Effect of some atherosclerosis risk factors on cholesterol, triacylglycerols and serum proteins levels in west Algerian adults

Djilali Larbaoui

College of Life Sciences, Ibn-Khaldoun University – Tiaret 14000, Algeria.
E-Mail: djlarbaoui@yahoo.fr. Tel. +213 697669000.

Abstract: The aim of this study was to determine the effect of some atherosclerosis risk factors such as obesity, diabetes and coronary artery disease on total cholesterol, triacylglycerols and serum proteins in hypertensive west Algerian adults undergoing surgery. Mean age and BMI of patients was 53 ± 4 years and 26 ± 2 Kg/m^2, respectively. Patients were divided into eight groups according to hypertension with/ or without other associated pathologic factors (obesity, diabetes and coronary artery disease) and compared with 51 controls (M:W, 25:26) with a mean age of 50 ± 6 years and BMI of 22 ± 1 Kg/m^2. Total cholesterol gradually increases according to atherosclerosis risk factors number and coronary artery disease. Triacylglycerols were also increased in all groups but remain within the normal range. Increased Apo A-I and decreased Apo B100 were observed in all patients. No significant differences in total proteins, albumin and globulins were noted in all hypertensive patients compared with controls. In addition, intergroup differences as well as that of patient groups with two or more risk factors for atherosclerosis with the GI (hypertension alone) show no significant difference. In conclusion, hypertension causes an alteration in different parameters, increased significantly total cholesterol, triacylglycerols and Apo A-I levels and decline in ApoB100 and that this alteration is proportional to the number of associated risk factors (e.g. diabetes and obesity) which may be considered in this study as good markers for cardiovascular disease.

1. Introduction

Hypertension and atherosclerosis are two closely associated pathological disorders. They are responsible for most of the deaths due to cardiovascular diseases (Carbone et al., 2017).

Through its effects on the arterial wall, hypertension acts as a "promoter" of lipid metabolism disorders and the development of atherosclerosis in hypercholesterolemic subjects (Mazzaglia et al., 2009).

Whatever the initial process of arterial injury, it develops more quickly and intensely when the subject has other risk factors such as diabetes or obesity. Several studies have shown that hypertension increases the prevalence and severity of coronary heart disease in diabetics. Among other investigators, the Framingham`s study shows that mortality from cardiovascular disease in diabetics is significantly higher when subjects are hypertensive (Kannel& Wolf, 2008).

In addition, serum lipid abnormalities are more frequently observed in non-insulin-dependent diabetics than in insulin-dependent diabetics, with an increase in serum levels of cholesterol and triacylglycerols (Tomoko et al., 2006).

The presence of obesity is 1.5 to 3 times more frequent in non-insulin-dependent (Taskinen, 1990).

Cardiovascular effects of arterial hypertension and obesity are noticeably different but are potentiating to impair cardiac function and coronary circulation (Raison, 1992).

In addition, there is a positive correlation between weight and blood pressure and is most important in populations with high prevalence of obesity and hypertension (United States, Western countries) or if it exists a family history of hypertension. Weight and blood pressure relationship is of the same order of intensity in men and women, but decreases markedly with age (Verdecchia & Trimarco, 2008).

Hypertension and obesity are often accompanied by other metabolic abnormalities such as hypertriglyceridemia and diabetes, which increase the risk of cardiovascular complications (Reaven, 1991).

The pathogenic mechanisms by which hypertension accelerates atherosclerosis in individuals with hypercholesterolemia and other risk factors have not clearly elucidated (Raison, 1992).

Therefore, the aim of our study is to evaluate the effects of arterial hypertension associated with or/without other risk factors of atherosclerosis such as diabetes or obesity, and in the presence or absence of coronary heart disease, on serum levels of lipids and proteins. In addition, this work allows to detectany of

these parameters can be taken as good markers for atherosclerosis high risk.

2. Material and Methods

Fifty one control subjects were recruited among apparently healthy, normolipidemic Algerian peoples, of them 25 men and 26 women with a mean age of 50 ± 6 years and 22 ± 1 Kg/m²body mass index (BMI). Four hundred and forty eight hypertensive patients with or without other pathological disorders e.g diabetes, obesity and coronary artery disease (previous myocardial infarction or angina pectoris) were recruited at the general medicine service of the Tiaret hospital (west of Algeria). Blood pressure levels were retrieved from medical recordsof participating patients. Hypertensive people are those who had blood pressure levels > 140/90 mmHg or used antihypertensive medications. There were 223 men (M) and 225 women (W) with a mean age of 53 ± 4 years. All men were current smokers but not women. No physical activity was practiced by all patients (men and women). Patients were divided into eight groups: Group I (GI), (n=54, Men/Women 27/27) with hypertension alone (mean age 52 ± 6 years, BMI 23 ± 1 Kg/m²); GII (n=57, M/W, 28/29) with hypertension and diabetes (mean age 49 ± 4 years and BMI 23 ± 1Kg/m²); Group III (GIII), (n=54, M/W,26/28) with hypertension and obesity (mean age 54 ± 4 years and BMI 28 ± 1Kg/m²); GIV (n=57, 28/29) with hypertension, diabetes and obesity (mean age 51 ± 6 and BMI 29 ±2Kg/m²); Group V (GV), (n=57, M/W,28/29) with hypertension and coronary artery disease (mean age 50 ± 7 years and BMI 22 ± 2Kg/m²); group VI (GVI), (n=57, M/W,30/27) with hypertension, diabetes and coronary artery disease (mean age 54 ± 5 years and BMI 23 ± 1Kg/m²); group VII (GVII), (n=55, 27/28) with hypertension, obesity and coronary artery disease (mean age 55 ± 5 years and BMI 29 ± 2) and Group VIII (GVIII), (n=57, 29/28) with hypertension, coronary artery disease and obesity (mean age 56 ± 3 years and BMI 32 ± 4). The purpose of this study was explained to the subjects and the investigation was carried out with their consent. The experimental protocol was approved by the West Hospital Committee of Tiaret on Human Subjects.

Measurements

Blood samples were drawn after a 12-h overnight fast by anticubital venipuncture in tubes containing anticoagulants (0.1% Na_2EDTA) from all subjects, then centrifuged at 3000xg at 5°C, for 15 min and preserved with 0.02% sodium azide in refrigerator (-20⁰C) until analyzed.

Triacylglycerols (TG) and total cholesterol (TC) were assayed in all subjects (controls and patients) by enzymatic methods (Boehringer Kits, Mannheim, Germany).

Total protein contents were measured using the method of Lowry et al. (Lowry et al., 1951) with bovine serum albumin (Sigma Chemical Co, St Louis, MO, USA) used as a standard.

Albumin and serum globulins are determined by electrophoresis using cellulose acetate membranes (BECKMAN, France) serving as supports for the separation of the different protein fractions. The migration is done at 250 volts for during 18 minutes.

Serum apo A-I and apo B100 amounts were determined by immunoelectrophoresis using monoclonal antibodies and ready-to-use plates (Hydragel Sebia kit, Issy-Les-Moulineaux, France).

Statistical Analysis

Values are given as means ± Standard Deviation. Statistically significant differences in the values between different groups was evaluated by Student's t test for parametric data and by Mann-Whitney U test for non-parametric data, and were initially analyzed by ANOVA. Correlation coefficients were determined by linear regression analysis. Statistical significance level was set at P< 0.05.

3. Results

No significant difference between values among men, compared with women regarding age and BMI was observed in this study.

Serum levels of protein, albumin, globulin and apo-proteins

No significant difference in serum levels of total protein, albumin and globulin was noted in all hypertensive patients compared with controls. In addition, intergroup variations as well as that of patient groups with two or more risk factors for atherosclerosis with hypertensive patients in group I (GI), show no significant difference (Table1).

Apo A-I levels were decreased in the GI (P <0.05), GII, GIII, GIV, GV, GVI, GVII and GIII group (P <0.001) compared to the control group (Table 2). With respect to patients in GI and group with hypertension alone, A progressive decrease in Apo A-I according to atherosclerosis risk factors is noted in patients in groups GII, GIII, GIV (P <0.05), GV (P <0.01). The most diminished values were noted in hypertensive patients with coronary events and who were obese and / or diabetic GVI, GVII and GVIII (P <0.001). A significant increase in Apo B100 levels was noted in GII (P <0.05), GIII, GIV, GV, GVI (P <0.01), GVII and GVIII (P <0.001) patients compared to those of controls. Highest value of Apo B100 is noted in the group of patients with hypertension associated with diabetes and / or obesity and who had coronary heart disease (GVIII), compared with controls [1.45±0.18 g / l (GVII), 1.49 ± 0.12 g / l (GVIII) vs. 1.00 ±0.25 g / l (controls)]. Compared with patients of GI group with hypertension alone, there

was an increase in Apo B100 levels in GVI, GVII (P <0.01) and GVIII (P <0.001) patients. However, patients of GII, GIII and GIV also have high but not significant Apo B100 levels compared to those of GI.

Serum levels of total cholesterol and triglycerides

A significant increase in total cholesterol (CT) levels was noted in Groups I, II, and III (P <0.01), IV, V, VI, VII, and VIII (P <0.001) patients compared to control group (Table 3). Total cholesterol levels recorded are 1.3- to 1.6-fold higher in all patients at high risk of atherosclerosis compared to controls. Total cholesterol levels are 1.2-fold higher (P <0.05) in patients with three risk factors (GVI, GVII) and four risk factors (GVIII), compared to patients with hypertension alone (GI). These levels of total cholesterol (6.87 ± 0.39 mmol / l, 7.34 ± 0.31 mmol/ l, 7, 22 ± 0.29 mmol / l and 7.39 ± 0.39 mmol/ l) in groups GV, GVI, GVII and GVIII) respectively, are

the most important when patients have had a coronary accident. Compared to GI patients (hypertension alone), total cholesterol levels are significantly different from those of patients with coronary troubles (groups, V (P <0.05), VI, VII and VIII, P<0.01).

A significant increase in triacylglycerols (TG) concentrations was noted in all eight patient groups (P <0.001) (Table 3). These elevations were 1.8- to 2.3-fold higher in all patient groups compared to controls. TG levels (1.79 ± 0.55 mmol / l, 1.91 ± 0.54 mmol / l, 1.88 ± 0.57 mmol / l and 1.96 ± 0.69 mmol / l) were higher in patients who had a coronary troubles (groups, V, VI, VI and VIII respectively), compared to controls (0.85 ± 0.36 mmol / l). Other comparisons between groups of patients with two or more risk factors for atherosclerosis with the GI group (hypertension alone) showed no significant difference.

Tableau 1: Serum total proteins, albumin and globulins in patients and controls

Parameters	Controls	GI	GII	GIII	GIV	GV	GVI	GVII	GVIII
Total proteins (g/l)	68,52 ± 4,74	78,22 ± 21,04	79,40 ± 21,47	79,06 ± 20,93	78,03 ± 20,57	78,37 ± 20,37	78,81 ± 21,13	79,27 ± 21,25	80,63 ± 23,75
Albumin (g/l)	43,38 ± 5,35	46,93 ± 12,62	47,64 ± 13,05	47,43 ± 12,56	46,82 ± 12,34	47,02 ± 12,22	47,28 ± 12,67	47,56 ± 12,75	48,38 ± 14,25
α₁ globulins (g/l)	2,74 ± 0,19	3,13 ± 0,84	3,18 ± 0,87	3,16 ± 0,83	3,12 ± 0,82	3,13 ± 0,81	3,15 ± 0,84	3,17 ± 0,85	3,22 ± 0,95
α₂ globulins (g/l)	5,48 ± 0,38	6,26 ± 1,68	6,35 ± 1,74	6,32 ± 1,67	6,24 ± 1,64	6,27 ± 1,63	6,30 ± 1,69	6,34 ± 1,70	6,45 ± 1,90
β globulins (g/l)	8,22 ± 0,57	9,39 ± 2,52	9,53 ± 2,61	9,49 ± 2,51	9,36 ± 2,47	9,40 ± 2,44	9,45 ± 2,53	9,51 ± 2,55	9,67 ± 2,85
γ globulins (g/l)	10,96 ± 0,76	12,52 ± 3,37	12,70 ± 3,48	12,65 ± 3,35	12,48 ± 3,29	12,54 ± 3,26	12,61 ± 3,38	12,68 ± 3,40	12,90 ± 3,80

Values are mean ± SD

Tableau 2: Serum Apo A-I and Apo B100 in patients and controls

Groups	Apo A-I (g/l)	Apo B100 (g/l)
Controls	1,49 ± 0,25	1,00 ± 0,25
GI	1,08 ± 0,06[*]	1,17 ± 0,13
GII	0,72 ± 0,05[***#]	1,23 ± 0,19[*]
GIII	0,74 ± 0,11[***#]	1,31 ± 0,23[**]
GIV	0,71 ± 0,06[***#]	1,29 ± 0,15[**]
GV	0,45 ± 0,06[***#]	1,37 ± 0,16[**##]
GVI	0,23 ± 0,05[***##]	1,39 ± 0,17[**##]
GVII	0,25 ± 0,04[***###]	1,45 ± 0,18[***##]
GVIII	0,19 ± 0,04[***###]	1,49 ± 0,12[***###]

Values are mean ± SD. [*]: Patients vs. controls; [#]: GI vs. (GII, GIII, GIV, GV, GVI, GVII and GVIII).[**]P<0.05; [##**] P<0.01; [*** ###] P<0.001.

Tableau 3: Total cholesterol (CT) and triacylglycerols (TG) in patients and controls

Parameters	Controls	GI	GII	GIII	GIV	GV	GVI	GVII	GVIII
CT (mmol/l)	4,59 ± 0,85	6,13 ± 0,75[***]	6,42 ± 0,59[***]	6,49 ± 0,62[***]	6,60 ± 0,31[***]	6,87 ± 0,39[***#]	7,34 ± 0,31[***##]	7,22 ± 0,28[**##]	7,39 ± 0,39[***##]
TG (mmol/l)	0,85 ± 0,36	1,57± 0,45[***]	1,69 ± 0,44[***]	1,66 ± 0,47[***]	1,71 ± 0,40[***]	1,79 ± 0,55[***]	1,91 ± 0,54[***]	1,88 ± 0,57[***]	1,96 ± 0,69[***]

Values are mean ± SD. [*]: Patients vs. controls; [#]: GI vs. (GII, GIII, GIV, GV, GVI, GVII and GVIII).[*#]P<0.05; [##**] P<0.01; [*** ###] P<0.001.

4. Discussion

Hypertension associated or without obesity or diabetes, with or without coronary artery disease does not modify serum proteins and albumin levels in the patients of our study. A significant decrease in apoprotein (Apo A-I) concentrations was noted in all hypertensive patients compared to controls. This decrease is progressive and the deceased values are observed in GVI, GVII and GVIII, patients with the highest number of atherosclerosis risk factors, compared to patients of GI with hypertension alone. A non-significant difference was found between diabetes and obesity regarding Apo A-I levels in GII patients, compared to GIII and GVI, compared to GVII. Apo A-I levels ranging from 1.08 ± 0.06 g / l (GI) to 0.19 ± 0.04 g / l (GVIII) are below normal limits according to other studies which reported that Apo A-I level in normolipidemic control subjects was 1.25 ± 0.25 and 1.55 ± 0.19 g / l in men and women, respectively, their ages averaged 51 to 60 years, versus 1.39 ± 0.21 g / l in men and 1.64 ± 0.35 g / l in women over 60 years. This shows the existence of an increase of Apo A-I levels according to age and sex. (Alaupovic et al., 1988; Turpin, 1989 and Ferrer et al., 2002). The decrease in Apo A-I levels in patients of this study and especially in those who had a coronary event is in agreement with the results of some studies that showed that Apo A-I concentrations increase in coronary lesion and that there is an inverse relationship between Apo A-I levels and degree of coronary involvement (Breier et al., 1989; Steinmetz et al., 1998; Meisinger et al., 2005 and Vasan, 2006). Some investigators in their studies reported that Apo A-I levels may be considered in this study as a good predictor and prevention indicator of coronary heart disease (Tohidi et al., 2010; Patel et al., 2010).

Apo B100, representative of LDL, a fraction considered to enhance the risk of atherosclerosis (Banget al., 2008), increased gradually and significantly in groups II (P <0.05); III, IV, V, VI (P <0.01); VII and VIII (P <0.001), compared to control group. A significant increase is noted in patients who have had a coronary diseases and have several atherosclerosis risk factors [(groups, V, VI, VII (P <0.01) and VIII (P <0.001)], compared to GI (with hypertension alone). The results showed that patients with hypertension associated with obesity and / or diabetes and with coronary artery disease have significantly higher Apo B100 levels than control one. This Apo B100 levels, associated with obesity or diabetes, potentiate and increase the risk of atherosclerosis, especially when these levels exceed the upper normal limit (1.30 g / l) (Turpin, 1989).

Our results in patients of the groups I and II are close to the values presented by (Fruchart et al., 1982) in patients with coronary artery disease and with

different degrees of coronary involvement (0.98 ± 0.19 to 1.24 ± 0.13 g / l versus 1.17 ± 0.13 to 1.23 ± 0.19 g / l). Apo B100 levels in groups II, III, IV, V, VI, VII and VIII were significantly higher and ranged from (1.31 ± 0.23 to 1.49 ± 0.12 g / l). This increase in Apo B100 was generally associated with hypertriglyceridemia (Turpin, 1989; Paul, 2002 and Superko, 2009), since Apo B100 is also carried by VLDL (Badaloo et al., 2005), and the majority of hypertriglyceridemia is related to an increase in VLDL concentration (Bruckert et al., 1992; Hokanson, 2002; Vanderlaan et al., 2009).

Indeed, patients of this study have high levels of triacylglycerols compared to control group. High levels of Apo B100 were also noted in patients with diabetes or obesity with or without coronary artery disease, compared to controls. In addition, a significant positive correlation was noted between total cholesterol levels and Apo B100 in the eight hypertensive groups. The most important correlation coefficients were found in hypertensive patients with several risk factors and who had a coronary accident: (GV: r = 0,83; P< 0,01; GVI: r = 0,85; P< 0,01; GVII: r = 0,89; P< 0,01 et GVIII: r = 0,92; P<0,01 respectively. Angiographic case-control studies suggest that Apo B100 assay is a good marker of coronary risk. On the other hand, the assay of Apo A-I does not appear to provide more information than that of HDL-C (Luc et al., 2006; Contoiset al., 2009).

A significant and similar increase in total cholesterol (TC) and triacylglycerols (TG) levels was noted in all groups of hypertensive patients, compared with controls. In addition, the highest concentrations of these two parameters (CT and TG) are found in patients who have had a coronary accident (groups V, VI, VII and VIII). Thus, other risk factors, diabetes or obesity, also increase concentrations of the two parameters. Indeed, high levels of total cholesterol and triacylglycerols are two independent factors, but they are potentiating to increase the degree of coronary involvement and their combination gives the highest incidence of coronary events. In addition, Turpin, 1989 proposed "normal" serum levels for CT and TG: ≤ 2g / l for cholesterol with tolerance until 2.2 g / l at 40 years and 2.4 g / l at 1 to 60 years and 1.5 to 2 g / l for triacylglycerols.

In the patients studied, was noted an increase in TG levels, compared with controls. However, with values of 1.38 ± 0.39 to 1.96 g / l, TG levels remain within normal limits. These results are superior to those presented by (Fruchart et al., 1982) with values of 1.12 ± 0.49 to 1.13 to 0.63 g / l. But high levels of cholesterol (> 3 g / l), which exceed the threshold of tolerance indicated by (Turpin, 1989) and which are the best indicator of coronary heart disease. The

highest levels of CT but which remain in the upper limit of normal are found in hypertensive patients with coronary artery disease and several atherosclerotic risk factors (GV: 2.66 ± 0.15g / l, GVI: 2.84 ± 0.12 g / l, GVII: 2.80 ± 0.11 and GVIII: 2.86 ± 0.15 g / l).

Turpin, 1989 has proposed some recommendations for the control of hyperlipidemia: total cholesterol of 2.5 to 3 g / l and a triacylglycerols< 2 g / l, with necessary assessment of global coronary risk, family history of coronary artery disease, high blood pressure, diabetes, smoking, sex, low HDL-C (< 0.35 g / l). The population studied has the same criteria, high levels of CT and TG values below 2 g / l. These patients are hypertensive, some are diabetic and some have a family history of coronary artery disease. The incidence of coronary atherosclerosis is closely related to cholesterolemia and to a lesser degree with hypertriglyceridemia (Turpin, 1989; Ingelssonet al., 2007; Tiroshet al., 2007). In addition, clinical data provide daily evidence of an inter-relationship between the atherogenic power of hyperlipidemia and other diseases such as diabetes and obesity (Taskinen, 1990; Fruchart & Duriez, 2001). Indeed, during diabetes, an increase in serum levels of cholesterol and triacylglycerols is observed (Tomoko et al., 2006). In addition, hypertension and its mechanical effects on the arterial wall, promotes lipid infiltration and lipid streaks formation that evolve into plaques of atheroma, the final step of atherogenesis process.

Conclusion

This study has shown that hypertension, whether or not associated with another risk factor (obesity or diabetes), with or without coronary artery disease, does not modify the serum protein and albumin levels. Apo A-I, the main apoprotein of HDL and Apo B100, the main LDL apoprotein, are correlated with coronary artery disease. However, the associated increase (total cholesterol and triacylglycerols) is considered a good indicator to detect the onset of atherosclerosis, resulting in coronary events.

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4/9/2019