COMPARISON OF CARDIOVASCULAR FUNCTION IN OLD AND YOUNG RATS

THESIS

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INTRODUCTION

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Aging may be defined as, irrevesible process that begins or accelerates at maturity and results in either increased range of deviation from ideal state or decreased rate of return to the ideal state.

A major characteristic of aging is gradual diminution in the functional reserve capacity of organ systems. However the age induced changes in body function is differential and lacks uniformity among different cells, tissues, organs and systems of the same individual.

As a matter of fact the physiologic changes during aging process does not represent the aging process per se, which can be described by chronological age, but is usually complicated especially in the late senescent stage with two composite factors, that are not easily dissociated from aging, physical inactivity and disease.

Since cardiovascular disease is the most frequent cause of hospitalization and death among elderly particularly in "Western countries" it was important to assess the age related changes in cardiovascular function.

In a previous study, the effects of age on intrinsic properties of the heart were reported, (El-Garph, 1990). The present study was planned to examine the age-related differences in the in vivo cardiovascular functions.

AIM OF THE WORK

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The aim of the present study is to investigate the age related differences in the invivo cardiovascular parameters packed cell volume,arterial blood pressure, heart rate and ECG changes. Also cardiac weights were determined. The parameters which may affect the cardiovascular performance such as time of induction of anesthesia and blood glucose were also estimated.

This cross sectional study was performed in intact anesthetized rats from two age groups, a younger and an older one. In order to avoid early postnatal and developmental changes postpubertal rats above 4 months were used as the younger age group. Also in order to avoid marked degenerative lesions encountered in the senescent stage of life, presenescent rats were used as the older age group.

REVIEW OF LITERATURES

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Age induced alteration in arterial blood pressure

Many studies were undertaken to investigate the effects of aging on arterial blood pressure.

In humans, studies have documented that systolic blood pressure increases with age in both sexes, and continues to rise with each successive decade throughout adulthood whereas diastolic blood pressure tends to plateau after the age of 40 or 50 years, *(Schoenberger et al., 1972, Sowers and Zawanda, 1985, Saltzberg, et al., 1988, Vandenberg, et al., 1989).*

According to *Lakatta and Gerstenblith (1990)* although diastolic blood pressure was found to increase with age, the extent to which this occurs is very small compared with the change in systolic blood pressure. This was also supported by a more recent study by *Lever and Harrap, (1992).*

Also, De Swiet et al., (1992) reported relatively little changes in blood pressure of children from 6 months to 10 years age. On the other hand *Bush et al., (1989)* observed, in his prospective study in participants aged 65-98 years, that systolic and diastolic blood pressure tend to decrease with age. Although many studies have shown tendency for blood pressure to rise with advancing age and that systolic blood pressure increases linearly with age then showed fall or plateau, some other studies in primitive societies showed the blood pressure to be not affected by age *(Truswell et al., 1972, Oliver et al., 1975, and Poulter et al., 1984).*

In animal experiments, *Soltis (1987)* studied the effect of age on blood pressure in 3 groups of rats 5-7 weeks, 24-26 weeks and 50-52 weeks. In this study systolic blood pressure increased significantly with age, and the rats in all 3 age groups were considered normotensive.

Relation of body weight to age induced alteration in blood pressure

Pan et al., (1986) used a cross sectional data to investigate whether body weight explains the association between age and blood pressure or whether increased blood pressure by age is due to aging process apart from overweight. They concluded that age and blood pressure were generally associated in absence of overweight.

Relation of vascular changes to age-induced alteration in blood pressure

Vascular changes which occur with advanced age in the aorta and its branches include progressive increase in the rigidity of the aorta and its branches *(Franklin, 1983)*. There is also deposition of increased amounts of calcium and collagenous matrix with fracturing of the elastic fibres within the media *(Tarazi et al., 1975)*.

The aging of the precapillary arterioles with patchy hyaline degeneration within the medial wall results in an increase in the wall to lumen ratio and an overall decrease in lumen cross sectional area *(Adamopoulas et al., 1975)*.

Rosenthal, (1987) has also reported variety of structural and biochemical changes that occur in arteries with advancing age summarizing the same changes reported above.

These vascular changes in the aorta and its branches lead to increase vascular stiffness and rigidity with early reflection of pulse waves. These changes together with increasing blood volume in the aorta with aging cause aortic input impedance to increase with age. Not only the aortic input impedance that increase but also total peripheral resistance, and both form a major increased vascular impedance *(Nichols et al., 1985).*

Lakatta, 1989 explained the increase in wave reflections with increasing age due to stiffness in the arterial wall that transmit pulse waves with a higher velocity and such that reflected waves return to the aortic root during the ejection of blood and this causes arotic input impedance to increase.

The increase in vascular impedance with age is supported by a study of *Morely and Reese, (1989)* who observed that vascular impedance increases by 13.7% by age due to decrease in the aortic distensibility and increased pressure wave reflections from peripheral vasculature, and total peripheral resistance increased by about 37% by age due to decrease in arteriolar cross sectional area.

Thus, with increasing age there is increase in both pulsatile component (aortic input impedance and wave reflections) and non pulsatile component (total peripheral resistance and the increased vascular load) and that may explain the tendency of blood pressure to rise with age reported by many studies.

Lakatta (1989) Added another factor to explain the tendency of rise of blood pressure with age which was the load imposed by volume of blood in the aorta as inertia which increases by age due to increase in both aortic volume and volume of blood inside it and both significantly increase by age.

He also reviewed that the changes in the vascular tree with aging in otherwise healthy individuals can occur at a younger age in clinical hypertension and can be produced in young experimental animals by hypertension, thus aging has sometimes been referred to as blunted hypertension and on the other way round, hypertension has been looked at, as accelerated aging.

Effect of age on heart rate and rhythm

Davis, (1976) reviewed that the total number of pacemaker cells decreases with age and the most part to be affected is the sinoatrial node and the number of sinoatrial nodal cells may be less than 10% in persons aged 75 years in relation to the number present in persons 20 years old. There was also less affection in muscle cells with invasion of fibrous tissues in the internodal tracts.

Lakatta and Gerstenblith (1990) reviewed that resting heart rate is not markedly affected by age.

In a previous study in this department *El-Garf, (1990)* showed that the baseline heart rate of spontaneously beating isolated hearts of young rats were higher than their older counterpart, although the difference was not significant. However, on stimulation by graded isoproterenol infusion, the older rats exhibited significantly higher heart rate than the younger group.

By examining heart rate regulation by means of rhythmography in 90 subjects aged 20-89 years *Korkusko et al.,*