Effect of Lisinopril versus amlodipine on QTc-dispersion among patients with stage I hypertension

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الخلاصة:

الخلفية: تفرق QT المصحح هو الفرق بين أعلى و أدنى QT في ١٢ قطب لتخطيط القلب الكهربائي يمثل الاختلافية في أعادة الاستقطابية لبطين القلب و لنتيجة الخطر القلبي الوعائي.
الهدف: لتوضيح الاختلاف بين الليزينوبريل و الاملوديبين كعلاج لارتفاع ضغط الدم على تفرق QT المصحح وهكذا على نتيجة الخطر القلبي الوعائي.
المرضى وطرق البحث: ٥٠ مريض من المراجعين للعيادة الخاصة والذين لديهم ارتفاع معتدل في ضغط الدم (ضغط الدم الانقباضي ١٤٠-١٥٩ ملم زئبقي) أو (ضغط الدم الانبساطي ٩٠-٩٩ ملم زئبقي) ، ٢٥ رجل و ٢٥ امرأة مع متوسط عمر ٣٨ سنة ومتوسط وزن ٨١ كلغم . تم تقسيم المرضى عشوائيا إلى مجموعتين، كل مجموعة تحتوي على ٢٥ مريض .تم إجراء تخطيط القلب الكهربائي لكل مريض قبل وبعد إنهاء فترة العلاج . مرضى المجموعة الأولى استلموا عقار الليزينوبريل ١٠ ملغم يوميا كجرعة واحدة ، مرضى المجموعة الثانية استلموا عقار الاملوديبين ٥ ملغم يوميا كجرعة واحدة .العلاج استمر لمدة ١٢ أسبوع وتم حساب تفرق QT المصحح من خلال قياس أعلى و أدنى لفترة QT وتصحيحها.
النتائج: حساب تفرق QT المصحح لعقاري الليزينوبريل و الاملوديبين كان -٠,٠٣٠ و ٠,٠٣٢ على التوالي وبدون فرق معنوي [p>0.05].
الاستنتاج: هذه الدراسة لم تبين فرق معنوي بين عقار الليزينوبريل وعقار الاملوديبين من حيث التأثير على تفرق QT المصحح لدى مرضى ارتفاع ضغط الدم المعتدل

Summary:

Background: QT dispersion is the difference between maximum QT and minimum QT across the 12 ECG leads, it represent ventricular repolarization variability and cardiovascular risk outcome stratification .

Aim: To clarify the difference between lisinopril and amlodipine as anti-hypertensive drugs on QTc dispersion and thus the cardiovascular risk outcome stratification.

Patients and Methods: A 50 patients consulted the private clinic with newly diagnosed stage I hypertension [systolic BP = 140-159 mm/Hg and or diastolic BP = 90-99 mm/Hg] , 25 were males and 25 females with age mean was 38 years and body weight mean was 81 Kg . Patients were randomly divided into 2 groups , each group contained 25 patients . Group I received lisinopril 10 mg daily as a single dose , group II received amlodipine 5 mg daily as a single dose. Treatment continued for 12 weeks and at the end of the study , a 12 leads ECG was done for each patient and QTc dispersion was examined by measuring the difference between maximum and minimum QT interval and QT correction.

Results: Calculation of QTcD for both lisinopril and Amlodipine treated group was -0.030 and -0.032 respectively with no significant difference [P>0.05].

Conclusion : This study showed no significant difference between lisinopril and amlodipine in affecting QT dispersion among patients with stage I hypertension.

Introduction

QT dispersion [QTD] is defined as the difference between maximum and minimum QT on the 12-lead electrocardiogram [ECG](1). QTD values are calculated and corrected with Bazett,s formula = [corrected QTD = QTcD= QTD ⁄ √RR (2).Greater QTD usually represents more electrical heterogeneity and ventricular myocardium instability (3).Abnormal values are found in heart failure and after MI and are predictive of high rate of malignant arrhythmias and of sudden death (4).In the healthy elderly population , a raised QTcD > 60 milliseconds is associated with a 2 fold increase in sudden cardiac death (5).QTD is increased in left ventricular hypertrophy [LVH] (6) and hypertension and abnormal QTD may be an early indicator of end-organ damage involving the heart in hypertension (7).Since angiotensin II and aldosterone have been implicated in myocyte hypertrophy and cellular matrix modification (8). A relation between QTD and the extent of myo-cardial ischemia has been reported indicating a direct correlation between myocardial lactate extraction ratio[a metabolic marker of myocardial ischemia] and QTD in patients undergoing rapid atrial pacing (9). In both experimental animal and patient studies , it has been shown that the QT interval shortens in acutely hypoperfused areas , whereas in infarcted myocardium there is a prolonged repolarization time associated with QT prolongation on the ECG (10).There are some controversial data that QTD insignificantly decreases during positive dobutamine stress testing in patients with CAD or fails to correlate with changes in regional wall motion during dobutamine stress echocardiography (11).It is claimed that increased QTD is related to susceptibility to reentry ventricular tachyarrhythmia , independent of degree of left ventricular dysfunction or clinical characteristics of the patients suggesting that the simple , noninvasive measurement of this interval from a standard 12 – lead ECG makes significant contribution to identifying patients at risk for life-threatening arrhythmias after a previous myocardial (12).

Patients and methods: This study was conducted in private clinic, in al- Najaf al-Ashraf city from 7th of October 2009 to 7th of January 2010 . A 25 males and 25 females with average weight 81 kg and age 39 years old with newly diagnosed stage I hypertension [systolic blood pressure 140-159 and or diastolic blood pressure 90-99 mm of mercury] are enrolled in this study. Exclusion criteria included seated systolic BP > 200 mm Hg and known or suspected secondary hypertension . other exclusion criteria are subjects with cardiovascular , neurological and renal diseases . Each patient stayed for 5 minutes before BP measurement , using sphygmomanometer with 3 readings taken 1 minute apart average.

Study Design: This study was a randomized clinical study , a 50 patients with mild hypertension were divided into 2 groups , each group contained 25 patients. Each patient in The 1st group took lisinopril 10 mg single daily dose while in the 2nd group , each patient took amlodipine 5 mg as single daily dose. The treatment duration continued for 3 months. A standard 12- lead ECGs were recorded using a paper speed of25 mm ⁄ s .These were obtained at baseline and after completion of the study after 3 months of therapy and QTcD were measured for each patient before and after finishing the treatment.

Statistical Analysis: A probability value ≤ 0.05 was considered significant . Paired t-test was used between treatment groups.

Results

After exclusion of patients with bad quality ECG [atrial fibrillation , left bundle branch block , or ventricular ectopics] , QTD is measured by subtracting the minimal QT distance from maximal one . The QTcD was measured according to Bazett,s equation .

Table [1] shows the demographic characters:

Character	Lisinopril treated group	Amlodipine treated group
Male	12	13
Female	11	14
Body weight[Kg]	80.9	81.1
Duration of hypertension[yr]	8.5	9

Table [2] shows changes in blood pressure recording before and after 3 months of treatment

	Before treatment	After treatment	P-value
Lisinopril treated group	DBP= 95 mm Hg SBP= 150 mm Hg	DBP= 86 mm Hg SBP= 135 mm Hg	P< 0.05
Amlodipine treated group	DBP= 92 mm Hg SBP= 155 mm Hg	DBP= 83 mm Hg SBP= 130 mm Hg	P< 0.05

This table explain the significant systolic and diastolic pressure reduction in both lisinopril and amlodipine treated groups [p < 0.05].

Table [3] shows changes in QTcD from baseline with treatment

Parameter	Lisinopril treated group	Amlodipine treated group	P-value
QTcD value	-0.030	-0.032	P>0.05

This table shows no significant change in QTcD value in between lisinopril and amlodipine treated group [P > 0.05]

Discussion

This study showed no significant reduction in QT indexes within or between groups. Changes in QT dispersion in the lisinopril and amlodipine treated group did not relate to BP lowering , suggesting that at least some of this effect may be independent of anti-hypertensive effect. Amlodipine failed to significantly reduce QT indexes , the changes in QT indexes correlated positively with the corresponding reduction in SBP. Any agent that reduces BP may also reduce QT dispersion to some degree because of a mechano-electrical feedback mechanism (13). 6 months combination of ramipril and felodipine by Mayet and colleagues study showed alerting response may be partly due to sympathetic activation, which may have increased QT dispersion at baseline (14). Gonzalez-Juanatey and colleagues study reported a significant reduction in QT

dispersion with treatment. The positive result in their study may be partly explained by the significant increase in serum K+ that occurred which has been shown to reduce QT dispersion(15). Angiotensin II alters autonomic function through multiple pathways, including the release of catecholamines from the adrenal glands, stimulation of the cardiac and peripheral sympathetic nervous system and centrally reduction of vagal tone (16). A previous study from our group suggested a positive link between sympathetic activity and QT dispersion (17). Hypertensive individuals have an increased risk of sudden cardiac death (18). QT dispersion has been shown to be increased in LVH in hypertensive patients (19).

Conclusion and Recommendation: This study shows No statistical significant difference between lisinopril and amlodipine in QTD reduction in patients with mild hypertension.
Further studies are needed to determine whether effect of anti-hypertensive drugs on QTD is due to blood pressure lowering effect or related to myocyte hypertrophy or cardiac fibrosis.

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