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Original Article

Effect of Atenolol on Hepatic Dysfunction by Evaluating Level of AST

Maria Fareed Siddiqui[1*], Mehreen Rasheed[1], Imran Shahid[2], Imrana Tanvir[3] and Sidra Khalid[4]

[1]Faculty of Pharmacy, The University of Lahore, Lahore, Pakistan
[2]Department of Pharmacology and Toxicology, Faculty of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia
[3]Department of Pathology, Faculty of Medicine in Rabigh, King Abdulaziz University, Kingdom of Saudi Arabia
[4]Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan

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***Corresponding Author:**
Maria Fareed Siddiqui
Faculty of Pharmacy, The University of Lahore, Lahore, Pakistan
maria.pharmacist@gmail.com

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ABSTRACT

Hypertension is one of the most important risk factors for morbidity and mortality around the world. Many drugs used to treat hypertension have several side effects. Atenolol used to control hypertension, is an anti-beta-adrenergic agent. It has found to significantly affect the hepatic functions. **Objective:** To study the effects of atenolol on hepatic dysfunction by measuring AST level in hypertensive patients, taking atenolol alone or in combination with other anti-hypertensive drugs. **Methods:** The variation in AST level was measured upon use of atenolol alone or in combination with other anti-hypertensive drugs. Out of total 80 patients, 43 were treated with atenolol alone, 37 with atenolol in combination with other anti-hypertensive drugs and 20 were healthy controls. Micro lab tests were used for measurement of AST level. **Results:** Significant results were found as atenolol cause increase in AST level. Other anti-hypertensive drugs did not affect the AST levels much and the increase in AST level was more significant in patients taking atenolol alone. **Conclusions:** Atenolol may have efficacy in controlling hypertension, but it causes disturbance in AST levels therefore any other drug in combination with atenolol is recommended to avoid AST variation and eventually hepatic dysfunctions. Further this study may be employed on large scale for strengthening the outcomes of this study.

INTRODUCTION

Hypertension is a chronic medical condition in which the blood pressure in the blood vessels is too high i.e., 140/90 mmHg or higher [1]. Major causes of hypertension include the complex interplay of pathological conditions including genetic predisposition as well as different environmental factors [2, 3]. Various systems including autonomic nervous system, the renin-angiotensin-aldosterone system, and nitric oxide and endothelin, which are secreted by the endothelium, are the major regulators of blood pressure and control cardiovascular homeostasis [4-6]. Any variation or disturbance in these systems can lead to hypertension. So, these systems are targeted for developing anti-hypertensive drugs. Different anti-hypertensive drugs have been developed to treat high blood pressure, including: alpha blockers, ACE inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, central alpha agonists, diuretics, renin inhibitors and vasodilators [7, 8]. Among these drugs one of the widely use drugs is beta blockers including Atenolol which is a selective β1 receptor antagonist. Atenolol was developed in 1976 as a replacement for propranolol in the treatment of hypertension. Atenolol has the beta-adrenergic receptor blocking activity by reducing the blood pressure at resting and after exercising, inhibition of the tachycardia and reduction of orthostatic tachycardia. Atenolol also decreases the cardiac output without affecting the total peripheral resistance [9]. When atenolol is used to treat hypertension, it has found to be responsible

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for some side effects including hepatic dysfunction. It causes damage to the liver cell and produce a variety of symptoms but the main problem originates from glucose insufficient supply to the brain leading to functions impairment. Liver function tests (LFTs) are performed in clinical biochemistry which indicate the condition of patient's liver [10, 11]. Abnormal liver function tests (LFTs) have been reported in people with high blood pressure [12]. AST (Aspartate transaminase) is a sensitive indicators of liver damage or injury from different forms of diseases. The elevated level of AST indicates the damaged liver however there could also be some others factors responsible for this increase in AST level e.g., muscle damage also causes an increase in AST level in blood its normal range for male lies within <35U/L and for females <31 U/L [13]. This study was based on finding the effect of atenolol on hepatic functions by measuring the AST level in hypertension patients after they are treated with atenolol alone or in combination with other anti-hypertensive drugs.

METHODS

In this study, total of 80 subjects were selected with hypertension taking atenolol alone or in combination and 20 subjects with normal blood pressure were taken as control. Patients were selected from Punjab Institute of Cardiology, Lahore for the evaluation of hypertension status. Those with hypertension taking atenolol alone or in combination were selected and their AST levels were checked. All positive hypertensive patients were included and those on multidrug therapy and with concomitant disorder were excluded in this study. Those with normal blood pressure were taken as control for comparison. After collection of blood from the patients, blood was centrifuged, and serum were separated. The AST level was determined by measuring the change in absorbance with time due to the conversion of NADH to NAD^+ which was measured by using a by using a photometer 5010plus at 340/400nm rate technique. Addition of pyridoxal-5-phosphate (P-5-P), recommended by IFCC, stabilizes the activity of transaminases and avoids falsely low values in sample containing insufficient endogenous P-5-P, from patients with hypertension.

RESULTS

The effect of atenolol on liver was studied by measuring the level of AST in blood of hypertensive patients. Figure 1 indicates the significant change (increase) in AST level in patients treated with atenolol alone (mean value = 49.9) as compared to patients treated with atenolol in combination with other anti-hypertensive drugs (mean value = 42.2) and while the mean value in control patients was 32.

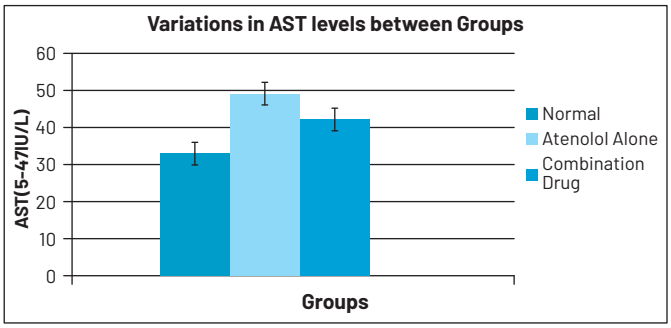

Figure 1: Graphical representation of variation in AST level between patients divided in three groups

In control group of 20 people of random age and gender with normal blood pressure have AST levels in normal range for males lies within <35U/L and for females <31 U/L (Table 1).

Table 1: Evaluation of AST in control population

Sr. No.	Gender	Age	AST
1	Male	35	12
2	Male	45	23
3	Male	37	30
4	Male	48	32
5	Male	51	39
6	Male	36	25
7	Male	42	36
8	Male	41	29
9	Male	55	49
10	Male	34	23
11	Female	35	28
12	Female	44	40
13	Female	45	36
14	Female	46	34
15	Female	44	25
16	Female	55	36
17	Female	35	37
18	Female	33	24
19	Female	57	43
20	Female	42	41

The group of patient's takings atenolol alone having random age and gender have significant disturbance in AST levels as compared to control group (Table 2).

Table 2: Evaluation of AST level in hypertensive patients taking atenolol alone

Sr. No.	Gender	Age	Duration of Administration	Dose (mg)	AST
1	Female	34	2 years 2 months	100	38
2	Female	35	1 week	50	66
3	Female	38	8 years	50	30
4	Female	38	1 years	50	24
5	Male	39	4 months	100	43
6	Female	42	1 year 1 month	50	60
7	Female	43	7 months	50	38
8	Female	43	7 years	100	41
9	Female	45	1 week	100	42
10	Male	45	9 months	100	32
11	Female	45	4 months	100	44
12	Male	47	6 months	25	43
13	Male	47	1 year	100	44
14	Female	47	1 year 3 months	100	50
15	Female	48	2 years 10 months	100	278

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16	Female	48	1 year 1 month	50	41
17	Male	48	7 months	25	28
18	Male	50	1 year 3 months	100	33
19	Male	50	1 year 1 month	50	55
20	Female	50	3 years	100	52
21	Female	50	1 year 2 months	50	38
22	Female	50	6 months	100	50
23	Female	50	5 months	50	51
24	Female	51	7 months	20	50
25	Female	52	9 months	100	57
26	Female	54	1 year 3 months	50	35
27	Male	56	2 years	50	35
28	Male	60	1 month	20	34
29	Male	60	1 month	25	37
30	Female	60	6 years 1 months	50	82
31	Female	60	10 months	100	56
32	Female	60	2 years 2 months	100	27
33	Female	60	1 year 9 months	50	36
34	Female	60	5 months	100	50
35	Female	60	7 years	50	42
36	Male	61	7 years	100	63
37	Female	62	4 months	100	36
38	Male	65	2 years 7 months	50	58
39	Female	67	6 months	50	38
40	Male	70	1 year	50	43
41	Female	70	5 months	100	36
42	Female	70	1 year 2 months	50	38
43	Male	77	2 weeks	100	53

While, in the group of patient's takings atenolol in combination with other antihypertensive drugs having random age and gender have lower disturbance in AST levels as compared to group of patients taking atenolol alone(Table 3).

Table: 3 Evaluation of AST level in hypertensive patients taking atenolol in combination

Sr. No.	Gender	Age	Duration of Administration	Dose (mg)	AST
1	Male	33	1 year	100	58
2	Female	35	8 years 2 months	100	35
3	Male	40	3years 3 months	100	29
4	Female	40	8 months	50	41
5	Male	41	1 year 3 months	100	53
6	Male	43	1 month	50	54
7	Male	44	5 years 4 months	50	36
8	Female	45	9 months	100	58
9	Male	45	5 months	50	56
10	Male	48	1 week	100	45
11	Female	48	4 years 5 months	50	28
12	Female	50	1 week	100	38
13	Male	50	6 years	100	44
14	Male	50	1 week	100	26
15	Female	50	1 year	50	60
16	Female	50	1 week	50	46
17	Female	54	3 years 3 months	100	60
18	Male	54	2 months	50	61
19	Female	55	9 years	50	63
20	Male	55	4 years 3 months	100	52
21	Male	56	1 year 1 month	100	29
22	Male	57	4 years 3 months	100	39
23	Male	58	1 year 5 months	50	32
24	Male	58	10 years	50	46

The results were further subjected to statistical analysis by applying standard deviation and standard error. In case of AST values evaluation, the significant results with 0.049 value were obtained(Table 4).

Table 4: Significance of measured AST values

values	N	Mean ± SD	Standard. Error	Significance
AST	.00	32.10 ± 8.69	1.94246	0.049
	1.00	49.46 ± 37.51	5.72064	
	2.00	42.24 ± 11.53	1.89689	
	Total	43.32 ± 26.49	2.64983	

DISCUSSION

Hypertension is a medical condition attributed to high blood pressure in blood vessels (140/90 mmHg or higher). According to world health organization ~1.28 billion adults with age between 30 to 79 years have hypertension across the world, with almost two-thirds of them living in low and middle economic countries. Some common factors include; age, genetics, obesity, non-active lifestyle, diet with high salt content and alcohol consumption [14]. Different anti-hypertensive drugs have developed to control blood pressure which targets different systems of the body that control and regulates the blood pressure. These anti-hypertensive drugs include; alpha blockers, ACE inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, central alpha agonists, diuretics, renin inhibitors and vasodilators [15]. Among beta blocker, a known drug is Atenolol (2-{4-[2-Hydroxy-3-(propan-2-ylamino) propoxy] phenyl} acetamide), which is a beta-adrenergic agent that blocks beta receptors on the heart and slow it down and decreases the blood pressure [9]. Some side effects of atenolol have been found when it is used in treatment of hypertension including; indigestion, dry mouth, depression, hepatic dysfunction, constipation, confusion, insulin level disturbance, central nervous system side effect, gastrointestinal and cardiovascular dysfunction [16]. Among these side effects the main focus of study is to study the effect of atenolol on hepatic dysfunction. As it is reported to cause damage to the liver cells. Liver function tests (LFTs) are important clinical assay used in clinical laboratory to give information about the condition of patient's liver [17]. Aspartate transaminase (AST) also known as serum glutamic oxaloacetic transaminase (SGOT) is an important biomarker among these LFTs but it doesn't indicate the absolute dysfunction of liver as its value can also be increase in some other inflammatory conditions such as muscle damage [13]. However, it is most commonly used test in clinical laboratories. In this study the effect of atenolol is studies on liver dysfunction by measuring AST level from blood of 80 patients either treated with atenolol alone or with atenolol in combination with other hypertensive drugs. While 20 persons with random age and gender with blood pressure within normal range were taken as control. After

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blood sampling the serum was separated and AST level was measured by measuring the change in absorbance with time due to the conversion of NADH to NAD+ which was measured by using photometer at 340/400nm rate technique. The significant results were obtained as there was more increase in level of AST in patients treated with atenolol alone (mean value = 49.9) as compared to patient group treated with atenolol in combination with other anti-hypertensive drugs (mean value = 42.2) and control (mean value = 32). The effect of atenolol on hepatic dysfunction has found in literature, as one study has reported that out of 76408 people having side effects due to atenolol, 393 (0.15%) have abnormal liver function tests. While in sixty the rate of hepatic dysfunction increases while using atenolol. In females this chance of hepatic dysfunction increases while using atenolol [12]. Many other studies have also reported the hepatic dysfunction due to atenolol treatment for hypertension as one study has reported that in two patient's hepatic dysfunction was reported and in another complicated case the liver cirrhosis (acute hepatitis) was reported on administration of atenolol in hypertensive patient [18, 19]. Result of this study supports these previous studies of effect of atenolol on hepatic dysfunction by evaluating the AST value [20, 21].

CONCLUSIONS

This study has showed that atenolol may have efficacy in controlling hypertension but it also causes disturbance in AST levels so any other drug in combination with atenolol is recommended to use to control hypertension to avoid AST variation. Further this study can be performed on larger patient groups with more cases for validating the outcomes of this study.

Authors Contribution

Conceptualization: MFS
Methodology: MR, IS
Formal analysis: IT, SK
Writing-review and editing: MFS, IS, IT, SK

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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