Study of the Effect of Capoten and Tenormin Drugs on Lipid Profile and Renal Function in Patients with Hypertension

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Abstract

High blood pressure, also called hypertension: it is an elevated pressure of the blood in the arteries. Although the body can tolerate increased blood pressure for months and even years, eventually the heart may enlarge, which is a major factor in heart failure. Such pressure can also injure blood vessels in the heart, kidneys, the brain, and the eyes. Tenormin used to treat hypertension may be chemically described as a benzene acetamide, 4 - [21 – hydroxyl 1-3-[methyl ethyl) amino] prosody]. Tenormin has a molecular weight of 266.34 D. Capoten used to treat hypertension, chemically described as a 1-(3-mercapto-2-D-methyl-1-oxoproppyl) -l-proline (S, S), is used therapeutically as an antihypertensive agent. It acts as a potent and specific inhibitor of angiotensinogen-converting enzyme. This study includes forty patients with high blood pressure whom divided into two groups: group (A) which included twenty patients use Tenormin and group (B) which included twenty patients use Capoten, and Twenty healthy subjects group (C) with matched age, sex and BMI, were included in this study as control group. Lipid profile, urea, creatinine, albumin, glucose were determined by enzymatic method. The results of group (A) show that there were significant elevation ($P< 0.05$) of total cholesterol, Triglycerides, VLDL, glucose, urea and creatinine, the result also revealed negative correlation between the treatment with Tenormin with LDL and glucose. The results of group (B) revealed significant elevation ($P< 0.05$) of cholesterol, LDL, triglyceride, glucose, urea, creatinine and albumin. Negative correlation was found between Capoten with LDL and albumin as Conclusion Tenormin is more appropriate to treat patients with diabetes mellitus or kidney disease in addition to hypertension.

Keyword: hypertension, Tenormin and Capoten.

Introduction

High blood pressure (hypertension) is, simply, elevated pressure of the blood in the arteries. Hypertension results from two major factors, which can be present independently or together:1-The heart pumps blood with excessive force. 2-The body's smaller blood vessels (known as the arterioles) narrow, so that blood flow exerts more pressure against the vessels' walls.[1]

Although the body can tolerate increased blood pressure for months and even years, eventually the heart may enlarge (a condition called hypertrophy), which is a major factor in heart failure. Such pressure can also injure blood vessels in the heart, kidneys, the brain, and the eyes.

Tenormin may be chemically described as a benzene acetamide, 4 - [21 – hydroxyl 1-3-[methyl ethyl) amino] prosody]. Tenormin (free base) has a molecular weight of 266.34D. It is a relatively polar hydrophilic compound with water solubility of 26.5 mg/ml at 37^0C and a log partition coefficient (octane /water) of 0.23. Lipid insoluble hydrophilic compounds (atenolol, sotalol, nadolol) are excreted only by the kidneys and have low brain penetration. Metoprolol and propranolol are morelipophilic compounds and so are more often used in migraine and have more cerebra side effects of b-blockers. [2] Tenormin is incompletely absorbed (about 50%), but most of the absorbed dose reaches the systemic circulation. Peak blood levels are reached between two and four hours after ingestion atenolol undergoes little or no metabolism by the liver and the absorbed portion is eliminated by renal excretion. Over 85% of intravenous dose is excreted in urine within 24 hours compared with 50% for an oral dose. Only a small amount (6-16%) is protein-bound resulting in relatively consistent plasma drug levels with about a four-fold inter-patient variation. The elimination half-life of atenolol is 6 to 7 hours and there is no alteration of kinetic profile of drug by chronic administration. Following oral doses of 50 mg or 100 mg both b-blocking and anti-

hypertensive effects persist for at least 24 hours. The drug accumulates in patients with renal failure and dosage should be adjusted for patients whose creatinine clearance is less than 35 mL/min/1.73m^2[2].

Captopril (CPL) 1-(3-mercapto-2-D-methyl-1-oxoproppyl) -l-proline (S, S), is used therapeutically as an antihypertensive agent. It acts as a potent and specific inhibitor of angiotensinogen-converting enzyme [3].

Its beneficial effects in hypertension and heart failure appear to result primarily from suppression of the renin-angiotensin-aldosterone system. However, there is no consistent correlation between renin levels and response to the drug. Capoten prevents the conversion of angiotensinogen I to angiotensinogen II by inhibition of ACE, a peptidyldipeptide carboxyl hydrolyses. This inhibition has been demonstrated in both healthy human subjects and in animals by showing that the elevation of blood pressure caused by exogenously administered angiotensinogen by Capoten. ACE is identical to "bradykininase", and Capoten may also interfere with the degradation of the vasodepressor peptide, bradykininase. Increased concentrations of bradykininase or prostaglandin E2 may also have a role in the therapeutic effect of Capoten. Inhibition of ACE results in decreased plasma angiotensinogen II and increased plasma renin activity (PRA), the latter resulting from loss of negative feedback on renin release caused by reduction in angiotensinogen II. The reduction of angiotensinogen II leads to decreased aldosterone secretion, and, as a result, small increases in serum potassium may occur along with sodium and fluid loss. The antihypertensive effects persist for a longer period of time than doe's demonstrable inhibition of circulating ACE. It is not known whether the ACE present in vascular endothelium is inhibited longer than the ACE in circulating blood[4].

Subjects and Methods

This study conducted during the period from April 2012 to August 2012. This study includes forty patients with high blood pressure (hypertension) whom divided into two groups: group (A) which included twenty patients use Tenormin and group (B) which included twenty patients use Capoten. All patients admitted to Al- Numman Hospital. Blood samples were taken from patients after having thoroughly examined. Twenty healthy subjects group (C) with matched age, sex and BMI, were included in this study as control group. From each patient and control, five ml of venous blood were aspirated from a suitable vein. Samples were collected between (8-9 A.M.) after 10 hours fasting. Blood samples were transferred to a plane tube to measure the levels of (lipid profile, urea, creatinine, albumin, glucose). The non heparinized blood in the plain tubes were left to clot and then centrifuged at 4000 rpm for 5 minutes to measure the parameters using Kits which were supplied by Randox (United Kingdom).

Results and Discussion

The results of this study show negative correlation between treatment with Tenormin with cholesterol and LDL, while there were positive correlation between treatments with Tenormin with HDL, the result of treatment with Capoten shows the same correlations. The elevated levels of triglyceride; cholesterol and LDL-C are documented as risk factors for atherogenesis lipid. LDL-C in particle; as it not only load macrophages with cholesterol for the formation of foam cells but also because it ischemotactic for circulating monocytes, is cytotoxic and can adversely alter coagulation pathways. The blood level of HDL-C in contrast bears an inverse relationship of the risk of atherosclerosis and coronary heart disease that is higher the level, smaller the and cardiovascular.[5] So these drugs also may play good rule as protective factor for cardiovascular disease.

Tenormin negatively correlated with glucose this mean it may increase the insulin sensitivity. There are several possible explanations for the diminished glucose disposal mediated by insulin during β-1 selective adrenergic blockade. The decrease in cardiac output during β-1 blockade may lead to reduced blood flow in muscles, thereby reducing the availability of glucose to the prime target tissue for glucose disposal. Two other studies have shown that clearance of insulin is reduced after blockade selective for

the type of β adrenergic receptor [5]. Capoten show positive correlation with glucose this indicate it may decrease the insulin sensitivity. The results show negative correlation between treatment with Tenormin with urea, creatinine and albumin, the result of treatment with Capoten also revealed the same correlation with these parameters. Elevated serum creatinine and protein, in addition to presence of protein in urine might be to direct effect of hypertension and its related complications on renal function. Creatinine test also provide a base line measurement of renal function that can be used as monitoring for side effects of certain antihypertensive drugs on renal function. Similarly testing of urine samples for protein can be used as a secondary indicator of renal disease. [6] There were negative correlations between Capoten treatment with urea, creatinine and albumin levels. The rises in blood urea nitrogen and serum creatinine indeed, this is an indication that the drugs are exerting their desired actions to help preserve renal function. [7].

Table (1)
Comparison between group (A) and group (C) for (high blood pressure, age, height, weight, BMI, waist circumference, hip circumference and neck circumference).

Parameters	***Patients (group A) Mean ±SD No.20***	***Control (group C) Mean ±SD No.20***	***P-value***
systolic pressure mmHg	14.8±1.01	12.2±1.2	<0.05
Diastolic pressure mmHg	9.8±1.1	8.7±1.1	0.329
Age years	49.39±8.08	47.2±7.3	0.148
Height cm	164.3±7.8	166.6±6.2	0.158
Weight kg	82.9±6.7	82.8±7.4	0.470
BMI Kg/m2	30.8±1.9	30.0±2.3	0.273
Waist circumference cm	102.2±5.7	101.8±6.2	0.404
Hip circumference cm	105.9±6.5	105.9±5.6	0.494
Neck circumference cm	37.9±2.9	39.0± 3.1	0.133

Table (2)
Comparison between group(A) and group (C) for (lipid profile and glucose).

Parameters mmole/l	***Patients (Group A) Mean ±SD No.20***	***Control(group C) Mean±SD No.20***	***P-value***
Total cholesterol	4.9±0.8	4.5±0.3	<0.05
Triglyceride	2.3±1.1	1.5±0.6	<0.05
VLDL	1.0±0.5	0.6±0.2	<0.05
LDL	2.8±0.8	2.8±0.5	0.482
HDL	0.9±0.1	1.0±0.2	0.408
Glucose	5.7±0.9	5.1±0.4	<0.05

Table (3)
Comparison between group (A) and group (C) for (Urea, Creatinine and Albumin).

Parameters	*Patients (group A) Mean ±SD No.20*	*Control (group C) Mean ±SD No.20*	*P-value*
Urea mmole/l	6.6±2.4	5.5±0.8	<0.05
Creatinine mmole/l	85.2±26.9	68.7±4.3	<0.05
Albumin g/l	41.6±5.3	39.9±3.0	0.111

Table (4)
Comparison between group (B) and group(C) for (High blood pressure, Age, Height, Weight, BMI, Waist circumference, Hip circumference and neck circumference).

Parameters	*Patients (group B) Mean ±SD No. 20*	*Control (group C) Mean ±SD No. 20*	*P-value*
Systolic pressure mmHg	15.0±0.79	12.2± 1.2	<0.05
Diastolic pressure mmHg	9.9±0.4	9.8±1.1	0.329
Age years	50.9±6.9	47.2±7.3	0.128
Height cm	164.8±7.2	166.6±6.2	0.100
Weight cm	85.6±8.9	82.8±7.4	0.140
BMI Kg/m^2	31.7±4.0	30.0±2.3	0.244
Waist circumference cm	100.9±6.3	101.8±6.2	0.339
Hip circumference cm	105.0±6.0	105.9±5.6	0.122
Neck circumference cm	39.2±3.7	39.0±3.1	0.407

Table (5)
Comparison between group (B) and group (C) for (lipid profile and glucose).

Parameters mmole/l	*Patients (groupB) Mean±SD No.20*	*Control (group C) Mean±SD No.20*	*p-value*
Cholesterol	5.5±1.1	4.5±0.3	<0.05
Triglycerides	2.3±0.7	1.5±0.6	<0.05
VLDL	1.03 ±0.3	0.6±0.2	<0.05
LDL	3.3±1.1	2.8±0.5	<0.05
HDL	1.00±0.1	1.005±0.2	0.471
Glucose	5.5±0.6	5.1±0.9	0.180

Table (6)
Comparison between group (B) and group (C) for (Urea, Creatinine and Albumin).

Parameters		*Patients (group B) Mean±SD No.20*	*Control(group C) Mean±SD No.20*	*P-value*
Urea	mmole/l	7.5±3.6	5.5±0.8	<0.05
Creatinine	mmole/l	97.4±45.	68.7±4.3	<0.05
Albumin	g/l	47.1±5.7	39.9±3.0	<0.05

Table (7)
The correlation(r) between , group (A) and group (B) with (lipid profile and glucose).

Parameters mmole/l	*group (A) (r)*	*group (B) (r)*
Cholesterol	-0.175	-0.230
Triglycerides	0.124	0.056
VLDL	0.160	0.086
LDL	-0.406	-0.468
HDL	0.171	0.268
Glucose	-0.398	0.083

Table (8)
The correlation(r) between group (A) and group (B) with (urea, creatinine, Albumine).

Parameters		*group (A) (r)*	*group (B) (r)*
Urea	mmole/l	-0.218	-0.017
Creatinine	mmole/l	-0.236	-0.123
Albumine	g/l	-0.356	-0.326

Conclusions

- The treatment with Tenormin or Capoten was negatively associated with total cholesterol and LDL while positively associated with HDL, so these drugs also may play good rule as protective factor for cardiovascular disease.
- Treatment with Capoten show positive correlation with glucose this indicate it may decrease the insulin sensitivity.
- Treatment with Tenormin show negative correlation with glucose this indicate it may increase the insulin sensitivity.
- Treatment with Tenormin and treatment with Capoten show negative correlation with kidney function parameters. These parameters are more negatively association with treatment with Tenormin than treatment with Capoten thus Tenormin is more appropriate to treat patients that had hypertension and kidney disease.

References

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بضغطِ الدمّ العالي (إرتفاع ضغط الدم) الذي قسّمَ إلى مجموعتين: مجموعة (A) التي تَضمّنتْ عشرون مريضَ يَستعملونَ Tenormin ومجموعة (B) التي تَضمّنتْ عشرون مريضَ يَستعملونَ Capoten. كُلّ المرضى ادخلوا لمستشفى النعمان. أُخِذتْ عينات الدمّ مِنْ المرضى بعد أن تم فَحصوا. عشرون شخص اصحاء اعتبروا كمجموعة قياسية مجموعة (C) متناظرة بالعُمرِ، جنس معامل كتلة الجسم، تم قياس الدهون و السكر واليوريا والكرياتنيين حيث تم القياس باستخدام الطريقة الانزيمية. اظهرت نَتائِج المجموعةِ (A) ان هناك إرتفاعَ معنوي في مستوى الكلوستيرولِ، والبروتين الدهني واطئ الكثافة ومستوى الكلوكوز و مستوى اليوريا و الكرياتنيين، كَشفتْ النتائج إرتباطَ سلبيَ بين المعالجةِ باستخدام Tenormin مَع البروتين الدهني واطئ الكثافة ومستوى الكلوكوز. نَتائِج المجموعةِ (B) كَشفتْ إرتفاعَ معنوي للكلوستيرولِ والبروتين الدهني واطئ الكثافة, الدهون الثلاثية، كلوكوز، اليوريا، والكرياتينين.وجد بان معامل الارتباط كان سلبيا الإرتباط السلبي وُجِدَ بين Capoten والبروتين الدهني واطئ الكثافة ومستوى الكرياتنيين. Tenormin أكثرُ ملائمة لمُعَالَجَة المرضى الذين يعانون من داء السكّري او المرضى الذين يعانون امراض الكلية بلاضافة الى مرض ارتفاع ضغط الدم.

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الخلاصة

ضغط الدمّ العالي، أيضاً يسمّى إرتفاع ضغط الدمِ: هو ضغطُ مرتفعُ مِنْ الدمّ في الشرايينِ. بالرغم من أن الجسمِ يُمْكِنُ أَنْ يَتحمّلَ زيادة ضغطَ الدمّ المتزايدَ لشهورِ ولسَنَواتِ، في النهاية يؤدي الى تضخم القلبُ والذي يكون العامل الرئيسي في عجزِ القلب. مثل هذا الضغطِ يُمْكِنُ أَنْ يؤذي الأوعية الدموية في القلبِ، الكِلى، الدماغ، والعيون. يَستعملُ Tenormin لمعالجة إرتفاع ضغط الدمُ قَدْ يُوْصَفُ كيمياوياً (بنزين acetamide، 1-3 hydroxyl - 21] - 4 – [أثيل ميثيلِ) أميني] بروسيدي]. وزنه الجزيئي ٢٦٦,٣٤ دالتون . يَستعملُ Capoten لمعالجة إرتفاع ضغط الدمَ، وَصفَ كيمياوياً 3 -2- mercapto-) - 1 a دي ميثيل oxoproppyl l proline. يعمل كمثبط فعّال للإنزيمِ المسؤول عن ايض angiotensinogen. هذه الدراسةِ أجريتْ أثناء الفترةِ مِنْ أبريل/نيسانِ ٢٠١٢ إلى أغسطس/آبِ ٢٠١٢. تَتضمّنُ هذه الدراسةِ أربعون مريضِ مصابيين