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Evaluation of The Effects of Amlodipine Therapy on Blood Pressure and Kidney Function among Hypertensive Patients in Mosul City.

*** Zeina Abdul Munim Abdul Majeed , ** Isam Hamo Mahmood**
* Dept. Of Clinical Pharmacy, Mosul, College of Pharmacy
**Dept. Of Pharmacology, Mosul, College of Medicine

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Abstract

The present study was conducted to evaluate the effect of amlodipine on blood pressure and kidney function in hypertensive patients in Mosul city. Thirty hypertensive patients participated in this study (14 female and 16 male) Amlodipine was administered for a period of 8 weeks in doses of 5 to 10 mg once daily. Antihypertensive efficacy was assessed by measurement of blood pressure by standard mercury sphygmomanometer before and after treatment . Blood samples were obtained from each patient before and after treatment and the obtained sera were analysed for renal parameters which they all measured in serum by using colorimetric and enzymatic method. Creatinine clearance was calculated by using the Cockroft and Gault equation.

The results of the study showed that amlodipine therapy lead to a significant reduction in blood pressure throughout the study and about 50% of the patients exhibit BP reduction to normal values after therapy. Creatinine clearance was significantly increased after the end of the study . All other renal parameters including urea , creatinine, sodium and potassium concentrations showed a significant reductions. It was concluded that therapy with amlodipine can be useful and effective therapy in hypertensive patients with deteriorated kidneys function in once daily dosage.

تقييم تاثير علاج املوديبين على ضغط الدم ووظيفة الكلية للمرضى المصابين بضغط الدم العالي

زينة عبد المنعم عبد المجيد عصام حمو محمود

المستخلص

يعد عقار الاملودبين من الجيل الثاني لمثبطات قناة الكالسيوم والذي يتميز بفعالية جيدة وفترة مديدة الاستعمال ..إن الهدف من هذه الدراسة هو لتقييم تأثير هذا العقار على ضغط الدم وعلى بعض فحوصات وظائف الكليتين عند المرضى المصابين بارتفاع ضغط الدم في مدينة الموصل. أجريت هذه الدراسة على 30 مريضاً مصابين بفرط ضغط الدم بغية معرفة تأثير الدواء المخفظ للضغط (الاملودبين) على بعض المتغيرات الكلوية المهمة والمتضمنة : اليوريا ، الكرياتنين وتصفية الكرياتنين و الصوديوم والبوتاسيوم قبل وبعد العلاج بهذا الدواء. تم تقييم فعالية الدواء الخافضة للضغط باستخدام جهاز قياس الضغط،كما تم اخذ نماذج من دم كل فرد في مجموعة المرضى قبل وبعد العلاج بعقار الاملودبين لقياس تراكيز كل من اليوريا ، الكرياتنين الصوديوم والبوتاسيوم في مصل الدم باستخدام طرق المقياس اللونية والأنزيمية ، أما تصفية الكرياتنين فقد تم قياسها باستخدام معادلة الكوكروفت والكولت . تم إعطاء العقار بجرعات تتراوح بين 5-10ملغ يوميا ولمدة 8 أسابيع.وقد أظهرت النتائج أن عقار الاملودبين يخفض ضغط الدم بصورة معنوية كما يؤثر أيضا على هذه المتغيرات الكلوية حيث أظهرت الدراسة أن هناك فرق معنوي بين تراكيز اليوريا ، الكرياتنين وتصفية الكرياتنين و الصوديوم والبوتاسيوم قبل وبعد العلاج بالاملودبين استنتج أن استخدام هذا العقار لضغط الدم(الاملودبين) يمكن أن يكون مفيد، أمين وفعال في تخفيض ضغط الدم لدى المرضى المصابين بخلل في الكليتين. بالإضافة إلى تحسين تصفية الكرياتنين لديهم ، إضافة إلى الاستخدام الفعال لهذا العقار مرة واحدة يوميا .

Introduction

Calcium antagomnists are being increasingly used in the treatment of hypertension, they differ in their sites and mode of activity (1). A large number of the second generation calcium antagonists have been developed. They are mainly dihydropyridine derivatives, and most have longer plasma half-lives and great vascular selectivity than the prototypical agent nifedipine.. Amlodipine which is one of the second generation of calcium antagonists, is more water soluble than nifedipine, has slow, smooth onset and ultralong duration of action (1) . It causes marked coronary and peripheral dilatation and is useful in the treatment of hypertension (1,2). Moreover, amlodipine has a good antianginal efficacy and safety with once daily dosage regimen for patients with coronary artery disease (3) . Since its release in 1992, amlodipine, a vasoselective dihydropyridine calcium channel blocker ,has become a frequent component of antihypertensive regimens in adults (2). It offers several potential advantages compared to other agents in this class, including once daily dosing (3), slow rate of elimination character (elimination half lifes of 40-60 hours) offers several pharmacokinetics properties that are not seen with other calcium antagonists (4), high oral bioavailability of 60 to 80% (5), steady state plasma concentrations in healthy volunteers are achieved after the 7^{th} dose without accumulations since this drug follows linear kinetics order (6) , few significant drug interactions, and a relatively mild adverse effects profile (2).

Medicine has long recognized association between hypertension and kidney .The kidney may be a culprit or a victim in the process. As a culprit, the kidney may be responsible for the pathogenesis of hypertension in many patients, and in virtually all patients the renal response to antihypertensive therapy is a major process determinant . Indications for a potential renal protective activity of calcium antagonists have recently been obtained.(7).

Among patients with end stage renal failure, 29% have hypertension, as the underlying cause secondary only to diabetes in (36%) (8). Treatment of hypertension in patients with renal diseases needs therefore to be directed at both the prevention of cardiovascular disease and halting the progression of renal disease.. The well - known antihypertensive activity of calcium antagonists can be thought of as a renal protective measure. In addition more specific renal effects of the calcium antagonists have been recognized as potentially beneficial mechanisms in certain forms of renal disease (8). As far as no study has been conducted on Mosul population which is concerned with amlodipine effects on blood pressure and kidneys. So, the present study was designed for this purpose.

Patients and Methods

With the co-operation of the medical staff in the out-patient clinic in IBN-SINA teaching hospital, thirty patients with hypertension were allocated to treatment with Amlodipine (Amlodis 5mg, Eczacibaçi Ilac Sanayi ve Ticaret A.S Lüleburgaz Kirklareli Turkey) in doses ranged from 5-10mg daily. Duration of treatment was 8 weeks. The patients included in the study were 14 females (age range 32 – 62 years) and 16 males (age range 27 -60 years). They have diastolic blood pressure between 90 – 115 mmHg and systolic blood pressure between 135 – 165 mmHg .

The study protocol specified that patients should be 18 years or older to be included in the study. Secondary hypertension patients with other cardiac or systemic diseases, and patients with a history of allergic reactions to amlodipine or other dihydropyridines were excluded from the study. The patients were joined an open, non comparative study. Antihypertensive efficacy was assessed by measurement of blood pressure by standard mercury sphygmomanometer. Blood pressure was measured at baseline (i.e. before treatments) and at the end of 8 weeks treatment period with amlodipine . Goal blood pressure after treatment was less than 140/90 mmHg.. Analysis include mean changes in blood pressure and percentage of patients achieving blood pressure less than 140/90 mmHg .

Blood samples were obtained from each patient before and after treatment and the obtained sera were analysed for renal parameters. Serum Urea concentrations is determined enzymatically by using Urea kit supplied by bioMerieux laboratory reagents, Marcy L'Etoile, France. Serum creatinine concentrations is determined by using creatinine kit supplied by RANDOX laboratories reagents, Co. Antrium, United Kingdom .Estimation of creatinine clearance was made by measuring the serum creatinine concentration and collecting those patient factors affecting the mass of muscle, viz. age, sex and

weight. The equation of Cockroft and Gault is a useful way of making such estimation.(9). Serum sodium and potassium concentrations was determined by using flame emission photometery(10). The results of the laboratory tests for the patients group have been statistically compared by using ANOVA test(One Way Analysis of Variance) with a significant level at 5%.

Results

The patients involved in this study were hypertensive. They were thirty; 16 males and 14 females. The age of the patients ranged from 27-62 years, with a mean age of 45.5 years. Thier blood pressure were significantly decreased. The reductions in systolic blood pressure after 8 weeks were significant (151.47± 8.13 to 143.30± 8.08 mmHg, P= 0.000) ,where as the reductions in diastolic blood pressure was from 101.23± 9.93 to 85.43 ± 8.26 mmHg (P=0.000). The number of patients achieving blood pressure less than 140/90 equal 15(50%). Table 1 shows the renal parameters values obtained before and after treatment. Statistical comparison between the measured parameters before and after treatments yields a significant reductions for urea (P=0.000) , creatinine (P=0.003) ,sodium (P=0.000) and potassium (P=0.018) concentrations, and a significant elevation for creatinine clearance (P=0.002).

Table (1): Renal parameters before and after treatment with amlodipine

Parameter	Before treatment	After treatment
Urea(mg/dl)	Mean ± SD: 49.17±6.2 Range: 36-58	Mean ± SD: 40.00±6.1 Range: 30-51
Creatinine (mg/dl)	Mean ± SD: 1.03±0.24 Range: 0.63-1.6	Mean ± SD: 0.86±0.21 Range: 0. 34-1.1
Creatinine Clearance(ml/min)	Mean ± SD: 86.8±24.3 Range: 48-136	Mean ± SD: 106.31±31.1 Range: 72-150
Sodium mmol/L	Mean ± SD: 141.0 ±4.73 Range: 133-150	Mean ± SD: 136.12±5.02 Range: 125-145
Potassium mmol/L	Mean ± SD: 4.63±0.58 Range: 3.7-5.7	Mean ± SD: 4.25±0.6 Range: 3.3-5.3

DISCUSSION

In the present study blood pressure was significantly controlled by amlodipine .Both systolic and diastolic blood pressures were significantly dropped at the end of the treatment period compared with the baseline and a number of patients showed a reduction of their blood pressure below 140/90. The results obtained in this study proved that amlodipine is an effective antihypertensive drug and can be given once daily . Our results thus may document results obtained in many previous studies. In a study comparing the efficacy , tolerability and cost of amlodipine and felodipine . Amlodipine produced blood pressure control in a greater percentage of patients (87%) than did felodipine(33%) at a lower total cost to achieve blood pressure control (11). The long term effects of amlodipine (6 months) were examined in patients with moderate to severe hypertension blood pressure was significantly lowered from 176/97 to 144/82 mmHg after treatment. The study suggests that amlodipine is effective antihypertensive agent in lowering blood pressure associated with the improvement of vascular function (12). Pepine et al(13) in their study, compared the antihypertensive effects of nislodipine and amlodipine, both drugs resulted in similar blood pressure response rates (diastolic blood pressure < 90mmHg) in 87% of patients who received nislodipine and 78% of patients on amlodipine .

Burges (14) demonstrated that the pharmacodynamics and pharmacokinetic properties of amlodipine make this drug an optimal choice of treatment for the control of hypertension with once daily administration. Renal protection is a very important goal in treating patients with hypertension with or without kidney disease (15). In chronic renal disease, renal function often continues to deteriorate even if the initiating insult is no longer present. Hypertension is one of the most prominent risk factors for the progression of renal disease and antihypertensive treatment is considered the cornerstone therapy for slowing the progression of chronic renal failure (16). In the present study a significant reduction of some renal parameters was noted after therapy with amlodipine including urea ,creatinine ,sodium and potassium concentrations. The demonstrated data may suggest a beneficial effect of amlodipine on the renal functions of the hypertensive patients.

The effects of calcium channel blockers on the renal function were studied in a number of clinical trials, some of those trials compared renal effects of calcium channel blockers with those of angiotensin converting enzyme inhibitors(ACE Inhibitors) Angiotensin converting enzyme inhibitors were the first agents demonstrated to have a beneficial effect on both diabetic and non diabetic renal diseases (17,18). The mechanism of the renoprotective effect of angiotensin converting enzyme inhibitors is not clear, but reduction in proteinuria via beneficial effects on glomerular haemodynamics and / or the permeability and size selective function of the glomerulus may play an important role (18,19).

Calcium antagonists, in addition to their pronounced blood pressure reduction , also have a favourable effects on renal haemodynamics and renal tubular sodium reabsorption (20). As this class of drugs also has other properties that could contribute to their ability to protect the kidney (21,22)., they have also been used with the intention to attenuate progression of renal disease. In some experimental studies, calcium antagonists have been shown to retard progression of renal insufficiency (23,24) but in others no beneficial effect has been demonstrated (25).

The beneficial effect of amlodipine demonstrated in this study is in agreement with the results obtained from other previous studies . Ghareeb et al .(26) demonstrated a significant increase in glomerular filtration rate (GFR) after amlodipine therapy. In a study comparing the effects of amlodipine and perindopril on renal haemodynamics and tubular function in cyclosporine treated hypertensive renal allograft recipient, both drugs maintained GFR and effective renal plasma flow and lowered mean arterial pressure but the excretion of sodium is not affected by either drugs (27). In another study performed by Agodoa *et al. (28)* compared the effect of ramipril and amlodipine on renal outcomes in hypertensive nephrocalcinosis, they found that both drugs retards renal disease and proteinuria .

It has been concluded from the data obtained in this study that amlodipine is a useful agent when given to hypertensive patients with deteriorated renal function and once daily dosage of amlodipine proved to be effective in hypertensive patients.

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