

Effects of L-Carnitine Supplement on Serum Levels of Estrogen, Progesterone and Testosterone in Felines Following Ovariohysterectomy

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Abstract

Background: The benefits of the addition of L-carnitine to the diet of cats to control weight gain after the removal of their ovaries have been highlighted recently. It is also used in women after menopause. Whether its supplementation alters the sexual hormones is a concern.

Objectives: The objective of this study was to evaluate the effect of dietary supplementation of L-carnitine on estrogen, progesterone and testosterone in cats following ovariohysterectomy.

Methods: Conventional midline ovariohysterectomy was performed in 14 DSH adult and healthy female cats. 10 days after the surgery, the cats were divided into two groups randomly. In group 2, a single dose of 100 mg/kg/day L-carnitine was added to the regular diet for 50 days. The cats in group 1 received no L-carnitine in their diet. Blood samples were taken from all cats prior to surgery, and then again 10 and 60 days post-operatively. Serum levels of estrogen, progesterone and testosterone were measured using a commercially available AMH enzyme-linked immunosorbent assay (ELISA).

Results: Serum levels of estrogen and progesterone significantly decreased at 10 days after the surgery in all cats ($P < 0.05$). There was no significant difference in serum level of testosterone prior and after the surgery between the groups. Also, no significant difference was observed in serum levels of estrogen, progesterone and testosterone at 60 days after the surgery between the groups ($P > 0.05$).

Conclusions: It is concluded that dietary supplementation of L-carnitine has no effect on serum levels of estrogen, progesterone and testosterone in cats following ovariohysterectomy. Long-term study is recommended.

Keywords: L-Carnitine, Sexual Hormone, Ovariohysterectomy, Feline

1. Background

The benefits of the addition of L-carnitine to the canine and feline diet to control weight gain have been highlighted recently. L-carnitine is a vitamin-like compound made in the body from the amino acids lysine and methionine. It is an important nutrient that acts as a transport for fatty acids into the mitochondria of cells and is essential for the cellular production of energy (1). It promotes cardiovascular health and prevents increases in body weight. Recent scientific works indicate that it helps reduce weight in overweight dogs and cats (2, 3). Dietary supplementation of L-carnitine to obese cats' diet was shown to affect the metabolic rate and cause rapid weight loss (4). Ovariohysterectomy is one of the most common surgical procedures performed in small animal practice (5). It is the method of choice for sterilization in dogs and cats (6, 7). Although ovariohysterectomy helps to effectively control overpopulation, it is a risk factor for feline obesity (8). It has been shown that the changes in feeding behavior and

increase in calorie intake after ovariohysterectomy are responsible for changes in body composition and weight gain in cats (9, 10). In addition, it has been proved that energy requirements are 20% lower after the removal of the ovaries (11). Therefore, we would expect weight gain in cats after spaying. Veterinarians have worked to prevent weight gain in cats following ovariohysterectomy. Exercise, restriction in dietary intake, special post-operative diets and dietary supplements are recommended for the prevention of obesity in spayed cats (9, 12). Among food supplements, L-carnitine is very frequently prescribed for cats to manage weight gain after sterilization.

All steroid hormones are synthesized from cholesterol. The ovaries and adrenal cortex are traditionally responsible for most of the production of steroids in female cats. However, it is shown that adipose tissue significantly contributes to the production of estrogen (13). This means fatter animals could be expected to have higher levels of estrogen, especially after gonadectomy (14). In addition, L-

carnitine is typically considered to be a fat burner and has been used for fat metabolism in other species (5, 6). It may affect levels of sexual hormones following ovariohysterectomy by affecting fat cells and cholesterol, which are basic components of steroid hormones. Limited studies have been conducted to evaluate the effects of L-carnitine on sexual hormones like testosterone and prolactin in humans, especially in males. It is reported that carnitine deficiency is independently associated with low free testosterone levels in male hemodialysis patients. Also, testosterone and carnitines proved to be effective in the treatment of male aging syndrome (14, 15). L-carnitine leads to significant weight loss and is recommended in women following menopause (16). Reports are available regarding disturbances in sexual hormones following the use of L-carnitine. Fenkci in 2008 showed that decreased total L-carnitine levels may be associated with hyperandrogenism and/or insulin resistance in non-obese women with polycystic ovaries (17).

2. Objectives

Therefore, we designed the present study to investigate any changes in serum levels of testosterone, progesterone and estrogen in cats following ovariohysterectomy after supplementation of L-carnitine to their daily diet. We aimed to characterize whether supplementation of L-carnitine to spayed cats is safe in terms of not altering the sexual hormones.

3. Methods

3.1. Animals

Fourteen adult and healthy female DSH cats, mean weight 3.2 ± 0.3 kg, were selected for the study. The present experimental exploratory study started on 23/1/93 in Tehran/Iran after approval was received from the university research committee, in accordance with the guidelines of its institutional animal experimentation ethics committee No # 302386, 1/12/1384.

3.2. Procedure

The cats were maintained in the same place at ambient room temperature and humidity with a 12h day/night cycle a few days prior to surgery. They were fed with standard laboratory pellets and allowed free access to water. The subjects' weight was recorded at the beginning of the study. A control blood sample was taken in all cats to measure the serum levels of testosterone, progesterone

and estrogen before removal of the gonads. Serum levels of testosterone, progesterone and estrogen were measured with a commercially available AMH enzyme-linked immunosorbent assay (ELISA, DRG, Germany) designed for use with canine and feline samples.

Under general anesthesia and aseptic preparation of the abdomen, conventional midline ovariohysterectomy was performed in all cats. The same surgeon performed all surgeries. Prior to the surgery, the cats were divided into two groups randomly. 10 days after the surgery, in group 2, a single dose of 100 mg/kg L-carnitine (250 mg tablets, Osve, Iran) was supplemented to the regular diet for 50 days. No L-carnitine was added to the diet of group 1. Blood samples were taken from all cats at 10 and 60 days post-operatively. The subjects' weight was recorded at the end of the study in both groups.

3.3. Statistical Analysis:

Data were summarized as Mean \pm SD. A general linear model procedure was used by SAS software version 9.2. Single point measurements, at any particular times, were analyzed using the repeated measure ANOVA, which tests the equality of means between groups across time points while accounting for the correlation between the repeated measures. A P value less than 0.05 was considered statistically significant.

4. Results

All animals survived the surgery and recovered from anesthesia without any complications. Also, no complications were observed following supplementation of L-carnitine in group 2. Mean serum levels of estrogen significantly reduced at 10 days after the surgery in both groups ($P = 0.00$). Although mean serum levels of progesterone decreased after the surgery in both groups, the changes were not significant ($P = 0.78$). There was no significant difference in serum level of testosterone prior and after the surgery between the groups. No significant difference was observed in serum levels of estrogen, progesterone and testosterone at 10 and 60 days after the surgery between group 1 and 2 ($P > 0.05$). Data are illustrated in [Table 1](#).

5. Discussion

The main clinical applications of L-carnitine supplementation are for pets affected with heart disease; ketoacidosis, a serious metabolic consequence of uncontrolled diabetes; and hyperlipidemia. It also appears beneficial in the management of both obesity and fatty liver syndrome in cats (17, 18). Obesity in small animals has emerged as a

Table 1. Mean \pm SD of Estrogen, Progesterone and Testosterone in Group Test and Controls at Prior to Surgery, 10 and 60 Days after the Surgery

Groups	Group 1			Group 2		
	Days					
	Prior to Surgery	10 Days After the Surgery	60 Days After the Surgery	Prior to Surgery	10 Days After the Surgery	60 Days After the Surgery
Estrogen, pg/mL	18.7 \pm 3.2	9.4 \pm 1.4 ^a	9.2 \pm 2.8	17.4 \pm 4.4	8.8 \pm 1.7*	7.8 \pm 2.5
Progesterone, ng/mL	1.6 \pm 0.88	1.2 \pm 0.35	1.4 \pm 0.68	1.2 \pm 0.98	0.91 \pm 0.44	0.88 \pm 0.32
Testosterone	0.4 \pm 0.21	0.5 \pm 0.24	0.54 \pm 0.33	0.4 \pm 0.18	0.4 \pm 0.15	0.4 \pm 0.21

^aDenotes a statistically significant difference within the groups at different measured times.

very important issue over the past decade and is reported to be the most common nutritional disorder identified in veterinary practice. Therefore, weight management remains a challenge for practitioners (19). Neutering is one of the leading causes of weight gain both in dogs and cats. Although ovariectomy is recommended in small animal practice, it is believed that reduction in sex hormones may directly affect the brain through the hormone regulators of food intake and play a role in weight gain following the removal of the ovaries in cats (11, 20). In the proposal of the present study, the subjects' weight loss during the study was considered as a parameter to measure. Unfortunately, we had many missing data during the experiment, due to challenges in handling the patients and lack of exact information from the owners. Therefore, we could not report the results regarding weight loss. Because this would not affect the objective of the study, we decided to omit this parameter. However, obvious weight loss was observed in cats at the end of the study.

Studies have confirmed a decrease in metabolic rate following ovariectomy in dogs and cats that leads to obesity (21). Mitsuhashi reported significant weight gain in cats following spaying. He defined that the maintenance energy requirement for spayed adult cats is about 25% lower than the cats' requirement prior to surgery (22). Fat cells can produce estrogen in addition to other sources like the adrenal cortex, liver, brain and skin (23). Because L-carnitine targets fat cells, its effects on sexual hormones that are produced through these tissues after sterilization are relevant. A marked decrease in both estrogen and progesterone would be expected, since basal levels are usually less than 10 pg/mL and 1.0 ng/mL, respectively, after removal of the ovaries. This would happen in 48 hours following the surgery (24, 25). The serum levels of estrogen and progesterone were decreased 10 days after the surgery in both groups in the present study, but there were no significant changes in the parameters after supplementation of L-carnitine between the groups. The results indicated

that the addition of L-carnitine in the diet of the cats does not affect the serum levels of estrogen, progesterone and testosterone after ovariectomy. Mustafa et al. conducted the study on ovariectomized rats (26). The rats were gavaged with 100 mg/kg L-carnitine for 60 days. He concluded that the administration of L-carnitine resulted in non-significant changes in serum levels of estrogen in rats. The results of the study are in agreement with the results we obtained in the present study. It has been reported that decreased total L-carnitine levels may be associated with hyperandrogenism in non-obese women with polycystic ovary syndrome (17). We did not observe significant changes in serum levels of testosterone prior and after the surgery between the groups.

Ovariectomy is mainly performed to control population and to prevent estrus and other unwanted behaviors in small animals. However, it is proved to prevent mammary gland tumors and many other sex-hormone-related diseases like pyometra as well (27, 28). Any supplementation to the diet that might affect the production of sex hormones may interfere with the effect of ovariectomy. This may cause the cat to become affected with sex-hormone-related diseases as well as possible demonstration of estrus behavior. However, the lack of influence of L-carnitine on serum levels of estrogen, progesterone and testosterone that was evaluated in this study suggests that L-carnitine can be supplemented to the cats' diet safely after removal of ovaries. Further studies on sexual hormone disturbances following long-term dietary addition of L-carnitine are recommended.

It is concluded that dietary supplementation of L-carnitine has no effect on serum levels of estrogen, progesterone and testosterone in cats following ovariectomy. Long-term study is recommended.

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