levels in pituitary stalk plasma of anesthetized rabbits. While the number of corpora lutea was higher in control group and differed significantly than that anesthetized does (where it was 8.5 for control and 6.5 for treated does with anesthesia, respectively). The previous observations can explain the negative effects of anesthesia on ability of ovaries for maximum ovulation capability. Where there is a synergism relationship between anterior pituitary and ovarian steroids to reach maximum ability of ovulation. The number of large Graffian follicles was also higher for control group and did not differ significantly than that anesthetized does as shown in Table 2.

It could be concluded that, anesthesia can alter and affect ovulation ability of female rabbits through its effect on higher centers of the brain and can alter physiological functions especially pulse rate when it was applied for a long period.

Table 1. Effect of anesthesia for four hours on values of respiration rate(R.R), pulse rate(P.R) and rect (R.T) temperature of female rabbits.

| Treatment | B.W[3] (K.g) | R.R/min 1st | 2nd | 3rd | 4th | Mean | P.R/min 1st | 2nd | 3rd | 4th | Mean | R.T°C 1st | 2nd | 3rd | 4th | Mean |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control group[1] (Average)[4] | 3.575 | $106^{a}$ | $112^{a}$ | $102^{a}$ | $104^{a}$ | $106^{A}$ | $110^{a}$ | $91^{a}$ | $107^{a}$ | $93^{a}$ | $100.3^{A}$ | $40.5^{a}$ | $39.5^{a}$ | $40.2^{a}$ | $39.8^{a}$ | $40.0^{A}$ |
| ±SE | 0.25 | 6.4 | 4.2 | 8.2 | 4.3 | 2.2 | 5.3 | 4.2 | 7.6 | 6.8 | 3.5 | 0.44 | 0.59 | 1.22 | 0.88 | 0.23 |
| Anesthetized[2] Does (Average) | 3.720 | $92.3^{a}$ | $102.7^{a}$ | $100.3^{a}$ | $101.3^{a}$ | $99.2^{A}$ | $138.7^{a}$ | $149.7^{a}$ | $153.3^{a}$ | $160^{b}$ | $150.4^{B}$ | $39.6^{a}$ | $39.7^{a}$ | $39.7^{a}$ | $39.6^{a}$ | $39.6^{A}$ |
| ±SE | 0.43 | 4.7 | 6.1 | 7.3 | 9.9 | 3.2 | 10.4 | 4.56 | 5.67 | 7.85 | 4.85 | 0.32 | 0.12 | 0.35 | 1.5 | 0.55 |

[1] Control group contained 8 does

[2] Anesthetized does group contained 8 does and subjected to anesthesia for 4 hours

[3] Body weight of does expressed in Kg

[4] Averages which contained the same letters have no significant differences at $P<0.05$

Table 2.Effect of anesthesia on ovarian activities (ovulation rate O.R, number of large Graffia follicles GF)

| Treatment | Ovulation Rate Average No. of C.L | No. of ovulated does | Average Number of Large G.F Right Ovary | Left Ovary | Total |
|---|---|---|---|---|---|
| Control[1] | $8.5^{A}$ | $7^{A}$ | $3.6^{a}$ | $4.6^{a}$ | $8.3^{A}$ |
| ±SE | 0.66 | | 0.89 | 0.52 | 0.44 |
| Anesthetized Does[2] | $6.5^{B}$ | $6^{A}$ | $3.3^{a}$ | $4.2^{a}$ | $7.5^{A}$ |
| ±SE | 0.52 | | 0.74 | 0.82 | 0.56 |

[A]Averages which contained the same letters have no significant differences at $P<0.05$

[1] Control group contained 8 does

[2] Anesthetized does group contained 8 does and subjected to anesthesia for 4 hours

## References

Ganong, W. F. (1999). Review of medical physiology. Appelton & Lange, Norwalk, Connecticut / San Mateo, California, pp: 80-113.

Guyton, A. C. and Hall, J. E. (1996). Textbook of medical physiology. W. B., Saunders Company, pp: 209-220.

Kalra, S. P. and Kalra, P. S. (1989). Do testesterone and estradiol-17 beta enforce inhibition or stimulation of luteinizing hormone –releasing hormone secretion? Biology of Reproduction, 41: 559- 570.

Kaplan, H.M. and Timmons, E. H. (1979). The rabbit. New York, New York: Academic Press, pp: 41-52.

Marai, I. F. M. and Habeeb, A. A. (1994). Thermoregulation in rabbits. Options Mediterraneenes, 8: 33-41.

Pau, K.-Y. F. and Spies, H. G. (1984).Release of GnRH and gonadotropins in the rabbit: Intrahypothalamic perfusion of norepinefhrine stimulates GnRH release. 17th Ann. Meet. Soc. For the study of reproduction, Laramie.

Pau, K.-Y. F. and Spies, H. G. (1986). Effects of cupric acetate on hypothalamic gonadotropin-releasing hormone release in intact and ovariectomized rabbits. Neuroendocrinology, 43: 197- 204.

SPSS/PC+ and SPSS for Windows, Jeremy, J. Foster(1993).

Steel, R. G. D. and Torrie, J. H. (1984). Principals and procedures of statistics. Mc Graw-Hill. Int. Book Comp.

Tsou, R. C., Dailey, R. A., McLanahan, C. S., Parent, A. D., Tindall, G. T. and Neill, J. D. (1977). Luteinizing hormone-releasing hormone (LHRH) levels in pituitary stalk plasma during the preovulatory gonadotropin surge of rabbits. Endocrinology, 101: 534-539.