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Relation of atenolol with development of myocardial infarction in hypertensive patients

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Abstract
Atenolol is one of the β-adrenergic receptor antagonists. It is widely used for the treatment of hypertension as a selective antihypertensive drug. However, long-term use of atenolol may cause myocardial infarction (MI). To prove the relationship between atenolol and myocardial infarction, measurement of creatine phosphokinase-MB (CPK-MB) enzyme as a diagnostic indicator in early and long-term usage of this medication by hypertensive patients is recommended. This study was conducted in Al-Thoura Teaching Hospital, Emergency Department, El-beida, Libya, on 30 hypertensive patients using atenolol. They were divided into two groups (A and B) according to the duration of the drug usage. Group A consisted of 15 patients with a mean age (56±6) years. They used atenolol for a period of 1-5 years. Group B also consisted of 15 patients with a mean age (60±6) years. They used atenolol for a period of 6-20 years. Both groups were with nearly the same number of males and females. Venous blood samples were taken in the first 8 hrs. after onset symptoms of cardiac attack from each patient and the levels of CPK-MB were estimated and compared between the two groups. There was a significant correlation between levels of serum CPK-MB of group A and group B (P<0.05). Atenolol caused an increased level of serum CPK-MB, and this increase was directly proportional to the duration of the drug usage. CPK-MB is one of the cardiac markers that is released from the heart muscle when it is damaged as a result of myocardial infarction. Thus, atenolol has a significant correlation with the development of myocardial infarction.

Keywords: hypertension, atenolol, β blocker, cardiac enzyme CPK-MB, Myocardial Infarction (MI)

1. Introduction
Atenolol is one of the β blockers that acts by blocking β receptors that are found in various parts of the body, and prevents the action of adrenaline and nor-adrenaline [1]. Atenolol is rapidly absorbed from the gastrointestinal tract (GIT). Blood level reaches a peak concentration in 2-3 hrs. [2]. Metabolism of atenolol is minimal and almost the total absorbed drug (85-100%) is cleared via excretion in the urine in an unaltered manner [3]. Even though atenolol is the drug of choice in different cardiovascular diseases such as angina pectoris, hypertension, arrhythmias and in the prevention of heart attack [4], the prolonged use of this drug as an antihypertensive may show different adverse effects which may develop to symptoms of cardiovascular diseases. CPK-MB is one of the isoenzymes of creatine kinase which is mostly found in the heart. We measured CPK-MB as an essential biological marker when it appears in abnormal level >10μ/L in serum. This means that there is a myocardial injury. CPK-MB shows an increase above normal in a person's blood test about 4-6 hrs. after the start of a heart attack. It reaches its peak level in about 18 hrs. and returns to normal in 24-36 hrs. [5]. CPK-MB is both a sensitive and specific marker for myocardial infarction, most commonly used to confirm the existence of heart muscle damage.

2. Materials and Methods
This study was done in the Emergency Department in Al-Thoura Teaching Hospital in El-beida, Libya from October 2018 to February 2019 on 30 hypertensive patients (48-68 years) who received atenolol tablet 100mg as an antihypertensive drug for a duration of 1-20 years. The patients were divided into two groups according to the duration of the drug use:
Group A: It comprised of 15 patients with a mean age (56±6) years. They used atenolol for a period of 1-5 years.
Group B: It also comprised of 15 patients with a mean age (60±6) years. They used atenolol for a period of 6-20 years.
Venous blood samples were obtained from each patient of both groups for measuring the level of CPK-MB. The method used for measuring CPK-MB is Immunoinhibition Assay (RANDOX) in which an antibody is incorporated in the CPK reagent. This antibody will bind to and inhibit the activity of the M subunit of CPK-MB. This means that only the activity of the B subunit in serum is measured [6, 7]. The sample is serum, heparinized, or EDTA plasma. Hemolysis interferes with the assay. Reagents are a mixture of CPK-MB Buffer/Glucose (Imidazole Buffer, Glucose, Mg-Acetate, and EDTA) with Enzymes/Coenzymes/Substrate/ Antibody (ADP, AMP, Diadenosine Pentaphosphate, NADP, HK, G-6-PDH, N-Acetyl Cysteine, Creatine Phosphate, and Antibody to CPK-MB). A patient sample is added to the reagent mixture to read the absorbance directly at 340 nm (A1). The second reading is after 5 minutes exactly (A2). $\Delta A = A2 - A1$
ΔA multiplied by 1651 (kit factor) gives the concentration of CPK-MB in μ/L. This procedure is done at room temperature 25ºC.

3. Results

After the collection and categorization of data from the 30 patients included in the study, statistical analysis was done (Table 1 and Figure 1), which revealed the following:

1. The correlation between atenolol duration 1-5 years and CPK-MB (μ/L) in patients included in the study {y= 2.4336x+2.5759, R2=0.236, r=0.486, P=0.066 (not significant)}.
2. The correlation between atenolol duration 6-20 years and CPK-MB (μ/L) in patients included in the study {y=-0.3751x+24.188, R2=0.277, r=-0.166, P=0.553 (not significant)}.
3. The correlation between atenolol duration of use (years) and CPK-MB (μ/L) in total 30 patients included in the study {y=0.9507x+9.3164, R2=0.1757, r=0.419, P=0.021 (significant direct correlation)} as shown in (Figure 2).

Table 1: CPK-MB (μ/L) concentration-atenolol duration of use (years) in hypertensive patients included in the study.

Atenolol duration of use (years)		1-5 years	6-20 years
CPK-MB (μ/L)	Mean	10.12	20.59
	SD	8.58	8.60
	Minimum	1.60	7.10
	Maximum	31.30	36.90

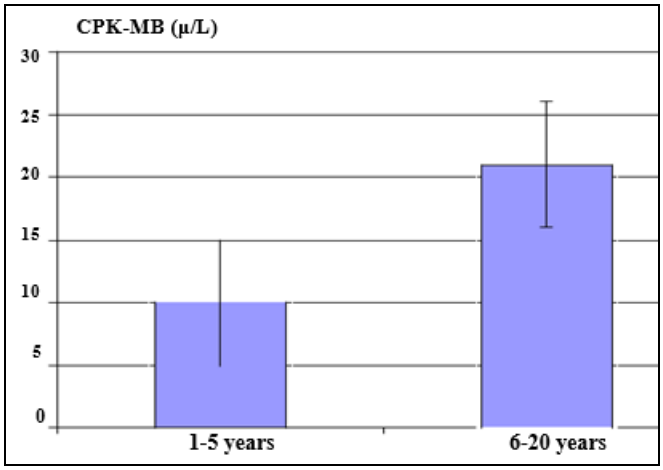

Fig 1: Correlation between time of atenolol usage and serum CPK-MB.

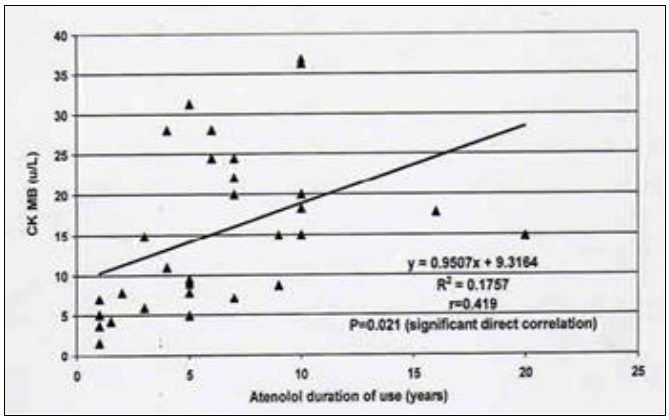

Fig 2: Correlation between atenolol duration of use (years) and CPK-MB (μ/L) in total 30 patients included in the study.

4. Discussion

Atenolol is widely used all over the world for the treatment of hypertension. It is an effective antihypertensive drug, however; it has many side effects which sometimes they might be serious. Enzymology is a diagnostic indicator for

cardiovascular disease in hypertensive patients with atenolol treatment [8]. CPK-MB is a primary indicator used to diagnose a heart attack because it exists in the highest amount in the heart that helps in converting creatine to creatinine, a reaction that is necessary for metabolism and energy production. Thus, the level of CPK-MB determines the effectiveness of the antihypertensive drug, which provides diagnostic clinical evidence [8]. Increase in the level of CPK-MB enzyme has been reported in hypertension with myocardial infarction patients [9, 10]. Enzymes always have been identified as a specific and sensitive marker of both clinical and subclinical myocardial injury [11]. Therefore, a biological marker such as CPK-MB to quantify myocardial injury has been widely used in clinical practice. In cardiac muscle, they are tightly bound to the contractile apparatus, and therefore, plasma concentrations are extremely low. In case of an acute myocardial injury, there is a release of CPK-MB into the serum, and the extent of the elevation in serum depends on the severity of the myocardial injury. And the entry of this enzyme in circulation depends upon the rate of passive diffusion of the enzyme from the myocardial infarct cells [12]. One of the most reliable and commonly tested cardiac enzymes is CPK-MB, which is specifically released from the injured heart muscle [13]. Increased serum levels of CPK-MB in hypertensive patients taking atenolol is directly proportional to the duration of the atenolol usage. Long exposure of cardiac muscle to atenolol leads to escape of CPK-MB to circulation. The mechanism by which atenolol causes myocardial injury is not yet known, and this may be due to the cardiac muscle which becomes fatigued with prolonged exposure to atenolol causing it unable to contract efficiently and ending with failure [14].

5. Conclusion

Atenolol should be used selectively and in acute and urgent cases for different cardiac diseases. For hypertensive patients of long-term usage, checking should be followed up continuously to make sure if any symptoms of cardiac injury appear and in such a case, termination of using atenolol and other antihypertensive drugs should be described.

6. Conflicts of Interest

We hereby declare that there are no conflicts of interest regarding the publication of this research article.

7. Acknowledgment

Data have been obtained from Al-Thoura Teaching Hospital, Emergency Department, El-beida, Libya. We would like to express our appreciation and thanks to all the participants in this research study.

8. Ethics

All patients provided written permission and consent before collecting data to conduct this research study.

9. References

1. Fisherman WH. Atenolol and timolol two newsystemic β-adrenoceptor antagonists, N. England J. Med. 1999; 306(24):1456-1462.
2. Fitzgerald JD, Ruffin R., Smedstad KG, Roberts R., *et al*., Studies on the pharmacokinetics and pharmacodynamics of atenolol in man, Eur. J. Clin. Pharmacol. 2010; 13:81-89.
3. Williams DA, Lemke TL, Foye WO. Foye's principles of medicinal chemistry, Hagerstown, MD: Lippincott Williams & Wilkins, 2002.
4. Rosendorff C., Black HR, Cannon CP, *et al*. Treatment of hypertension in the prevention and management of ischemic heart disease: A scientific statement from the American Heart Association Council for High Blood Pressure Research and the Councils on Clinical Cardiology and Epidemiology and Prevention, Circulation. 2013; 115:2761-88.
5. Book-Wu A. Editor. Cardiac Markers, Washington, DC: American Association of Clinical Chemistry (AACC) Press, 1999.
6. Szasz G., Busch EW. Paper presented at 3rd Eur. Congr. Clin. Chem., Brighton/England, 1979, 3-8 (abstract).
7. Wurburg U., *et al*. Clin. Chem. 1990; 54:357.
8. Kamble MM, Vaidya SM. Effect of antihypertensive drugs on cardiac enzymes in hypertension with myocardial infarction in NIDDNM, Indian Journal of Clinical Biochemistry. 2015; 17(2):60-63.
9. Stein W. Med. Weit. 2007; 36:572.
10. Yi-Chun Z., Yi-Zhum Z., Heidi S., Peter G., Thomas U. Substrate metabolism, hormone interaction and angiotensin converting enzyme inhibitors in left ventricular hypertrophy diabetes. 2009; 45(Suppl- 1):559-565.
11. Adams J., Abendschein D., Jaffe A. Biochemical markers of myocardial injury=1s MB creatine kinase, the choice for the 1990s? Circulation. 1999; 88:750- 763.
12. Burton ES, Robert R., Kenneth BI. Considerations in the use of biological markers of ischemic injury, Circ. Res. 1976; 38(Suppl-1): I-99-I-106.
13. European Heart Journal. 2004; 25(14): 1187-1196; doi: 1016/j.ehj.2004 04.026 copyright©2004 by the European Society of Cardiology, Role and Importance of Biochemical Markers in Clinical Cardiology.
14. Fitzgerald JB. The biological and clinical effect of atenolol (tenormin) a cardioselective beta antagonist. In Goldberg ME ed. Pharmacological and biological properties of drug substances, Vol.2, American Pharmaceutical Association, Washington, 2013, 98- 147.