Association between drugs treatment ,glycemic control and serum level of c-reactive protein IN IRAQI patients receiving anti diabetic or antidiabetic with anti hypertensive drugs

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Abstract

Background

- The aim of this study was to investigate the association between drug treatments, glycemic control and serum level of C-reactive protein (CRP) in Iraqi patients receiving antidiabetic drugs or antidiabetic with antihypertensive drugs.

Methods:

- Patients receiving antidiabetic drugs or antidiabetic with antihypertensive drugs, not suffering from complications, were recruited from outpatient's clinics at Al-Mawanee Jeneral Hospital in Basra. Socioeconomic characteristics, blood pressure (BP) and treatment plans were recorded. Blood samples were obtained tre glycated haemoglobin (HbA1c), lipids profile and hs-CRP.

Introduction

- In Iraq, high rate of incidence of diabetes and hypertension has been documented. Diabetes and hypertension are the two main risk factors in the development of ischemic heart disease, cardiac hypertrophy, and cardiac failure. Cardiovascular diseases are the most common causes of mortality over the world. Previous studies have demonstrated that individuals with diabetes (1), hypertension (2, 3) have higher levels of C-reactive protein (CRP) compared with individuals without these conditions in the general population.

- Increased risk of cardiovascular disease has also been associated with increased levels of CRP (4). C-reactive protein (CRP) is synthesized and secreted mainly in hepatocytes (5) and regulated by interleukin-6 (IL-6), interleukin-1 (IL-1), and tumor necrosis factor-alpha (TNFα) (6). It is a sign of systemic inflammation in blood (7

- The normal plasma level of CRP in a healthy population without evidence of acute inflammation is 2 mg/L or less (8). There is a rapid rise in the circulating CRP by as much as 3000-fold in response to inflammation, infection or acute tissue injuries, which drop rapidly when inflammation or injury is, resolved (9). Many studies are focused on the association of chronic elevation of CRP with increased risk of cardiovascular disease and atherosclerosis (10-13).

- If CRP is concerned in the pathophysiology of cardiovascular disease, it could be accepted that lowering of CRP levels would reduce the progress of the disease and its complications. CRP causes atherosclerosis by various mechanisms, such as the release of reactive oxygen species (ROS), CRP increases the generation of ROS by monocytes and neutrophils (14, 15) directly

- ROS have been concerned in the beginning and continuation of atherosclerosis (16). Also CRP increases the expression of adhesion molecules (17). Furthermore, CRP has been concerned in the destabilization of atherosclerotic plaques (18). Moreover, CRP can mediate the uptake of LDL into macrophages to form foam cells (19).

- The aim of this study was to investigate the association between drug treatments, glycemic control and serum level of C-reactive protein (CRP) in Iraqi patients receiving antidiabetic drugs or antidiabetic with antihypertensive drugs.

Study design

- This study was conducted during the period from February to May, 2018 and the patients were selected during their visit to Diabetes Endocrine and Metabolism Centre in Al-Mawanee Jeneral Hospital in Basra

- Patients receiving antidiabetic drugs or antidiabetic with antihypertensive drugs, not suffering from complications, were recruited. A total of 76 diabetic patients aged between 42 and 67 years were included in this study 50 patients were females and 26 were males. 42 patients were diabetic and hypertensive, from which 30 were females and 12 were males.

- **The other 34 patients were diabetics only**. Patients were excluded from the study if they have any cognitive problems or if they were type1 diabetic patients. Socioeconomic characteristics, blood pressure (BP) and treatment plans were recorded. Fasting blood samples were obtained to measure glycated haemoglobin (HbA1c), lipids profile and hs-CRP

- HbA1c up to 7% reflected adequate glycemic control, while HbA1c greater than 7% reflected poor glycemic control, as recommended by the American Diabetic Association guidelines (20).

- Hypertension was defined as a systolic BP more than 140 mmHg or diastolic BP more than 90 mmHg, or current use of antihypertensive drug treatment (21). Ethics approval was obtained from Basra Health office, Ethics Committee for Human Research and from Al-Mawanee Jeneral Hospital in Basra.

Laboratory investigations

- Glycated hemoglobin (HbA1C) was measured by D-10 Dual Program Bio-Rad Laboratories, Inc., Hercules, CA 94547, 220-020, California; USA. D-10 Dual Program is based on chromatographic separation of the analytes by ion-exchange (HPLC).

Statistical analysis

- Statistical analysis was performed using GraphPad Prism software (version 7.0, GraphPad Software, Inc., San Diego, CA). Descriptive statistics, such as mean ± standard deviation (SD), were calculated for all estimated parameters. Comparison between two means was performed using unpaired Student t test for normally distributed parameters. Associations between variables were examined using Pearson's correlation coefficients

- . All p values that were less than 0.05 were considered significantly different.

Results

- A total of 26 men and 50 women were recruited. Lower mean HbA1c was found in patients receiving antidiabetic with antihypertensive drugs compared with those on antidiabetic drugs only ($p = 0.0013$). Lower mean systolic BP ($p < 0.0001$) and diastolic BP ($p = 0.0078$) were found in diabetic patients compared with diabetes and hypertension patients

- . Lower mean hs-CRP was found in women receiving antidiabetic with antihypertensive drugs compared with those on antidiabetic drugs only. Management treatment had no effect on mean hs-CRP in men, however there was a significant direct correlation of hs-CRP with HbA1c ($p = 0.002$) and triglycerides ($p = 0.009$), but inversely with high-density lipoprotein cholesterol (HDL-C) ($p = 0.011$) in women receiving antidiabetic drugs only. Furthermore, the management treatment had no effect on mean hs-CRP in men and women receiving antidiabetic with antihypertensive drugs.

- **Table 1:** Measured hs-CRP, HbA1c and blood pressure according to management treatment (Mean ± STDEV) of type -2 diabetic patients or type-2 diabetes with hypertension patients.

Variables	Mean ± STDEV Users of antidiabetic drugs[A]	Mean ± STDEV Users of both antidiabetics and antihypertensive drugs[B]	*P* value
Age (years)	54.1 ± 6.3	56.6 ± 5.7	0.0738
HbA1C (%)	10.36 ± 2.3	8.86 ± 1.6	**0.0013**
Systolic BP (mmHg)	122.7 ± 6.7	149.5 ± 18.8	**< 0.0001**
Diastolic BP (mmHg)	80.59 ± 7.3	85.2 ± 7.3	**0.0078**
hs-CRP (mg/liter)	2.00 ± 0.9	1.8 ± 0.8	0.3089
Male	6.7 ± 4.5	2.6 ± 1.4	**<0.000**
Female			**1**

[A] Total number = 34, men (14), women (20).

[B] Total number = 42, men (12), women (30).

STDEV, standard deviation; HbA1c, glycated haemoglobin; hs-CRP, highly sensitive C-reactive protein; Statistically significant values are shown in bold font (significance $P < 0.05$).

Table 2: Correlations between hs-CRP with HbA1c, lipid profile and blood pressure in men and women of type -2 diabetic patients or type-2 diabetes with hypertension patients

	HbA1c	Cholesterol	TG	HDL-C	SBP	DBP
	r = -0.328 *p* = 0.147	*r* = -0.043 *p* = 0.852	*r* = -0.052 *p* = 0.823	*r* = 0.01 *p* = 0.965	*r* = -0.045 *p* = 0.845	*r* = 0.142 *p* = 0.538
Female (N = 20)	*r* = 0.537 ***p* = 0.002**	*r* = 0.329 *p* = 0.147		*r* = -0.455 ***p* = 0.011**	*r* = -0.104 *p* = 0.584	*r* = -0.132 *p* = 0.487
hs-CRP (DM +HT group) Male (N = 12)	*r* = 0.314 *p* = 0.320	*r* = -0.310 *p* = 0.326	*r* = 0.150 *p* = 0.643	*r* = -0.370 *p* = 0.236	*r* = 0.023 *p* = 0.943	*r* = 0.002 *p* = 0.994
Female (N = 30)	*r* = 0.043 *p* = 0.822	*r* = 0.215 *p* = 0.254	*r* = -0.044 *p* = 0.818	*r* = 0.357 *p* = 0.053	*r* = -0.078 *p* = 0.682	*r* = -0.043 *p* = 0.821

- DM, diabetes mellitus; HT, hypertention; HbA1c, glycated hemoglobin; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; hs-CRP, highly sensitive C-reactive protein; Statistically significant values are shown in bold font (significance P <0.05).

Discussion

- This study was designed to investigate the association between drug treatments, glycemic control and serum level of C-reactive protein (CRP) in Iraqi patients receiving antidiabetic drugs or antidiabetic with antihypertensive drugs

- Diabetes mellitus is associated with a numerous complications. Hyperglycemia, increased blood pressure, dyslipidemia, oxidative stress, and inflammation are all characteristics of T2DM and are concerned in the development of vascular complications (22, 23). So that control of diabetes leads to decreased risk of these complications. Most of the diabetic patients involved in our study were uncontrolled regardless of which antidiabetic drug treatment was used

- This study revealed that lower mean of glycated haemoglobin (HbA1c) found in patients receiving antidiabetic with antihypertensive drugs compared with those on antidiabetic drugs only. Few studies are found concerned in the combined effects of antidiabetic and antihypertensive drugs on HbA1c level

- Previous study revealed that different classes of antihypertensive drugs have different effects on blood glucose metabolism. Certainly, angiotensin receptor blockers as well as angiotensin converting enzyme inhibitors have been associated with advantageous effects on glucose homeostasis. Calcium channel blockers (CCBs) in general have no effect on glucose metabolism

- . Though, some members of the CCBs class such as azelnidipine and manidipine have been revealed to have beneficial effects on glucose homeostasis. Conversely, diuretics and β-blockers generally have unfavourable effect on glucose metabolism. Important, carvedilol as well as nebivolol were different from the other β-blockers class, being more preferable concerning their effect on glucose homeostasis (24).

- Lower mean hs-CRP was found in women receiving antidiabetic with antihypertensive drugs compared with those on antidiabetic drugs only. Management treatment had no effect on mean hs-CRP in men; however there was a significant direct correlation of hs-CRP with HbA1c and triglycerides, but inversely with high-density lipoprotein cholesterol (HDL-C) in women receiving antidiabetic drugs only

- Furthermore, the
- These results indicated that high levels of hs-CRP are associated with poor glycemic control and dyslipidemia, therefore consequently increased cardiovascular risk. Due to the valuable effect of hs-CRP as a cardiovascular risk predictor, it should be included in routine monitoring of type-2 diabetic patients.

Conclusions

- High levels of hs-CRP are associated with poor glycemic control and dyslipidemia, therefore consequently increased cardiovascular risk. Due to its value as a risk predictor, hs-CRP should be included in routine monitoring of type-2 diabetic patients.

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