

The Effect of Atenolol on CK-MB Levels in Hypertensive Patients[#]

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Abstract

Atenolol is one of beta-adrenergic receptor blocking agent. It is widely used for the treatment of hypertension as a selective antihypertensive drug. But long term usage of atenolol may cause one of the cardiovascular diseases like myocardial infarction. To prove the relationship between atenolol and cardiovascular disease, measurement of creatine kinase-MB as a diagnostic indicator in early and long term usage of this drug by hypertensive patients is recommended. A comparative study was conducted in Al-Yarmouk Teaching Hospital–Emergency Department- on 30 hypertensive patients using atenolol. They were divided into (2) groups A and B according to the duration of the drug usage. Group A- (15) patients with a mean age (56±6) years. They used atenolol for a period of (1-5) years. Group B- also (15) patients with mean age (60±6) years. They used atenolol for (6-20) years. Both groups were with nearly the same number of males and females. All subjects of the study groups were screened to exclude evidence of hyper or hypothyroidism, diabetes and chronic renal failure. Venous blood samples were taken in first 8 hours after onset symptoms of cardiac attack from each patients and the levels of creatine kinase-MB were estimated and compared between the (2) groups. There is a significant correlation between levels of serum creatine kinase-MB of group A and group B (P<0.05). Atenolol causes increased level of serum CK-MB and this increase was directly proportional to the duration of the drug usage. CK-MB is one of cardiac markers that released from heart muscle when it is damaged as a result of myocardial infarction. So, atenolol has a significant correlation with development of myocardial diseases.

Key words: hypertension , Atenolol and side effects , creatine kinase-MB , Atenolol antihypertensive.

الخلاصة:

التينورمين هو واحد من مجموعة الأدوية التي تعمل على غلق مستقبلات بيتا، وهو يستخدم بشكل واسع في معالجة ارتفاع ضغط الدم ولهذا فإن هذا العقار قد يصنف كدواء اختياري لتقليل ارتفاع ضغط الدم ولكن استخدام هذا العقار على مدى طويل قد يسبب حدوث واحد من امراض الجهاز القلبي الوعائي. ولإثبات العلاقة بين عقار التينورمين وأمراض الجهاز القلبي الوعائي بواسطة قياس أنزيم الكرياتين كينيس م ب ككاشف تحليلي على المدى القصير والبعيد لاستخدام هذا العقار لدى مرضى ارتفاع ضغط الدم، ولهذا أجريت دراسة مقارنة حالات في مستشفى البرموك التعليمي- قسم الطوارئ- على (30) مريضاً يعانون من ارتفاع ضغط الدم ويستعملون تينورمين كعلاج وتم تقسيم هؤلاء المرضى إلى مجموعتين (أ وب) وفقاً إلى طول فترة استعمالهم لعقار التينورمين. المجموعة (أ) وتتألف من (15) مريضاً، معدل أعمارهم (6±56) سنة واستعملوا التينورمين لفترة زمنية تراوحت بين (1-5) سنة والمجموعة (ب) وتتألف أيضاً من (15) مريضاً، معدل أعمارهم (6±60) سنة واستعملوا التينورمين لفترة زمنية تراوحت بين (6-20) سنة. كلا المجموعتين تقريباً تضم نفس العدد من كلا الجنسين، وكل المرضى المشمولين بهذه الدراسة غير مصابين بأمراض الغدة الدرقية ولا بداء السكري أو عجز الكلية المزمن. تم أخذ عينات من دم كل مريض خلال الساعات الثمانية الأولى بعد ظهور أعراض الأزمة القلبية لقياس مستوى أنزيم الكرياتين كينيس م ب وتمت مقارنة النتائج بين المجموعتين. كان معدل الأنزيم كرياتين كينيس م ب في مصل دم المجموعة (ب) مقارنة بالمجموعة (أ) عالية وبمعنوية واضحة P<0.05. ومن خلال النتائج التي تم الحصول عليها تبين أن عقار التينورمين يؤدي إلى ارتفاع وزيادة مستوى الأنزيم كرياتين كينيس م ب وهذه الزيادة تتناسب طردياً مع طول الفترة الزمنية لاستعمال التينورمين وبما أن هذا الأنزيم مؤشر حيوي خاص لأمراض الجهاز القلبي الوعائي، لذا فإن عقار التينورمين له علاقة بمعنوية بحدوث أمراض الجهاز القلبي الوعائي وخصوصاً احتشاء العضلة القلبية.

Introduction:

Atenolol is one of beta blockers acts by blocking beta receptors that are found in various parts of the body, and prevents the action of nor-adrenaline and adrenaline⁽¹⁾. Atenolol is rapidly absorbed from the gut. Blood level reached a peak concentration in (2-3) hours⁽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⁾. Although atenolol is the drug of choice in different cardiovascular

diseases as angina pectoris, hypertension, arrhythmias and in prevention of heart attack⁽⁴⁾. The prolong use of this drug as antihypertensive may show different side effect which may develop to symptoms of cardiovascular disease. Creatine Kinase-MB is one of the isoenzymes of creatine kinase which is mostly found in the heart. I measured creatine kinase-MB as an important biological marker, when it appears in abnormal level>10u/L in serum.

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This means that there is a myocardial injury. CK-MB shows increases above normal in a person's blood test about four to six hours after the start of a heart attack. It reaches its peak level in about 18 hours and returns to normal in 24 to 36 hours⁽⁵⁾. CK-MB is both a sensitive and specific marker for myocardial infarction, most commonly used to confirm the existence of heart muscle damage.

Materials and Method:

This comparative study was done in the Emergency Department in Al-Yarmouk Teaching Hospital on (30) hypertensive patients (48-68) years who received atenolol tablet 100mg as antihypertensive drug for a duration of (1-20) years. The patients were divided into (2) groups according to the duration of drug use:

Group A: consists of (15) patients with a mean age (56 ± 6), they used atenolol for a period of (1-5) years.

Group B: consists of also (15) patients with a mean age (60 ± 6), 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 CK-MB. The method used for measuring CK-MB is Immunoinhibition Assay (RANDOX) in which an antibody is incorporated in the CK reagent. This antibody will bind to and inhibit the activity of the M subunit of CK-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. Haemolysis interferes with the assay. Reagents are a mixture of CK-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-Acetylcysteine, Creatine Phosphate and Antibody to CK-M).

A patient sample is added to the reagent mixture read the absorbance directly at 340nm (A_1), the second reading is after five minutes exactly (A_2). $\Delta A = A_2 - A_1$

ΔA multiplied by 1651 (kit factor) gives the concentration of CK-MB in u/L. This procedure is done at room temperature 25°C.

Results:

After collection and categorization of data from the (30) patients included in the study, statistical analysis was done [table 1 and Fig.1] which revealed the following:

1. The correlation between atenolol duration 1-5 years and CK-MB (u/L) in patients included in the study ($y = 2.4336x + 2.5759$, $R^2 = 0.236$, $r = 0.486$, $P = 0.066$ (Not significant)).
2. The correlation between atenolol duration 6-20 years and CK-MB (u/L) in patients included in the study ($y = -0.3751x + 24.188$, $R^2 = 0.277$, $r = -0.166$, $P = 0.553$ (Not significant)).
3. The correlation between atenolol duration (years) and CK-MB (u/L) in total 30 patients included in the study ($y = 0.9507x + 9.3164$, $R^2 = 0.1757$, $r = 0.419$, $P = 0.021$ (significant direct correlation) as shown in Fig. (2).

Table(1) : The CK MB(u/L) concentration duration of use of atenolol in hypertensive included in the study

Atenolol duration of use (years)		1-5 years	6-20 years
CK MB (u/L)	Mean	10.12	20.59
	SD	8.58	8.60
	Minimum	1.6	7.1
	Maximum	31.3	36.9

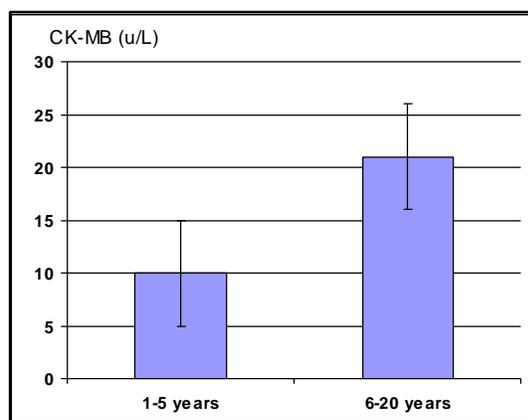
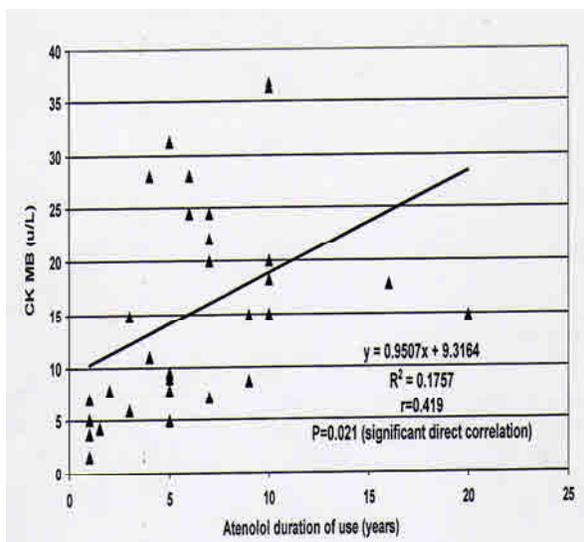


Figure (1) : Correlation between time of atenolol usage and serum CK-MB



Figure(2) : The correlation between the duration of atenolol treatment (years) and CK-MB (u/L) in total 30 patients included in the study

Discussion:

Atenolol is widely used all over the world for the treatment of hypertension. It is an efficient antihypertensive but 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⁾. CK-MB, the primary indicator used to diagnose a heart attack because it exists in the highest amount in the heart helps in converting creatine to creatinine, a reaction that is necessary for metabolism and energy production. So, the level of CK-MB determines the effectiveness of antihypertension drug which provides a diagnostic clinical evidence⁽⁸⁾. Rise in the level of this enzyme (CK-MB) has been reported in hypertension with myocardial infarction patients^(9,10). Enzymes always have been identified as a specific and sensitive markers of both clinical and subclinical myocardial injury⁽¹¹⁾. Therefore biological marker like CK-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 is extremely low. With acute myocardial injury, there is release of CK-MB into the serum, 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 infarct myocardium cells⁽¹²⁾. One of the most reliable and commonly tested cardiac enzyme is CK-

MB which released specifically from injured heart muscle⁽¹³⁾. Increased serum levels of CK-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 CK-MB to circulation. The mechanism by which atenolol causes myocardial injury is not yet known and this may be due to cardiac muscle which becomes fatigue with prolonged exposure to atenolol causing it unable to contract efficiently and ending with failure⁽¹⁴⁾.

Conclusion:

Atenolol should be used selectively and in acute urgent cases for different cardiac diseases. For hypertensive patients of long term usage checking should be followed continuously to make sure if any symptoms of cardiac injury appears and in such a case terminates using atenolol and other antihypertension drug should be described.

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