The effect of atenolol and combination of atenolol and thiazide diuretic on the lipid profile in hypertensive patients

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Abstract

Objectives: To assess the effect of atenolol and combination of atenolol and diuresam® (hydrochlorthiazide, ٢٥ mg and amiloride, ٥ mg) on the lipid profile including serum total cholesterol, triglyceride, very low density lipoprotein-cholesterol (VLDL-C), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein-cholesterol (HDL-C) in hypertensive patients.

Design: Case-control study.

Setting: The study was conducted in Outpatient department of Ibn-Senna Hospital in Mosul, during the period from December ٢٠٠٣ to July ٢٠٠٤.

Participants: Fifty hypertensive patients under atenolol therapy (١٠٠ mg/day) and ٤٠ hypertensive patients under combination therapy of atenolol (١٠٠ mg/day) and diuresam® (one tablet every other day). In addition to that, ٥٠ stage ١ hypertensive patients without treatment served as a control group.

Mean outcome measures: lipid profile in the treated hypertensive patients were compared with those measurements in the control group by using Duncan test.

Results: In the hypertensive patients treated with atenolol, serum total cholesterol, triglyceride, VLDL-C and LDL-C were significantly higher (P<٠.٠٥) than those values in the control group, at the same time HDL-C did not change. The measurements of the lipid profile of the atenolol group were not significantly different from those measurements in the combination treated group of atenolol and diuresam®.

Conclusion: Chronic use of atenolol or combination of atenolol and diuresam® is associated with a significant increase in serum lipid profile. However, diuresam® in moderate dose might not increase serum lipid profile.

الخلاصة

الأهداف: لتقييم تأثير عقار الأتينولول وتأثير العلاج التوافقي من عقار الأتينولول والدايريسام (هيدروكلورثايزايد ٢٥ ملغم واميلوراد ٥ ملغم) على واجهة الدهون والتي تشمل الكليستيرول الكلي والشحوم الثلاثية وكوليستيرول اللايبوبروتين واطئ الكثافة جدا وكوليستيرول اللايبوبروتين واطئ الكثافة وكولستيرول اللايبوبروتين عالية الكثافة في المرضى المصابين بفرط الدم الشرياني .

التصميم: مقارنة حالة مرضية مع حالة ضابطة

مكان أجراء الدراسة والإطار الزمني لها: نفذت هذه الدراسة في العيادة الخارجية في مستشفى ابن سينا التعليمي في مدينة الموصل وخلال الفترة من كانون أول ٢٠٠٣ ولغاية تموز ٢٠٠٤

المشاركون: خمسون مريض مصاب بفرط الدم الشرياني وتحت علاج الأتينولول (١٠٠ ملغم/اليوم) وأربعون مريض مصاب بفرط الدم الشرياني وتحت العلاج التوافقي من عقار الأتينولول (١٠٠ملغم / اليوم) والدايريسام (حبة واحدة بين يوم وآخر) .بالأضافة الى ذلك خمسون مريض مصاب بفرط الدم الشرياني المرحلة ١ دون علاج كمجموعة ضابطة.

القياسات المستخدمة: مقارنة واجهة الدهون في مصل الدم في مرضى فرط الدم الشرياني تحت العلاج مع واجهة الدهون في المجموعة الضابطة بأستخدام اختبار دانكن .

النتائج: كان مصل الكولستيرول الكلي والشحوم الثلاثية و كولستيرول اللايبوبروتين واطئ الكثافة جدا و كولستيرول اللايبوبروتين واطئ الكثافة اعلى معنويا (ب < ٠,٠٥)من هذه القيم في المجموعة الضابطة . وفي نفس الوقت لم تتغير كولستيرول اللايبوبروتين عالي الكثافة . كذلك لم تختلف معنويا هذه القياسات لواجهة الدهون

في المرضى تحت علاج الأتينولول مقارنة مع تلك القياسات في مجموعة العلاج التوافقي من الاتينولول والدايريسام .

الاستنتاج: أن الاستعمال المزمن لعقار الأتينولول والدايريسام يكون مصحوبا بزيادة معنوية في مصل واجهة الدهون وقد لا يؤدي الدايريسام بجرعة متوسطة الى زيادة في مصل واجهة الدهون.

Introduction

Atenolol is a relatively selective ß-blocker drug[١]. It is effective in stage ٢ hypertension[٢]. Atenolol can be used in many cardiovascular diseases as mitralstenosis[٣] and angina pectoris[٤]. The combination of ß-blockers and diuretics are used to control blood pressure, when first line treatment is not enough[٥].

The side effect of atenolol on lipid profile includes tendency to increase plasma concentration of total cholesterol[٦], as well as triglyceride, while high density lipoprotein cholesterol (HDL-C) is reduced[٧]. Furthermore, Talseth et al.[٨] found that the treatment with atenolol increases triglyceride, while HDL-C was decreased at dose ١٠٠ mg/day after one year of treatment. However, no consistent trends in the concentration of triglyceride, total cholesterol and HDL-C were noticed over ٩ years of treatment with atenolol[٩].

In short term treatment of less than one year with thiazide, total cholesterol increased by ٧% which resulted primarily by the increase in very low density lipoprotein-cholesterol (VLDL-C) and low density lipoprotein-cholesterol (LDL-C) but HDL-C did not change[١٠]. However, in long duration treatment with thiazide, the level of total cholesterol in patients treated with thiazide for at least ٣٠ months were not increased significantly[١١]. Furthermore, the use of low dose of thiazide at duration of more than ٥ years had negligible metabolic side effects[١٢].

The present study was designed to investigate the effect of atenolol and a combination therapy of atenolol and diuresam (hydrochlorothiazide and amiloride) on serum lipid profile in a number of hypertensive patients in Mosul.

Patients and Methods

This study was carried out in Ibn-Seena Hospital in Outpatient department in Mosul city, from December ٢٠٠٣ to July ٢٠٠٤. Three groups were included. The first group included ٥٠ patients, receiving atenolol at a dose of ١٠٠ mg/day (Limassol, Cyprus), the age ranged between ٢٩-٧٠ years (mean ± SD, ٥١.٦ ± ١٠.١ years). The second group included ٤٠ patients, receiving a combined therapy of atenolol at a dose of ١٠٠ mg/day and one tablet of diuresam® (SDI) (hydrochlorothiazide ٢٥ mg + amiloride ٥ mg), every other day, the age ranged between ٣٠-٧٠ years (٥٠.٧ ± ٩.٥ years). The third group included ٥٠ stage ١ hypertensive patients without any medication, the age ranged between ٢٩-٦٥ years (٥٠.٩ ± ٩.١ years). The duration of treatment for the first and second groups were between ١-١٠ years (٩.٣٧ ± ٣.٧ years and ٤.٦ ± ٣.٤ years respectively).

Patients with any other disease except hypertension were excluded from this study. In addition to that, patients with any other medication other than atenolol or thiazide were not included.

Five ml of blood were taken from all patients and controls, after over night fasting (١٢ hours) by venipuncture. The blood was allowed to clot and after centrifugation, the serum was collected in a plane tube and analysed for lipid profile.

Serum total cholesterol, triglyceride and HDL-C were measured by using the enzymatic method[١٣,١٤,١٥], using kits (Bio Merieux, France). LDL-C was calculated using Friedewald equation:

$$LDL - C = Total - cholesterol - HDL - C - \frac{triglyceride}{5}$$

In addition, VLDL-C was calculated according the following equation:

$$VLDL - C = \frac{triglyceride}{5}$$

Duncan-test was used to compare parameters among treated and control groups.

Results

In the hypertensive patients treated with atenolol, serum total cholesterol, triglyceride, VLDL-C and LDL-C were significantly increased (P<٠.٠٥), while HDL-C was significantly decreased (P<٠.٠٥) in comparison with the control group. Furthermore, the ratio of the total cholesterol to HDL-C was significantly increased (P<٠.٠٥) in the treated group in comparison with the control group. All these results were shown in Table ١.

In the hypertensive patients treated with a combination therapy of atenolol and diuresam®, serum total cholesterol, triglyceride, VLD-C and HDL-C were significantly increased (P<٠.٠٥), while HDL-C did not change. At the same time, total cholesterol to HDL-C ratio was significantly increased (P<٠.٠٥) as compared to the control group as shown in Table ١.

No significant difference was detected in the lipid profile between the patients treated with atenolol a lone and those patients treated with combination therapy of atenolol and diuresam®, as shown in Table ١.

No significant correlation was found between the duration of treatment with atenolol or combination therapy of atenolol and diuresam® and the lipid profile of the treated patients (data not shown). Furthermore, no correlation was noticed between the age of the control, atenolol treated patients or combination treated patients and the lipid profile (data not shown).

Discussion

In the present study, serum total cholesterol and LDL-C increased significantly in the hypertensive patients treated with atenolol. These results were in agreement with other studies[١٦,١٧]. However, Northcote[١٨] and Stearne et al.[٩] did not find a significant increase in serum total cholesterol and LDL-C in patients treated with atenolol. These latter results might be due to a low dose of atenolol. The mechanism of the increases of plasma lipid and lipoprotein by ß-blockers are not well understood[١٩,٢٠]. Krone[٢١] showed that the activity of LDL receptor of cells was regulated by catecholamine receptors.

Table (١): *Serum lipid profile in the control and patients treated groups.*

Parameters (mmol/l)	Control group (n=٥٠)	Atenolol group (n=٥٠)	Atenolol + diuresam® group (n=٤٠)
Total cholesterol	٤.١٤±٠.٧٤ a	٤.٧٢±٠.٩٣ b	٤.٧٥±٠.٨٠ b
Triglyceride	١.٢٨±٠.٥٨ a	١.٧٨±٠.٨٧ b	١.٦٣±٠.٨١ b
VLDL-c	٠.٢٥±٠.١٢ a	٠.٣٥±٠.١٦ b	٠.٤٠±٠.٤٣ b
HDL-c	١.٣٢±٠.٣٨ a	١.١٠±٠.٣٤ b	١.٢٤±٠.٤٠ ab
LDL-c	٢.٧٧±٠.٧٢ a	٣.٢٢±٠.٨٨ b	٣.١٤±٠.٩٠ b
Total cholesterol to HDL-c	٣.٣±٠.٧١ a	٤.٦٤±١.٤٦ b	٤.٠٣±١.١٧ b

Data are represented by mean±SD. Different symbols represent significant difference at level P<٠.٠٥.

In this study, triglyceride and VLDL-C was higher significantly, while HDL-C was lower significantly in the atenolol treated patients as compared with the

control group. These results were consistent with the results of other workers[٢٢,٢٣]. However, Lakshaman et al.[٢٤] found that atenolol tended to cause short term increases in triglyceride. The mechanism of the increase of triglyceride and decrease of HDL-C by cardioselective ß-blockers are poorly understood[٨]. One explanation is that all these changes in triglyceride and HDL-C might be mediated throw inhibition of lipoprotein lipase[١٦].

Serum total cholesterol and LDL-C were significantly higher in the studied hypertensive patients under the combination therapy. These results were in agreement with other studies[٢٢,١٧]. However, Neutel[٢٥] did not find a significant difference in total cholesterol level and LDL-C in the combination treated patients of atenolol and thiazide group, the finding of Neutel[٢٥] might be due to low dose of atenolol and thiazide.The mechanism for diuretics to induce an increase in cholesterol is still unclear and unknown[٢٦,١٠]. Prichard et al.[٢٧] related the change in cholesterol to catecholamine release in response to volume depletion which stimulated hepatic cholesterol synthesis.

Serum triglyceride level and VLDL-C were higher significantly, while HDL-C did not change in the present combination treated group. These results were supported by other studies[٢٨,٢٢]. However, Neutel[٢٥], did not find a significant increase in serum triglyceride level or decrease in HDL-C with low doses of hydrochlorothiazide.

The ratio of total cholesterol to HDL-C was increased in the present atenolol and combination treated groups. The same results were achieved by the study of Berglund and Anderson[٢٩], who showed that the ratio was increased with chronic use of atenolol.

In this study, no significant difference was noticed between atenolol and combination treated groups regarding serum lipid profile. The reason might be due to low dose of the hydrochlorothiazide in this study, since low dose of hydrochlorothiazide caused minimal changes in lipid profile[٣٠]. In addition, no correlation was found between the age of the studied patients with serum lipid profile for both the control and the treated groups. These results were consistent with Simon et al.[٢٢] and Ott et al.[٣٠].

In conclusion, atenolol causes significant increases in serum lipid profile. Combination therapy of atenolol and diuresam® causes minimal increases in serum lipid profile. Diuresam® might not affect lipid profile in the used dose. This study also encourage the use of thiazide diuretic in low dose. In addition, periodic biochemical measurements for serum lipid profile are indicated for both atenolol and thiazide treated patients.

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