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RESEARCH ARTICLE

EFFECT OF AGEING ON DIABETES MELLITUS AND HYPERTENSION

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ABSTRACT

Ageing is associated with an increasing prevalence of hypertension, atherosclerotic vascular diseases, reduced insulin sensitivity and non-insulin-dependent diabetes mellitus (NIDDM). It has been suggested that hyperinsulinaemia/insulin resistance and/or hyperglycaemia could play a role in determining and/or exacerbating the hypertension and vascular disease associated with diabetes mellitus and ageing. The effect of aging on blood glucose showed that high significant increase on blood glucose with increasing aging. Also, there were significant increases in blood elements (Na, K, Cl and Ca) in the population that increase in aging than young one. On the other hand there were a significant increase on blood urea, creatinine and uric acid in the population that increase in aging than young one. The liver enzymes AST, ALT and ALP were a significant increase in blood of human in the population that increases in aging than young one. Concerning lipid profile, we noted that variety induced high significant variation of different lipid parameters in the population that increase in aging than young one. The effect of aging on blood glucose showed that only the variety Tamesrit had a significative increase on blood glucose. Results generally showed that increase in aging were always high significant increase in their blood elements Na, K, Cl and Ca. Also, there is high significant increase in liver functions and kidney functions in the population that increase in aging than young one and high significant variation of different lipid parameters in the population that increase in aging than young one. We suggest that ionic disturbance might be the missing link responsible for the frequent clinical coexistence of hypertension, atherosclerosis and metabolic disorders. Ageing cells may become more vulnerable to ion disturbances, leading to possible elevation of intracellular free calcium and concurrent magnesium depletion. The "ionic hypothesis" of ageing supposes that an alteration in the cellular mechanisms which maintain the homeostasis of cytosolic calcium concentrations may play a key role in the ageing process, and that a sustained accumulation of cellular calcium and/or the depletion of cellular magnesium may also provide the final common pathway for many ageing-associated diseases, including hypertension and NIDDM.

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INTRODUCTION

Although hyperglycaemia is the characteristic metabolic abnormality of diabetes mellitus, the hypothesis that hyperglycaemia and inadequate metabolic control play a primary role in the pathogenesis of hypertension in NIDDM patients has been of little concern to clinical investigators in recent decades. Early epidemiological studies involving diabetic and non-diabetic subjects showed that both systolic and diastolic blood pressure were positively correlated with plasma glucose levels Sowers, *et al*., 1991, 1987 and plasma glucose response to an oral glucose tolerance test (OGTT) Brownlee, *et al*., 1988. The reduction of both systolic and diastolic blood after improvement in metabolic control is consistent with these epidemiological observations Sowers, *et al*., 1987. Experimen- tally, excess sucrose ingestion has raised blood pres- sure in different rat strains, even in the absence of clinical diabetes Stamler, *et al*., 1975. These observations indirectly confirm the early finding of Pell and D'Alonzo Swilocky, *et al*., 1987 that diabetic patients taking high daily doses of insulin had a lower incidence of hypertension than other dia- betic patients. Despite this evidence that hyperglycaemia probably contributes to the genesis of hyperten- sion in diabetic subjects and that

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metabolic control may reduce blood-pressure levels, the mechanisms of these actions have not been fully clarified. Diabetic hypertension is related to an increase both in total body exchangeable sodium and total peripheral resis- tance ELSayed Shokr 2016 and is often of the salt-sensitive, low-renin type ELSayed Shokr 2015. Hyperglycaemia may also play a cau- sative role in the hypervolemic state of diabetic individuals. An increase in glycaemia over the renal threshold for glucose results in glomerular hyperfiltra- tion of glucose, and consequent hyperactivation of the proximal tubular glucose-sodium cotransporter Avogaro, *et al*., 1967. Hyperglycaemia also leads to increased extracellular fluid osmolality, which generates an osmotic drive for water retention in vascular space Cerami, *et al*., 1985. Thus, hypergly- caemia probably contributes to the increase of total exchangeable sodium and the hypervolemic state of diabetic hypertensive subjects. Hyperglycaemia may also contribute to the increased peripheral vascular resistance of NIDDM, promoting accumulation of ad- vanced glycosylation end (AGE)-products in tissues and causing irreversible changes in vascular permea- bility and thickening of the vessel wall due to deposits of plasma proteins and proliferation of matrix and cells in response to AGE-induced secretion of growth-promoting factors (from macrophages and endothelial cells) Crane. 197 found a significant correlation between tissue accumulation of AGE pro- ducts and the presence of diabetes complications [DeFronzo., 1979]. Hyperglycaemia and hypertension accelerate the deve- lopment of atherosclerosis and macrovascular disease in NIDDM [Ferranini *et al*., 1985. Increased protein glycosylation is likely to be involved as well in the pathogenesis of atherosclerosis since hyperglycaemia promotes glyco- sylation of apolipoproteins, which increase the athero- genicity of lipoprotein molecules, whereas the trap-ping of low-density lipoproteins by AGE on collagen may promote lipid accumulation in the arterial wall Goldberg AP, Coon PJ. 1987. Aim of this work to show the influence of aging on different lipid parameters (total protein, albumin, triglycerides and cholesterol) and increase the LDLc level (bad cholesterol), thus increase the lipid profile in the aging of human being and increase blood glucose and hypertention.

MATERIALS AND METHODS

Blood samples were collected from three hospitals in Hail, KSA. To show the effect of aging in the population of hail. These samples were analyzed by using ICP emission instrument on Perkin Elmer ICP-400 at the University of Hail, KSA. Each hospital is represented by 50 blood samples for chemical and blood analysis with a total of 150 samples. Collect the blood samples to determine the Blood elements Na, K, Cl and Ca, liver functions and kidney functions in this population and different lipid parameters were measured. Blood sugar was measured in capillary blood samples with Lifescan One Touch II ® Glucometer, which has been tested for accuracy and precision against a Beckman Synchron CX7 analyzer of a laboratory that uses the glucose oxidase method.The assays of total cholesterol (TC), HDL-cholesterol, LDL cholesterol and triglycerides (TG) were performed by enzymatic colorimetric methods using kits marketed by Bio Systems, Spain. Reference values adopted are those given by the distributors of these kits. Liver functions and kidney functions in this population and different lipid parameters were measured were performed by enzymatic colorimetric methods using kits marketed by Bio Systems, Spain. Reference values adopted are those given by the distributors of these kits. The blood pressure measured by semi-automatic-blood-pressure-monitor-arm-67468-104993.

Statistical Analysis

Data were expressed as M ± SD. The SPSS program version 15 was used in analysis. One way analysis of Variance (ANOVA) followed by Duncan post hoc test and/or t-test were used in analysis. Pearson correlation Coefficient was used to study correlations. P-values less than 0.05 were significant.

RESULTS

The present study showed that the effect of aging on blood glucose showed that high significant increase on blood glucose with increasing aging. Also, there were significant increases in blood elements (Na, K, Cl and Ca) in the population that increase in aging than young one. On the other hand there were a significant increase on blood pressure with increasing age of human as shown in Table 1.

Table 1. Effect of ageing on the blood glucose and blood elements Na, K, Cl and Ca

Area /Contents	Hospital 1	Hospital 2	Hospital 3
	Mean ± SE	Mean ± SE	Mean ± SE
Age	62 ± 0.12	60 ± 0.22	65 ± 0.52
Hypertention	155 ± 0.71	158 ± 0.52	160 ± 0.12
Glucose	6.5 ± 0.42	9.63 ± 0.33	10.34 ± 0.85
Na	137.6 ± 0.54	139 ± 0.1	148.1 ± 0.711
K	4.38 ± 0.76	4.52 ± 0.7	4.84 ± 0.425
Cl	83.62 ± 0.74	113.6 ± 0.667	114.6 ± 0.083
Ca	2.41 ± 0.52	2.76 ± 0.667	2.94 ± 0.51

Table 2 and table 3 showed that the urea, creatinine and uric acid in the population that increase in aging than young one. The liver enzymes AST, ALT and ALP were a significant increase in blood of human in the population that increases in aging than young one. Concerning lipid profile, we noted that variety induced high significant variation of different lipid parameters in the population that increase in aging than young one. The effect of aging on blood glucose showed that only the variety Tamesrit had a significative increase on blood glucose.

Table 2. Effect of Ageing on the liver functions enzymes AST, ALT and ALP

Area /Contents	Hospital 1	Hospital 2	Hospital 3
	Mean ± SE	Mean ± SE	Mean ± SE
Creatinine	68.5 ± 0.22	73.02 ± 0.333	68.70 ± 0.469
Uric	265.1 ± 0.56	410.6 ± 0.667	307 ± 0.09
Urea	3.8 ± 0.92	3.75 ± 0.6667	3.81 ± 0.1652

Table 3. Effect of Ageing on the kidney functions enzymes Creatinine, Uric acid and Urea

Area /Contents	Hospital 1	Hospital 2	Hospital 3
	Mean ± SE	Mean ± SE	Mean ± SE
AST	20.04 ± 0.012	21.66 ± 0.667	19.28 ± 0.201
ALT	30.54 ± 0.331	48.66 ± 0.667	36.83 ± 0.088
ALP	70.28 ± 0.421	85.66 ± 0.667	74.8 ± 0.32

Results generally showed that increase in aging were always high significant increase in their blood elements Na, K, Cl and Ca. Also, there is high significant increase in liver functions and kidney functions in the population that increase in aging than young one and high significant variation of different lipid parameters in the population that increase in aging than young one as shown in Table 4.

Table 4. Effect of Ageing on the total protein, albumin, triglycerides, LDL, HDL and cholesterol

Area /Contents	Hospital 1	Hospital 2	Hospital 3
	Mean ± SE	Mean ± SE	Mean ± SE
T protine	71.04 ± 0.145	74.53 ± 0.333	71.3 ± 0.57
Albumin	35.92 ± 0.35	41.96 ± 0.667	39.74 ± 0.619
Cholesterol	4.694 ± 0.85	4.63 ± 0.3333	4.31 ± 0.8945
Triglyceride	1.362 ± 0.321	1.81 ± 0.6667	1.55 ± 0.4965
LDL	2.944 ± 0.235	3.1 ± 0.33	2.86 ± 0.26
HDL	1.096 ± 0.05	0.85 ± 0.3333	0.93 ± 0.2742

DISCUSSION

Ageing is associated with an increasing prevalence of hypertension and metabolic abnormalities such as hyper insulinaemia, insulin resistance, altered glucose tolerance and/or frank noninsulin-dependent diabetes mellitus (NIDDM) Harris, *et al*., 1987. Systolic blood pressure (SBP) increases throughout life, while diastolic blood pressure (DBP) rises much more modestly with age, increasing until 55 to 60 years and then declining after 70 elsayed shokr 2016 and Harris, *et al*., 1987. In the Fra- mingham Heart Study, SBP increased about 25 mmHg in men and 35 mmHg in women between the fourth and eighth decades [Kannel, Jarret]. Isolated systolic hypertension was present in 11.7 % of patients over 60 years of age enrolled in the Systolic Hypertension in the Elderly Program (SHEP) Kannel *et al*., 1991, Jarret *et al*., 1978 and Elsayed shokr, 2015 and 2016. The effect of aging on blood glucose showed that high significant increase on blood glucose with increasing aging. Also, there were significant increases in blood elements (Na, K, Cl and Ca) in the population that increase in aging than young one. Arterial hypertension and "nor- mal" ageing, in the absence of hypertension, have many similar effects on the cardiovascular system. Thus, increased arterial stiffness, increased peripheral vascular resistance and increased left ventricular mass are common in hypertensive patients and healthy nor- motensive elderly subjects. Etiologic factors in age- related hypertension include vascular structural chan- ges, such as increased rigidity and decreased compliance of the aorta, hyalin degeneration within the media of precapillary arterioles, and atherosclero- tic effects of baroreceptor sensitivity. Other important factors involved in rising blood pressure with age are a decreased ability to handle sodium, a tendency to accumulate calcium and reduce magnesium content in the cell, increased sympathetic nervous system acti- vity, and a decreased vascular beta-adrenenergic vaso- dilatation function, which leaves alpha-adrenergic re- ceptor vasoconstriction unopposed in response to elevated norepinephrine levels Kannel *et al*., 1976 Monnier *et al*., 1986. Since an in- crease in blood pressure is not inexorable, and not present in developing countries, cultural factors such as diet, decreased exercise, stress and obesity probably contribute to the age-related rise in blood pressure in Various clinical studies have emphasised the asso- ciation of hyperinsulinaemia per se with blood pres- sure. Patients with hypertension have been shown to be resistant to insulin-stimulated glucose uptake and to be hyperinsulinaemic compared to matched normoten- sive control groups Elsayed shokr, 2015 and 2016, Paolisso *et al*., 1967 and Perry *et al*., 1989. In the San Antonio heart study, hyperinsulinaemia was directly correlated with systolic and diastolic blood pressure in men Preuss *et al*., 1992. Lucas reported that fasting serum insulin levels were positively associated with systolic and diastolic blood pressure in obese women, independently of age, wei-ght, and blood glucose values Resnick *et al*., 1993. On the other hand there were a significant increase on blood urea, creatinine and uric acid in the population that increase in aging than young one. The liver enzymes AST, ALT and ALP were a significant increase in blood of human in the population that increases in aging than young one. Concerning lipid profile, we noted that variety induced high significant variation of different lipid parameters in the population that increase in aging than young one. The effect of aging on blood glucose showed that only the variety Tamesrit had a significative increase on blood glucose. Metabolic abnor- malities were present before the institution of antihy- pertensive therapy and did not necessarily improve when blood pressure was lowered since different anti- hypertensive therapies may improve, not alter or wor- sen, insulin sensitivity Elsayed shokr, 2015 and 2016, Paolisso *et al*., 1967. Altogether, the coexis- tence of hyperinsulinaemia and insulin resistance (the former causing renal sodium retention and increased sympathetic drive, the latter causing blunted insulin- dependent vasodilatation and catecholamine antago- nism) suggests that hypertension, at least in some circumstances, may be the result of a primary defect in insulin and glucose metabolism. In addition, prolon- ged hyperinsulinaemia may play a role in the promo- tion of atherosclerosis, vascular remodelling and other mechanisms that have not been thoroughly explored Sowers *et al*., 1995 Preuss *et al*., 1992. Calcium and magnesium ions play a crucial role in cellular physiology. Both ions are universal cellular messengers for extracellular signals for the regulation of cell, tissue and organ functions. The calcium ion is unique among all the mineral ion species due to its large intra- extracellular gradient (1:10,000) which is needed to maintain cellular responsiveness to a variety of extracellular stimuli as well as cell homeostasis. Cytosolic free calcium (Cai) concentrations in resting cells are constantly maintained within a very narrow range by a series of channels, pumps, and other trans- port mechanisms that controls the movements of the ion into and out of cells and between the cytosol and intracellular stores Teusher *et al*., 1989 and 1994. Intracellular free calcium is a determinant in regulating cardiac function and smooth muscle contraction, and acts as a final com- mon factor in mediating cellular responses to a wide variety of stimuli, including stimulus-secretion cou- pling in endocrine cells, glycogen metabolism and cell division Wilson *et al*., 1986. Results generally showed that increase in aging were always high significant increase in their blood elements Na, K, Cl and Ca. Also, there is high significant increase in liver functions and kidney functions in the population that increase in aging than young one and high significant variation of different lipid parameters in the population that increase in aging than young

one. Insulin-resistant states, such as essential hypertension and NIDDM, as well as "normal" ageing, are characterised by similar intracellular ionic defects. The importance of calcium and magnesium ions in regulating cell functions is well-known. A rise in cellular free calcium and depletion in cellular magnesium may induce cellular insulin resistance and vasoconstriction. Ionic levels quantitatively predict the extent of elevated blood pressure, fasting blood glucose. We suggest that ionic disturbance might be the missing link responsible for the frequent clinical coexistence of hypertension, atherosclerosis and metabolic disorders. Ageing cells may become more vulnerable to ion disturbances, leading to possible elevation of intracellular free calcium and concurrent magnesium depletion. The "ionic hypothesis" of ageing supposes that an alteration in the cellular mechanisms which maintain the homeostasis of cytosolic calcium concentrations may play a key role in the ageing process, and that a sustained accumulation of cellular calcium and/or the depletion of cellular magnesium may also provide the final common pathway for many ageing-associated diseases, including hypertension and NIDDM. Aim of this work to show the influence of aging on different lipid parameters (total protein, albumin, triglycerides and cholesterol) and increase the LDLc level (bad cholesterol), thus increase the lipid profile in the aging of human being and increase blood glucose and hypertention.

Conclusion

The causes of abnormalities of cellular ion content in hypertension and associated conditions remain uncertain. Genetic mechanisms and/or changes in in- tracellular control mechanisms such as altered mem- brane pump activities, phosphorylating and dephos- phorylating enzyme cascades, and intracellular regulating factors such as G-proteins and phospholipases, may be involved calcium metabolism is of crucial importance in regulating vascular tone, blood pressure homeostasis, and various other cardiovascular and metabolic processes. Hypertensive states and ageing and may be the direct cause of tissular insulin resistance and hyperinsulinaemia and also induce vasoconstriction and frank hypertension. These cellular ionic defects, present in many different organ systems, could produce a spectrum of altered tissue responses, resulting in the above-mentioned clinical disease states regarded as the normal ageing process, including universal cellular hypofunction and hyporesponsiveness to stimuli associated with ageing.

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