The effects of amiodarone on QT dispersion in patients with atrial fibrillation

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ABSTRACT **OBJECTIVE:** This study evaluated the effects of amiodarone on the myocardial repolarization in the patients with atrial fibrillation. **METHODS:** QT dispersions measured from 12-lead standard surface ECG were retrospectively assessed in 48 patients treated with Amiodarone, and compared with that of paroxysmal atrial fibrillation and health groups. **RESULTS:** No disparity in QT interval and QT dispersion was found between paroxysmal atrial fibrillation and health group(QT:405 ±44vs397 + 30 ms. QTc:448 ±47vs424 ±26 ms, QTD 29 ±17vs27 ±16 ms, QTcD:28 ±19vs26 ± 18 ms, $P > 0.05$). However, compared with these two group, we found that both of the QT interval and QT dispersion significantly increased in Amiodarone group(QT:465 ±53vs405 ±44 or 397 ±30 ms, QTc:449 ±54vs448 ±47 or 424 ± 26 ms, QTD:47 ±20vs29 ±19 or 27 ±16 ms, QTcD:49 ±21vs28 ±19 or 26 ±18 ms, $P < 0.01$). **CONCLUSION:** Amiodarone not only effectively control atrial fibrillation with QT interval prolongation but also increased QT dispersion.

KEY WORDS amiodarone, atrial fibrillation, QT dispersion, QT interval

胺碘酮转复心房纤颤时对 QT 离散度影响

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摘要 目的:评价胺碘酮在治疗心房纤颤中对心肌复极的影响。方法:测量了 48 例用胺碘酮转复和维持治疗房颤患者的 QT 间期与 QT 离散度,并与 21 例阵发房颤和 43 例健康对照组比较。结果:阵发房颤动组与健康对照组 QT 间期和 QT 离散度无差异(QT:405 ±44vs397 + 30 ms. QTc:448 ±47vs424 ±26 ms, QTD 29 ±17vs27 ±16 ms, QTcD:28 ± 19vs26 ±18 ms, $P > 0.05$),但与前两对照组比,胺碘酮明显延长 QT 期间并使 QTD 增大(QT:465 ±53vs405 ±44 or 397 ±30 ms, QTc:449 ±54vs448 ±47 or 424 ±26 ms, QTD:47 ±20vs29 ±19 or 27 ±16 ms, QTcD:49 ±21vs28 ±19 or 26 ±18 ms, $P < 0.01$)。结论:胺碘酮不仅延长心肌复极,且使复极离散。

关键词 胺碘酮;心房纤颤;QT 离散度;QT 间期

Quinidine was used as a classic drug for prevention and cardioversion of atrial fibrillation, Nowadays, however, Quinidine has been substituted by Amiodarone[1,2] in managing atrial fibrillation due to its proarrhythmic effect and enhanced mortality in patients with atrial fibrillation. Amiodarone was found[3] to have less proarrhythmic effect and proven to be relatively safer. Good efficacy was observed from the therapy of atrial fibrillation with Amiodarone in our patients. We evaluated the effect of Amiodarone to determine its impact on myocardial repolarization.

Data and Method

Subjective: All the patients were documented atrial fibrillation with EKG or Holter from 1994 to 1999.

Exclusion criteria: ①patients with cute myocardiac infarction or unstable angina; ② patients with hyperthyroidism; ③patients under the treatment of other antiarrhythmic medications class Ⅰ-class Ⅳ; ④patients with impaired liver and renal function; ⑤ patients with uncorrected electrolyte disorders. The atrial fibrillation

Group had 48 patients with persistent atrial fibrillation, aged 19 ~ 62 (mean age 39.8 ± 11.9 years), and administered Amiodarone. In this group, there were 33 patients who had undergone cardiomyopathy or valve replacement, 6 patients with isolated atrial fibrillation, 5 patients with coronary artery disease, 2 patients with dilated cardiomyopathy and 2 patients with hypertension. 43 cases were with NYHA class Ⅰ ~ Ⅱ and 5 cases were with NYHA class Ⅳ. Control group included, patients with paroxysmal atrial fibrillation achieved cardioversion spontaneously and healthy subjects accoreling to physical examination. Twenty-one patients were with paroxysmal atrial fibrillation (male 14, female 7), age 30 ~ 70 years (mean age 51.4 ± 13.5 years). This group included 7 patients with coronary artery disease, 4 patients with valvular heart disease, 8 patients with isolated atrial fibrillation and 2 patients with hypertension. Twenty patients had NYHA class Ⅰ ~ Ⅱ and one had NYHA class Ⅲ. There were 43 healthy subjects (male 19, female 24), 18 ~ 61 years old (mean age 35.6 ± 15.3 years).

Method: Patients continued to take both medications for underlying diseases and anticoagulation (Aspirin and/or Ticlid). All patients who were examined to have no thrombus in the atrium by echocardiography were administered 200 mg 3 times a day for 7 days. Patients with atrial fibrillation resistance to Amiodarone underwent electrical cardioversion. They kept on the same treatment (i.e. Amiodarone 200 ~ 400 mg/d) to maintain the sinus rhythm if their cardioversions were successful.

QT interval and dispersion measurement: standard 12 lead EKG were done at paper speed 25 mm/s. An unique technician was required to measure QT interval in all leads during maintenance treatment. Three consequent QT intervals of QRS complex to termination of T wave.

Confirmed criteria: QT dispersion is defined as the maximum minus the minimum of QT interval in different leads. QT and QTD are adjusted by Bazzet equation. (i.e.: $QTc = QT \sqrt{R - R}$. QTcD = QTcmax - QTcmin).

Analysis: All data were analyzed in spss system. Ordinal data were reported as mean ± SD. $P < 0.05$ was considered significantly.

Result

Therapeutic effect: Eleven patients (23 %) in Amiodarone group were converted to sinus rhythm spontaneously in 7 days and the rest 37 patients were in electrical cardioversion. Sinus rhythm were maintained in 35 patients (73 %) in short term observation (10 days).

Side-effects: Ⅰ° AVB, Ⅱ° AVB occurred in one patient respectively (Both of them disappeared after decreasing dosage of Amiodarone). No fatal arrhythmia happened.

QT and QT dispersion: ①Paroxysmal atrial fibrillation group was similar to the control group on QT, QTc, QTd, QTCD ($P < 0.05$). ②There was significant difference between Amiodarone group and the other two groups on myocardiac repolarization parameters ($P > 0.01$).

Tab. 1 The effect of Amiodarone on QT and QT dispersion in patients with atrial fibrillation patients (ms)

Group	QT	QTc	QTD	QTcD
H/ n = 43	397 ± 30	424 ± 26	27 ± 16	26 ± 18
PAF/ n = 21	405 ± 44	448 ± 47	29 ± 17	28 ± 19
A/ n = 48	465 ± 53*	499 ± 54*	47 ± 20*	49 ± 21*

* $P < 0.01$, A vs PAF or H, H = health, PAF = Paroxysmal Atrial Fibrillation, A = Amiodarone

Discussion

Amiodarone is one of class Ⅲ anti-arrhythmia medications, It has property of high efficacy and safety. It seldom induces malignant proarrhythmia. It can also decline mortality of acute myocardiac infarction, consequently, it is considered one of the best anti-arrhythmia medication[3~5]. We found Amiodarone could effectively control chronic atrial fibrillation, though spontaneous cardioversion rate is low within one week (23 %). But it increased the successful rate by direct currently cardioversion. Moreover, it has satisfactory result in prevention from recurrence of atrial fibrillation in short term (10 days) about 73 %. Compared with class Ⅰ anti-arrhythmia medication which has more adverse effect of malignant proarrhythmia, it has mild side-effect on myocardism[6]. Here only one patient began to suffer IAVB and another patients had degree Ⅱ type Ⅱ AVB. No Torsade de points or ventricular fibrillation emerged.

The electrophysiology mechanism of medication inducing Torsade De points or ventricular fibrillation perhaps is based on prolonged myocardial repolarization and repolarization dispersion. Some authors[6,7] pointed out that the reason Amiodarone seldom induces arrhythmia resulted from its property on myocardiac repolarization. In

another words compared with type I anti-arrhythmic medications, it does not increase QT dispersion, thought it has similar effect to prolong QT interval.

So far, the effect of Amiodarone on QT dispersion is controversial. Cui. *et al*[6] reported Amiodarone could reduce myocardiac repolarization dispersion in coronary artery disease. His opinions was confirmed in patients with hypertrophic cardiomyopathy. However, Hii *et al*[8] showed that Amiodarone has no effect on repolarization dispersion in patients with coronary artery disease, and similar conclusion deduced from the latest data[9]. Our results are different from either of above, even from our predictive result. We found that Amiodarone prolonged myocardiac repolarization, and meanwhile increased myocardiac repolarization dispersion when it was administered in patients with chronic atrial fibrillation. The reason is still unknown. It may be due to underline disease, arrhythmia or dosage of Amiodirone. Further study is needed.

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