PATTERN OF PRESCRIPTION OF ANTI-HYPERTENSIVE DRUGS AND THEIR EFFECT ON BLOOD PRESSURE

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ABSTRACT

Background: Hypertension, one of the most common diseases, with medical treatment ranging from monotherapy to combination of drugs. **Objective:** This study was conducted to determine the pattern of prescription of antihypertensive agents and their effect on blood pressure control among hypertensive patients with BMI above or below 25. **Patients and Methods:** This cross-sectional study was conducted on 150 hospital admitted hypertensive patients from 1st April to 30th June 2012, in the department of Medicine, in Khyber Teaching Hospital, Leady Reading Hospital, Peshawar and Ayub Teaching Hospital, Abbottabad. In the study were included only the previously known hypertensive patients with or without the complications of hypertension whereas, those who were either newly diagnosed cases or treated as outdoor patients, having white coat hypertension or having vague history of hypertension were excluded from the study. A detailed questionnaire including biographic details, BMI, BP record, associated comorbidities, baseline biochemical profile including RBS, antihypertensive drug or drugs combination used, and any adverse effects, was used. The data was processed using SPSS Version 20. **Results**: Amlodipine was only calcium channel blocker prescribed in our study, which was given to 43 (28.7%) of all the cases, ACEi were prescribed to 45 (30%) of cases (lisinopril 20%, enalapril 2.6%, ramipril 7.3%). ARBs were given to 7 (4.6%), diuretic were given to 48 (32%) of all the cases and beta blockers were given to 7 (4.6%) patients. Combination was given to 48 (32%) of the patients seen and as a second line therapy when one of the fore mentioned drug failed. It was noted that 125 (67%) of the patients achieved target BP of less than 140/90 mmHg, with the used of antihypertensive medication whereas, 33% of all the patients failed to achieve the target BP. It was noted that 54% of the study subjects were having DM and were obese, with 10% having nephropathy and protinurea. It was noted that 13% where having history of MI and 5% having history of strokes. **Conclusion:** It is concluded that Amlodipine, lisinopirl and diuretic are leading drugs used in tertiary care hospitals of Khyber Pakhtunkhawa. It was noted that antihypertensive drugs gradually lose their effectiveness in controlling BP as the BMI increases.

Keywords: Hypertension, Antihypertensive drugs, Side effects.

INTRODUCTION

Hypertension is one of the common diseases, and a major risk factor for myocardial infarction, stroke and chronic kidney disease. Worldwide, prevalence of raised blood pressure in adults aged over 25 years was 40% in 2008.[1] In United States, 75 million adults are affected by hypertension and only about one third of these have blood pressure under control.[2] In Pakistan, National Health Survey has shown that 18% of adults and 33% of adults above 45 years have hypertension.[3] It has been reported that the control of blood pressure remains poor with 35% in USA to 6% in India.[4] It was mentioned that only 50% of the people with hypertension were diagnosed and only half of those diagnosed were ever treated, thus only 12.5% of hypertension cases were adequately controlled.[5] Medical treatment of hypertension, ranges from monotherapy to combination therapy with more than one antihypertensive agents including calcium channel blocker, beta-blocker and diuretics among others.[6] Blood pressure control in obese patients is more difficult than in none obese patients.[7] Present study was conducted to determine the pattern of prescription of anti-hypertensive agents and their effect on blood pressure control among hypertensive patients with BMI above or below 25.

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PATIENTS AND METHODS

This cross-sectional study was conducted on 150 hospital admitted hypertensive patients from 1st April to 30th June 2012, in the department of Medicine, in Khyber Teaching Hospital, Leady Reading Hospital, Peshawar and Ayub Teaching Hospital, Abbottabad, and were followed up for 2 months after discharge to conclude the effectiveness of the prescribed antihypertensive drug/drugs, in achieving target

Blood Pressure in these patients in accordance with European Society of Hypertension and European Society of Cardiology, 2007 *(ESH-ESC)* and American Joint National Committee JNC-7 guidelines.[8] A blood pressure (BP) less than 140/90 mmHg was labeled as target BP, normal BP was taken as less than 120/80 mmHg, pre-hypertensive stage (Systolic BP 120-139 and diastolic BP 80-89 mmHg), stage I hypertension (systolic 140-159 and diastolic 90-99 mmHg), stage II hypertension (systolic BP more than 160 mmHg and diastolic more than 100 mmHg). In the study were included only the previously known hypertensive patients with or without the complications of hypertension whereas, those who were either newly diagnosed cases or treated as outdoor patients, having white coat hypertension or having vague history of hypertension were excluded from the study. The patients were followed up for a maximum of two months after discharge fortnightly and blood pressure measured in every visit. A detailed questionnaire including biographic details, BMI, BP record, associated comorbidities, baseline biochemical profile including RBS, RFTs, ECG and Echocardiography in patients, evidence of end organ damage, antihypertensive drug or drugs combination used, and any adverse effects was used. The study was approved by the ethics committee of the hospital and an informed consent was taken from all patients. The data was processed using SPSS Version 20.

RESULTS

A total of 150 patients with mean BMI of 23.96 were included. Amlodipine was only calcium channel blocker prescribed in our study, which was given to 43 (28.7%) of all the cases, ACEi were prescribed to 45 (30%) of cases (lisinopril 20%, enalapril 2.6%, ramipril 7.3%) . ARBs were given to 7 (4.6%), diuretic were given to 48 (32%) of all the cases and beta blockers were given to 7 (4.6%) patients. Combination was given to 48 (32%) of the patients seen and as a second line therapy when one of the fore mentioned drug failed. It was noted that 125 (67%) of the patients achieved target BP of less than 140/90 mmHg, with the used of antihypertensive medication whereas, 33% of all the patients failed to achieve the target BP. It was noted that 25.7% among these non responders have BMI > 25 and 17% were having diabetes as well. Of 43 (28.7%) patients who were put on amlodipine 37 (24.6%) have BMI less than 25 achieved target BP, while 6 patients who had BMI more than 25 still had BP in stage II hypertension. It showed adverse effects only in 4 of 43 patients, mainly constipation and Angioedema. Beta Blockers were given to 7 (4.6%) of all the patients and given mainly in females (5) out of (7). Amongest the beta blockers, atenolol was given to 5 patients; 2 with BMI in normal range achieved target BP while 3 with BMI more than 25 failed to achieved a target BP. In comparison bisoprolol was given to 2 patients (BMI, 23 and 27) and both of them achieved target BP.

ACE inhibitors/ARBs were given to 52 (35%) of the patients and they showed an effect almost similar to amlodipine. Out of these 52 patients, 30 (20%) were put on lisinopril; 27 (18%) patients with BMI less than 25 achieved target BP while 3 (2%) patients with BMI more than 25 failed to achieved target BP. Enalapril was given to 4 (2.6%) of the patients, with 3 patients achieving target BP on follow up, in both above and below 25 BMI groups. Ramipril was given to 11 (7%) of the patients, with 8 (5.3%) patients achieving target BP with BMI less than 25. ARBs were given to 7 (4.6%) of patients, with 6 patients achieving target BP.

Table I: Drug prescribed and blood pressure control (N =150)

Drug	Numbers	Percentage of patients	Percent achieved target BP	Percent not achieved target BP
Amlodipine	43	28.7%	24%	4.7%
ACEi	45	30%	25.5%	4.5%
Lisinopril	*30*	*20%*	*18%*	*2%*
Enalapril	*4*	*2.6%*	*2%*	*1%*
Ramipril	*11*	*7.3%*	*5.5%*	*1.5%*
ARBs	7	4.6%	4.1%	0.5%
Beta Blockers	7	4.6%	2.8%	1.8%
Diuretics (in combination)	48	32.1%	10.6%	21.4%
Total	150	100%	67%	33%

The Diuretics were given to 48 (32%) of the patients and amongst these furosemide 40-60mg was given stat intravenously for short term relief. In these patients 25% responded acutely to IV furosemide and 10% were shifted to oral furosemide, thiazide or spironolactone, for better control in addition to other drugs as combination therapy on long term. It was noted that 54% of the study subjects were having DM and were obese, with 10% having nephropathy and proteinurea. It was noted that 13% where having history of MI and 5% having history of strokes.

DISCUSSION

Hypertension and obesity are epidemic and are often seen in combination. The choice of antihypertensive agent for the patients has been the subject of several studies and resulting in national guidelines. Patient's age, associated clinical conditions and end organ damage also plays a part in determining dosage and type of drug administered.[9]

Weight gain is associated with increases in arterial pressure, and it has been estimated that 60-70% of hypertension in adults is attributable to adiposity.[10] Cross-sectional and longitudinal studies document an association of blood pressure with body weight and an association of blood pressure increases over time with weight gain,[11] even among lean individuals.

Our study revealed the pattern of antihypertensive drug therapy and effect of these drugs on patients with different BMI. It also showed the most commonly prescribed single drug was amlodipine, followed by ACEi and diuretics in combination with other antihypertensive agents. It was seen that control of BP becomes more difficult in patients with high BMI and to gain effective control over BP in obese patients either the antihypertensive drug be given in increasingly high doses or be given in combination with other drugs. Losing weight can lead to improved control over BP via medications, even moderate weight loss results in reduction of blood pressure and hypertension incidence, and improvement in insulin sensitivity and vascular endothelial function.[12,13] Our study also showed that most of the antihypertensive drugs lose their effectiveness in patients with increasing BMI in comparison to relatively lean individuals though Enalapril was the only drug found to be relatively more effective in overweight individuals than in patients with normal BMI, however, small number of patients, have been prescribed Enalapril.

The most widely prescribed drugs are amlodipine amongst the calcium channel blockers and lisinopril followed by ramipril, amongst the ACE inhibitors which are often prescribed in combination with ARBs especially losartan and valsartan. Several trials have documented the efficacy of the combination of hydrochlorothiazide with either an ACE, an ARB, in obese hypertensive patients.[14] All these drugs have been shown to be effective in controlling BP over long-term while diuretics (Furosemide,thiazide) and Captopril are used for symptomatic relief and have limited role in long-term BP control. However, these drugs (diuretics) stimulate both sympathetic nerve activity and the renin-angiotensin system, and long-term administration of the thiazide diuretic, hydrochlorothiazide, has been associated with increased insulin resistance and dyslipidaemia.[15] In a trial in 232 obese hypertensive patients, hydrochlorothiazide was as effective as the angiotensin converting enzyme (ACE) inhibitor, lisinopril, in decreasing blood pressure, but monotherapy with the diuretic showed a lower efficacy at lower doses and had a slower rate of response than was achieved with the ACE inhibitor.

In our study, we observed that most of the patients were free of adverse effects attributable to the antihypertensive medications and only 4% patients presented with adverse effects mostly constipation and angioedema with calcium channel blockers and cough with ACE inhibitors. 54 % of the patients in our study group were having concomitant diabetes mellitus and were obese showing the existence of metabolic syndrome. Amongst our study group 10 % of the patients were with diabetic nephropathy and hypertension and were put on ACE inhibitors and on follow up there was significant reduction in proteinuria and blood pressure. ACE inhibitors are probably the most appropriate form of antihypertensive agent for obese hypertensive patients, as they exert a range of hypotensive effects.[16] ACE inhibitors may also be the drugs of choice for the obese hypertensive patient because of the frequent association of obesity with left-ventricular hypertrophy, congestive heart failure, renal hyper filtration and micro albuminuria,[17] conditions known to be positively influenced by ACE inhibition.

We also found that 13% of the previously known hypertensive patients have a history of myocardial infarction and 5 % with stroke and on questioning it was seen that there was poor drug compliance in these patients leading to complications of hypertension.

CONCLUSION

It is concluded that Amlodipine, lisionopirl and diuretic are leading used in tertiary care hospital of Khyber Pakhtunkhawa. It was noted that antihypertensive drugs gradually lose their effectiveness in controlling BP as the BMI increases, though Enalapril is the drug which was found to be effective in controlling BP in patients with high BMI as well. Some classes of antihypertensive agents may have potentially unwanted effects on some of the metabolic and hemodynamic abnormalities that link obesity and hypertension, yet most hypertension guidelines fail to provide specific advice on the pharmacological management of obese hypertensive patients probably due to lack of sufficient studies examining the efficacy of anti-hypertensive drugs in obese patients, therefore it is highly recommended that further studies be done in this regard to establish the effectiveness of a specific class of anti-hypertensive agents in overweight and obese patients, so that specific guidelines regarding hypertension management in patients with high BMI could come to the surface.

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