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BLOOD PRESSURE LOWERING EFFECTS OF ATORVASTATIN IN ESSENTIAL HYPERTENSION

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ABSTRACT

Plenty epidemiologic data support association between hypertension and atherosclerotic related risk and supportive results has been established that treatment of hypertension can reduce the risk of atherosclerotic related event. There are limited trials based evidence that the cholesterol reducing statin, Atorvastatin is also effective in lowering blood pressure. Based on above said hypothesis our study is designed to evaluate the anti hypertensive effects of atorvastatin, in patients diagnosed to have essential hypertension, in combination other antihypertensive drug namely, Amlodipine. Our study results shows Blood pressure measurement at the end of second week and fourth week showed more reduction in the test group, where atorvastatin is added with another standard anti hypertensive, amlodipine, a calcium channel blocker group than control group in which only amlodipine was prescribed.This was statistically and clinically significant.

1. INTRODUCTION

1.1 Background

Affecting one billion people worldwide, hypertension (HT) is the most common easily recognizable and treatable risk factor for many cardiovascular diseases like infarction, stroke etc[1, 2]. There are plenty epidemiologic data support association between hypertension and atherosclerotic related risk and supportive results has been established that treatment of hypertension can reduce the risk of atherosclerotic related events. Hypertension and dyslipidemia occur together in a significant population , the constellation of hypertension , diabetes and insulin resistance (diabetes) is called metabolic syndrome and the prevalence of this syndrome worldwide is about 60% in women aged 45-49 and 45% in men aged 45-49 according to the national cholesterol education programme criteria[3]. The statins , HMG –CoA reductase inhibitors , statins are the most efficacious and better tolerated agents for treating dyslipidemia syndromes[4].More potent , newer statins like Atorvastatin reduce LDL-C significantly and are also effective in reducing triglycerides , elevated VLDL in dyslipidemia[13].

1.2 SCOPE OF THE PRESENT STUDY

There are trials based evidence that the cholesterol reducing statin , Atorvastatin is also effective in lowering blood pressure. Statins exert anti hypertensive effects irrespective of cholesterol reduction property , mainly by expressing endothelial nitric oxide synthase and release of endothelial nitric oxide (NO), as well as by several other mechanisms.

In an experimental study conducted , Atorvastatin has shown to prevent target organ injury in hypertension[7.] A related study published in the Journal of the American College of Cardiology' states that adequate therapy with Atorvastatin can significantly reduce systolic hypertension [5] .

In an another study , the group which received combination therapy with an antihypertensive drug and statin resulted with a sustained reduction in blood pressure than in the group which received the anti hypertensive drug alone[8].

Based on the outcome of the above said studies , it was decided to study the possible role of atorvastatin in reducing the blood pressure in hypertensive patients.

This is a comparative study , where antihypertensive effects of statin , atorvastatin was compared with the standard antihypertensive drug , namely amlodipne.

2 . MATERIALS AND METHODOLOGY

2.1. Aim : Evaluation of the effectiveness of Atorvastatin in essential hypertension.

2.2 . Objective : To evaluate the anti hypertensive effects of atorvastatin , in patients diagnosed to have essential hypertension, in combination with other antihypertensive drugs namely, Amlodipine .

2.3 .INCLUSION CRITERIA

- Age :30 – 60 years
- Sex :Both male and female
- Only cases diagnosed as essential Hypertension – stage I(Sys BP : 140 – 159mmHg) (Dias BP : 90 – 99 mmHg)

2.4. EXCLUSION CRITERIA

- Age below 30years and above 60 years.
- Other stages of Hypertension.
- Pregnant and lactating women.
- Patients having existing renal or liver diseases.
- Patients having associated cardiac illness.
- Patients with known Hyperlipidemias and other endocrine diseases.

2.5 METHODOLOGY

The study was conducted open , randomized ,active control studies , conducted between June and December 2012 , at Stanley medical college , hypertensive clinic. For all the patients in the trial groups, basic investigations such as hemogram , renal function test , liver function test was done before and after the study period. The permission was obtained from our institution ethics committee. Informed consent was obtained from all the patients after explaining about the study in their own language. Only patients who were willing to participate were included in the trial. Two hundred and sixty patients having essential hypertension stage I hypertension were selected for the study. These subjects were randomozied into two groups, the first group called IA , consists of one hundered and thirty patients . All the patients in group IA were given tab. Amlodipine 5 mg OD in the morning. This serves as the control group. The other one hundered and patients, who are allocated to group IB, were given Tab. Amlodipine 5 mg in the morning and Tab. Atorvastatin 10 mg at bed time . This is the study group. For subjects in trial , control group and IB study group , blood pressure was recorded on the day before drug administration . The patients were followed up and blood pressure was recorded once in every two days , but for analysis pre drug blood pressure, blood pressure at end of second week , fouth week treatment were taken.

3. RESULTS

3.1 AGE AND SEX DISTRIBUTION

Age group of the participants in trial I , in trial IA (control) 5 patients dropped out of the study and 9(study) patients dropped out of the study in trial IB. Statistical analysis of the age group of participants study and control between shows no significant difference (p- 0.843)in the age group and similarly gender distribution of the participants in trial shows no significant difference (p- 0.695) among study and control group .

Analysis done by using SSPS software .13 , parameters taken from the participants who were all completed the four weeks treatment procedure , per protocol analysis

3.2 Results on the effect of blood systolic BP and diastolic BP

Table six shows no significant difference of blood pressure among control and study group during pre treatment period both systolic and diastolic blood pressure were almost identical.

Blood pressure measurement at the end of second week showed more reduction in the test group than control group .This was statistically significant , with p value of difference in systolic blood pressure at the end second week , was (p- <0.001**) and diastolic blood pressure at the of second week (p – 0.007). Similarly systolic and diastolic blood pressure difference between control and study subjects at end of fourth week is significant with p value of (p-<0.001** , p- 0.008) respectively.

Analysis done by using SSPS software .13 , parameters taken from the participants who were all completed all the four weeks treatment procedure , per protocol analysis .

BLOOD PRESSURE ANALYSIS

	GROUP	N	Mean	SD	p-value
SBP_PRE	CONTROL BP MONITORING	125	149.28	3.781	0.076.
	TEST BP MONITORING	121	147.05	4.544	
DBP_PRE	CONTROL BP MONITORING	125	91.28	2.441	0.115
	TEST BP MONITORING	121	92.48	2.600	
SBP_2W	CONTROL BP MONITORING	125	133.04	5.004	<0.001**
	TEST BP MONITORING	121	125.43	6.361	
DBP_2W	CONTROL BP MONITORING	125	83.12	3.516	0.007*.
	TEST BP MONITORING	121	80.76	2.047	
SBP_4W	CONTROL BP MONITORING	125	131.76	4.910	<0.001**
	TEST BP MONITORING	21	122.86	4.881	
DBP_4W	CONTROL BP MONITORING	125	83.04	3.835	. 0.008*.
	TEST BP MONITORING	121	80.19	2.960	

Table -1, results of blood pressure recording (SBP-PRE : represents systolic blood pressure during pre treatment , DBP-PRE , represents diastolic blood pressure during pre treatment period. SBP-2W, DBP-2W : represents systolic and diastolic blood pressure at end of second week , SBP-4W , DSP-4W : represents systolic and diastolic blood pressure at the of fourth week).

4. DISCUSSION

This trial was designed to study the possible effects of Atorvastatin to reduce the blood pressure. Presently Atorvastatin is a drug given for dyslipdemia , since it was also found to have blood pressure lowering effect , a trial was carried out to determine its blood pressure lowering effect. Mean reduction of systolic and diastolic blood pressure among test subjects where atorvastatin was combined with one of the standard anti hypertensive drug was more when compared to the control group, which received the standard drug alone . This is clinically and statistically significant .This shows the possible effects of atorvastatin in lowering blood pressure.

Atorvastatin is now well known for its cardioprotective actions by its property other than LDL lowering property , has significant actions by its anti oxidant , anti inflammatory ,and lipid modulating effects. Antihypertensive property is also significant and irrespective of its cholesterol lowering effects , mainly by expressing endothelial nitric oxide synthase

The mechanisms by which atorvastatin lowers the blood pressure can be attributed to actions like endothelial nitric oxide levels and activity, decreade endothelins production , downregulate angiotensin II receptor subtype 1 (AT_1) expression, and inhibit NAD(P)H oxidase activity.

Statins interfere with cholesterol synthesis, by inhibiting rate limiting step of mevolanate formation . Mevolanate also destrolys ribonucleo proteins necessary for the synthesis od nitric oxide synthase proteins . Hence Inhibition of mevalonate formation by statins indirectly increases nitric oxide synthase enzyme and nitric oxide level. Our study reports coincides with the various supportive studies mentioned in the scope of the our study[5, 6, 12, 15] . At the end of our study all the patients was followed for two weeks to note is there any rebound increase of blood pressure or any other any other adverse effects , however no such effects found. Pharmacologic therapy is recommended for individuls for blood pressures more than or equal to 140/90 mmhg.Based on clinical trial data , the maximum protection is achieved with pressures < 135-140mHg and <80-85 mmHg. Even mere additional control of systolic BP 10-12 mmHg and diastolic BP 5-6 mmHg significantly prevents end organ injury by hypertension and reduce the risk of stroke , cardiac failure among hypertensives[3] , this can be utilized by Concomitant use of atorvastatin which also helps to normalize the altered lipid profile , if present in hypertensives and definitely valuable in patients with both hypertension and dyslipdemia, for patients of metabolic syndrome.

5. CONCLUSION

Atorvastatin which is a primary drug for dyslipidemia has been found to have significant blood pressure lowering effects. Atorvastatin can emerge as a promising antihypertensive drug or as an adjuvant drug in antihypertensive therapy .So multiple benefits can be obtained in patients with dyslipidemia and hypertension and in patients with metabolic syndrome.

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