Effects of Medroxy Progesterone Acetate (Inject-able Contraceptive) on Serum Cholesterol level of Female adult Albino rats.

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ABSTRACT

Objective: To analyze the effects of Medroxy Progesterone Acetate (Injectable contraceptive) on serum cholesterol level of adult female albino rats.

Study Design: An experimental study.

Place and Duration: At Department of Anatomy, Dow University of Health Science from 1st March 2012 to 30th August 2012.

Methodology: Total Seventy-two female albino rats Wister strain were used which were further divided into three groups, named Group A, Group B and Group C. These groups were then subdivided into three subgroups depending on the duration of treatment. Treatment was given for one, two and three months. Group A (n=24) animals were served as controls. Group B as treated (n= 24) and were given MPA (3mg/ kg) according to body weight of rat. Group C treated group (n= 24) was given double dose of MPA (6 mg/ kg). At the beginning of the experiment only one dose of Injections (MPA) was given to both treated groups; B and C. After 1, 2 and 3 months the animals were dissected and 2cc blood was obtained from the intracardiac puncture for the measurement of serum cholesterol level.

Results: Serum cholesterol level showed significant rise in all treated groups B and C, when it was compared with control group A. Serum cholesterol level in control group A was 53.87 mg/dl ± 13.26, in treated group B was 52.50 mg/dl ± 8.29 and in group C was 66.75 mg/dl ± 8.81. When the two groups A and C were compared (p-value < 0.046) the significant increase in serum cholesterol level was observed in group B and C.

Conclusion: Raised Serum Cholesterol level in this study may lead to cardiovascular problems like ischemic heart disease (IHD) and cerebro-vascular-accidents (CVA).

Keywords: Albino rats, Progesterone acetate**,** Serum cholesterol. Ischemic heart disease**,** Cerebro-vascular-accident.

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INTRODUCTION

Contraception is to prevent pregnancy by intervening with the physiological process ovulation, fertilization, and implantation[1]. Rapid increase in population and increase mortality rate is a problematic situation for developing countries. Therefore, systematic endeavors are conducted to investigate acceptable methods of birth control that are cheaper, reliable and effective for women[2,3]. However, despite the advancement in contraceptive technology, the ideal contraceptive has not yet been discovered as methods have their own hazards[4]. Hence, the objective of this experimental study is to evaluate the hazards associated with the contraceptive injections.

Injection MPA contains 150 mg Medroxy Progesterone Acetate (MPA) that is steroidal in nature[5]. MPA inhibits the production of gonadotropin hormone which prevents ovulation[6,7]. MPA is well known progesterone contains contraceptive injection that is extensively used worldwide and highly effective. This study pointed out towards the adverse consequences of drug[8]. Numerous family planning centers are functioning in Karachi where the drug is easily available without informing any hazards of the injection[9]. It is expected that lack of awareness of side effects will emerge as a major community health burden in coming years. This research will provide public awareness about the adverse effects of contraceptives injections on women's health and will have value in clinical practice. The user would be

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educated and encouraged to do the regular pap smear and measure serum cholesterol level to enhance the early detection of cervical carcinoma and consequences of hypercholesterolemia.

MPA is excessively used without any awareness of its side effects. The hypothesis of the study is that there are effects of MPA on serum cholesterol level of female rats. This study pointed out towards the ill-health consequences of drug. There are studies evaluating the effects of MPA on endometrium but the studies evaluating the effects of MPA on myometrium and correlate serum cholesterol level are lacking. Therefore, the present experimental study focused mainly on microscopic changes in endometrium, myometrium and ovary and serum cholesterol level. This study was conducted with an objective to analyze the effects of Medroxy Progesterone Acetate (Injectable contraceptive) on serum cholesterol level of adult female albino rats.

METHODOLOGY

This experimental study was conducted at Department of Anatomy, Dow University of Health Science (DUHS) from 1st March 2012 to 30th August 2012. The sample collection, processing, microscopy, micrometry, data entry and subsequent data analysis was conducted DUHS. The female albino rats of Wistar strain, age between 90 to 120 days and of 190g-220g weight were selected. The pregnant Female Rats were excluded from the experiment.

The selected albino rats were divided into three groups: Group A (Control group), Group B(1st treated group), and group C (2nd treated group). All three groups were further subdivided into three subgroups (each subgroup comprising 8 animals). Sample size was determined by applying statistical consideration which concluded that each sub- group should comprise at least 8 rats to obtain statistically significant results using statistical test. Control group A had 24 animals. First treated group B having 24 rats, was given MPA (3mg/ kg) according to body weight of rats. Group C, second treated group (n= 24) was given double dose of MPA (6 mg/ kg.).

At the commencement of experiment, Injections (MPA) were given only once to both treated groups B and C. After 1, 2 and 3 months, the female rats were sacrificed under deep Ether anesthesia. The animals were dissected through midline thoraco-abdominal incision from xiphoid process to pubic symphysis. Thoracic cavity was exposed after the dissection of sternum and direct cardiac puncture was done to collect 2cc blood for the measurement of serum cholesterol level. Blood samples were given in Biochemical Laboratory for measurement of serum cholesterol level.

Data Analysis: The data was recorded on different Performa for study variable on raw form it was then entered on SPSS 16 Version Kruskal Wallis and Tukey's test applied for non-parametric variable to test the difference between control and treated groups. The statistical significance of differences of various quantitative changes between treated animal and control was evaluated.

RESULTS

The mean serum cholesterol level was recorded in different groups at different time interval as shown in Fig-1.

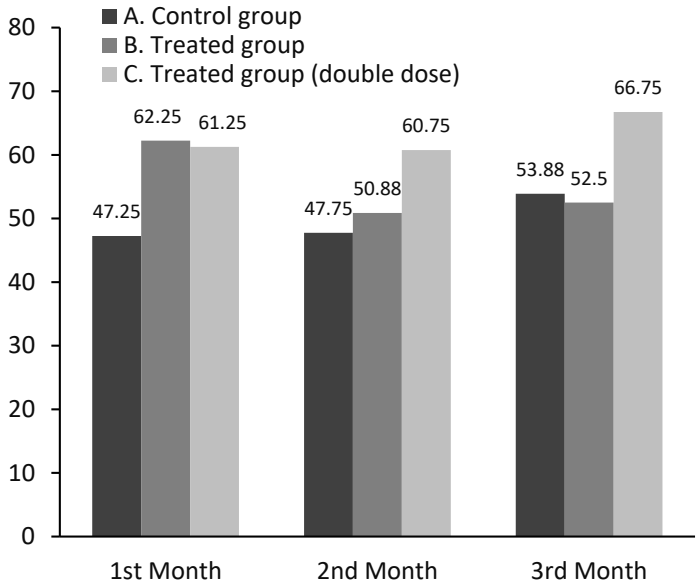

Figure-1: Mean serum cholesterol level (mg/dl) of female albino rats in different groups at variable time interval

Control group A1 and treated groups B1 and C1 after one month of treatment: The mean ± S.D value of serum cholesterol level in control group A1 was 47.25mg/dl ± 9.067 and in treated group B1 was 62.25 mg/dl ± 12.15. When the two groups A1 and B1 were compared (p-value < 0.03) the significant increase in serum cholesterol level was observed in group B1. Whenever mean ±S.D value in treated group C1 was 61.25mg/dl ± 10.26µm. When the two groups A1and C1were compared (p-value < 0.05) the significant increase was observed in group C1. When two treated groups B1 and C1were compared the (p value < 0.978) which was not significant (Fig-1)

Control group A2 and treated groups B2 and C2 after two months of treatment: The mean ±S.D value of serum cholesterol level in control group A2 was 45.75 mg/dl ± 4.71 and in treated group B1 was 50.87 ± 14.17. When the two groups A2 and B2 were compared the (p-value < 0.415) the non-significant increase in serum cholesterol level was recorded in group B2. However mean ±S.D value in treated group C2 was 6075 mg/dl ± 12.16. When the two groups A2 and C2 were compared the (p-value < 0.026) the significant increase in serum cholesterol level was observed in group C2. When two treated groups B2 and C2 were compared (p value< 0.297) which was not statistically significant (Fig-1)

Control group A3 and treated groups B3 and C 3 after three months of treatment: The mean ±S.D value of serum cholesterol level in control group A3 was 53.87 mg/dl ± 13.26 and in treated group B3 was 52.50 mg/dl ± 8.29. When the two groups A3 and B3 were compared (p-value< 0.969) at C.I of 95%. The non-significant was observed in group B3. However mean ±S.D value in treated group C3 was 66.75 mg/dl ± 8.81. When the two groups A3 and C3 were compared (p-value < 0.046) the

significant increase in serum cholesterol level was observed in group C3. When two treated groups B3 and C 3were compared the p value < 0.074 at C.I of 95% which was statistically non-significant.

DISCUSSION

World Health Organization's recent research highlights an estimated 16 million women using injectable steroids annually, for contraception. This has potential hazards as the results of our study demonstrates a gradual increase in serum cholesterol level in treated animal (group B and C). The study validates that Progesterone stimulates lipoprotein lipase activity, enhance the fat deposition and reduces the serum HDL (High Density Lipoproteins) level, previous studies also disclosed the similar finding[10,11].

Other researches support the finding of this study that MPA increases triglycerides, LDL (Low Density Lipoprotein) and cholesterol level that led to increased risk of ischemic heart disease[12]. Long-term administration of more potent MPA may decrease the glucose tolerance and increase the need for insulin or another anti-diabetic drugs[13-15]. When MPA used as a contraceptive, it increases the risk of venous thrombo-embolism (VTE) [16,17]. A study has shown, statistically significant 3-4-fold increase the risk of (VTE) with Injectable progestin[18]. If the females have family history of venous thrombosis or other risk factor like obesity, immobility or surgery the contraceptive should never be used[19,20].

MPA is known to Induced hypo estrogenic state. Progesterone receptors are present on adipose tissue therefore MPA directly acts on adipose tissue. In addition, MPA binds to the glucocorticoid receptor and in high doses result in glucocorticoid like changes in fat mass.

MPA increased serum cholesterol level and very low-density lipoprotein (VLDL)[20-22]. Many recent studies have indicated that the use of injectable contraceptive carries the increased risk of myocardial infarction, thrombotic stroke, hemorrhagic stroke and venous thrombosis, with or without pulmonary embolism. Therefore, IHD and CVA are the leading cause of maternal mortality in developing countries[23-25].

This research will provide the public awareness about adverse effects of contraceptive injections on women' health. Since the study indicated that Serum cholesterol level was increased significantly in treated animals (group B and C) and findings are confirmed by work done in previous study[26], it validates that MPA decreased the HDL and increased cholesterol level, triglyceride and VLDL (very low-density lipoprotein). This leads to Hypercholesterolemia which causes ischemic heart disease and cerebrovascular accident.

CONCLUSION

Raised Serum Cholesterol level in this study may lead to cardiovascular problems like ischemic heart disease (IHD) and cerebro-vascular-accidents (CVA).

AUTHOR'S CONTRIBUTION

Nigar S: Conceived idea, Design methodology, Data collection.
Haq AA: Data collection, Manuscript writing
Mubeen S: Literature review and search.
Jabeen S: Literature search, Manuscript writing.
Raza A: Literature search, Manuscript writing
Rehman D: Data analysis, Data collection.

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