Influence of oophorectomy on glycemia and lipidogram[1]

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Abstract

Purpose: To verify the influence of oophorectomy on lipidogram and glycemia.
Methods: Fifty six female rats were divided into the following 7 groups (n = 8): group 1 – sham group, group 2 – oophorectomy 30 days, group 3 – oophorectomy 35 days, group 4 – oophorectomy 40 days, group 5 – oophorectomy 45 days, group 6 – oophorectomy 70 days, group 7 – oophorectomy 55 days. Animals were following by number of days according the group. Was evaluated the serum levels of glucose and lipid profile.
Results: The oophorectomized rats presented higher glycemia. Groups 3, 4, 6 and 7 had a higher glycemia and LDL levels (except for group 6) and groups 6 and 7 had lowest levels of HDL. Group 7 had highest level of VLDL than oophorectomy groups. There was no difference in triglycerides levels.
Conclusion: Oophorectomy was related to dyslipidemia and insulin resistance, mainly after 50th days.
Key words: Ovariectomy. Climacteric. Dyslipidemias. Rats.

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■ Introduction

Low incidence of cardiovascular diseases has been reported in women due to protective hormone effect[1-3]. These illnesses are rare in the premenopausal period, because high levels of estrogen acts improving lipid profile by reducing cholesterolemy. After menopause, hormones promote an increase in weight[1,2,4], high insulin resistance[2-5] and high blood pressure[1,3-5]. In addition to lipidogram changes, leading to an atherogenic lipoprotein profile.

Cholesterol and triglycerides levels are influenced by several factors[4,6,7], such as: diet, life style, age, sex, changes in spleen e hormonal changes. The women's lipid profile has a high influence of this hormonal change, since physiological fluctuations in menstrual cycle change the lipidogram and glycemia[8]. Showing the importance of these sexual hormones. However, mechanisms underlying the influence of hormone in metabolism are controversial yet.

Human studies are being poorly feasible, so, experimental animal model can be used in medical testing to resemble events occurring among the human being as their genetic, biological and behavior characteristics mimic those of human[9]. Rodents are excellent experimental model of dyslipidemia, because they pass through hormonal fluctuations occurring in middle age, similar to those in women. However, rodents enter an estropause rather than a true menopause. Rodents show irregular acyclicity at middle age, after which, they enter a state of persistent estrus, with complete stoppage of reproductive cycles[10,11]. Due the importance of risk factors caused by oophorectomy and your relationship with lipid profile and insulin resistance, this paper aims to verify the influence of oophorectomy on lipidogram and glycemia.

■ Methods

This research followed the rules of the Brazilian Law for Animal Care (Law: 11.794/08) and was approved by the Animal Use and Care Committee, Universidade do Estado do Para (protocol Nº 22/11).

Fifty-six Wistar female rats (*Rattus norvegicus*) were kept in a controlled environment, with food and water *ad libitum*. All animals had the same birth date, 90 days old at baseline and were randomly divided into the following seven groups (n = 8):

Group 1 - Sham - identification and manipulation of the ovaries without removing them.

Group 2 – Bilateral oophorectomy and followed during 30 days after surgery.

Group 3 – Bilateral oophorectomy and followed during 35 days after surgery.

Group 4 – Bilateral oophorectomy and followed during 40 days after surgery.

Group 5 – Bilateral oophorectomy and followed during 45 days after surgery.

Group 6 – Bilateral oophorectomy and followed during 50 days after surgery.

Group 7 – Bilateral oophorectomy and followed during 55 days after surgery.

All surgical procedures were performed in anesthesia (ketamine and xylazine 70 and 10 mg/kg, respectively, IP). The bilateral oophorectomy was performed similar to described by Brito *et al*.[12]. At the end of the following period, 5ml of blood was collected from vena cava for glucose, cholesterol fractions and triglyceride studies, using colorimetric assay, using kits from Labtest®. The animals were killed under deep anesthesia by intravenous injection of KCl.

The software BioEstat© 5.4 was used. All data were expressed as means ±standard deviation. The serum levels of glucose and lipid profile were comparing by analysis of variance (ANOVA), followed by Tukey post hoc test correction when necessary. Statistical significance was assumed at p< 0.05.

■ Results

All animals survived during the study period. Table 1 presents the mean and standard error of mean glycemia and lipidograms of the 7 groups. Regarding the measurement of serum glucose, the groups 3, 4, 6 and 7 had a higher level than group 1 (p<0.01). With respect to total cholesterol, only the groups 2, 3 and 4 had a significant increase than group 1 (p<0.01).

By analyzing the cholesterol fractions, the groups 2 and 3 had increased and groups 6 and 7 had a reduction of HDL levels, comparing to group 1; already in relation to LDL, the group 7 show higher levels than group 1 (p=0.02). The group 7 had the highest levels of VLDL than other oophorectomy groups (p<0.01), however, its had similar levels than groups 1. There was no statistically significant difference in the analysis of serum triglycerides.

Table 1 – Mean levels of serum glucose, total cholesterol and fractions and triglycerides according groups.

Parameter	GROUP						
	1	2	3	4	5	6	7
Glucose	144 ± 27	236 ±86*	253 ±53*	165 ±22	148 ±20	219 ±44*	230 ±67*
Total Cholesterol	69 ±15	136 ±32	124 ±34	86 ±34	78 ±16	62 ±20	84 ±21
HDL	11 ±9.7	23 ±9.0	36 ±5.7*	22 ±14.6	15 ±3.4	02 ±1.8*	02 ±1.8*
LDL	45 ±12	107 ±35*	80 ±32*	56 ±24	54 ±18	48 ±19	65 ±19*
VLDL	12 ±4.6	06 ±1.6	08 ±2.4	09 ±4.9	08 ±4.4	11 ±5.6	16 ±7.4*
Triglycerides	62 ±23	30 ±8.2	39 ±11	44 ±24	41 ±21	56 ±28	83 ±37

■ Discussion

The mechanism by which ovarian hormones affect the women's physiology still not fully understood. However, the lack of these, due to ovarian failure (menopause) or surgical removal (oophorectomy) is associated with development of adverse conditions, such as: obesity[4,13], diabetes[4,5] and dyslipidemia[4,5]. Possibly these changes are linked to estrogen action, once the replacement of only estrogen in menopause rats and humans decrease the plasma cholesterol levels and glycemia[14,15].

We initiated these studies to characterize the better time to evaluation the lipidogram and glycemia levels in oophorectomized rats, since this time is not well defined. Cholesterol total was maintained at similar levels in all groups (p>0.05), however, its fractions showed a decrease of HDL and increase of LDL and VLDL, mainly from the group 6 (50 days). Well-known that after oophorectomy, sex hormones circulate in the body at a high level for 21-30 days[11,12]. Therefore, groups 2 to 5 were in adaptation to new condition of hormonal suppression, explaining fluctuations of serum levels identified in this period (30-45 days). Thus, studies evaluating these parameters at this time may be harmed.

In more than sixty days follow-up of oophorectomized rats[16-18], studies show similar levels of plasma cholesterol and glucose than groups 6 and 7. These findings strengthen the possibility that it is necessary at least fifty days for adaptation to hormonal suppression.

Triglycerides have a close relationship with diet and energy consumption, however is slightly influenced by sexual hormones. Vasconcellos *et al*.[13] reported that oophorectomy does not imply changes in dietary habits on female rats. Some studies that show increase of triglycerides have a bigger follow-up than this study and probably the obesity, associate to oophorectomy, influence the serum levels.

Menopause is associated with an increased risk of development of diabetes[19], related to increase of insulin resistance caused by estrogen depletion. The glycemia, as plasma cholesterol levels, shows fluctuations of serum levels (groups 2 to 5) before the fifty days of post-operation; strengthen the hypothesis of adaptation to hormonal suppression. This hormonal influence is important to be highlighted, because after menopause other risk factors involved in insulin resistance happen[4,5,19], such as obesity and muscle loss.

The data from this study favors the early use of hormone replacement in women, since the earlier they are used, the lower the metabolic changes suffered by women and the less the side effects they may present. However, more studies are needed to confirm these promising findings.

We limited to study the effects of oophorectomy on rats in lipidogram and glycemia in the first days of post-operative, to understand better the physiology. Meanwhile, it is necessary more studies evaluation the liver metabolism to confirm these findings and with a longer follow-up, correlated with weight of the animals.

■ Conclusion

Oophorectomy was related to dyslipidemia and insulin resistance, mainly after 50th days.

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