Efficacy and Safety Evaluation of Low- dose Sotalol on Atrial Fibrillation in the Elderly Patients of China

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ABSTRACT **OBJECTIVE:** To investigate the efficacy and safety of low- dose(80 ~ 160 mg/ d) sotalol on atrial fibrillation in the elderly patients of China . **METHODS**: Total 60 patients ,65 ~ 89 years old with atrial fibrillation entered the randomized study ,30 patients received sotalol and 30 received amiodarone . There were no significant differences in baseline clinical characteristics between groups . Patients randomized to sotalol began with 80 mg/ d . After first and second week ,the dosage was added 40 mg/ d for those who had not reached the responsible criteria , patients randomized to amiodarone began with 200 mg/ d , meanwhile 100 mg/ d would be added for those who had not reached the responsible criteria until the dose reached the maximum(400 mg/ d) . Holter monitoring was used to assess the arrhythmias . **RESULTS**: ①The total efficacy rate of sotalol was 63 .3 % and that of amiodarone was 62 .1 %($P > 0.05$) . ②Afterthe first week of treatment , the efficacy rate of sotalol reached 26 .8 % and that of Amiodrone was 10 .3 %($P < 0.05$) . ③There was signifcant relativity between efficacy rate of sotolol and average heart rate decreasing($r = -0.85$, $P < 0.001$) ,and there was also signifcant relativity between efficacy rate of sotalol and lengthened QTc interval($r = 0.74$, $P < 0.001$) . ④The accident rate of side effect of sotalol was 6 .7 % , no patients discontinued sotalol therapy . **CONCLUSION**: Low- dose sotalol(80 ~ 160 mg/ d) was efficient and safe in the Chinese patients with atrial fibrillation .

KEY WORDS sotalol ,arrhythima ,elderly ,clinical trial

低剂量索他洛尔治疗老年房颤的疗效及安全性评价

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摘要 目的 :探讨低剂量索他洛尔(80 ~ 160 mg/ d) 对老年房颤的疗效及安全性 。方法 :选择 60 例年龄大于 65 岁的房颤患者随机接受索他洛尔(施太可) 或可达龙治疗 。施太可的剂量每天 80 mg 开始 ,未达到疗效者每周增加 40 mg/ d ,直至达到疗效或剂量增加到 160 mg/ d 。可达龙组剂量每天 200 mg/ d 。未达疗效者每周增加 100 mg/ d ,直至达到疗效或剂量增加到 400 mg/ d 。疗效及不良反应采用临床及动态心电图结果评定 。结果 : ①施太可组及可达龙组治疗老年房颤的总有效率分别为 63 .3 %与 62 .1 %($P > 0.05$) ; ②治疗第一周后施太可组的有效率为 26 .7 %较可达龙组一周后的有效率 10 .3 %明显较高($P > 0.05$) ; ③施太可组房颤的有效率与平均心率下降呈显著的负相关($r = -0.85$, $P < 0.001$) 与 QTc 延长无显著的正相关($r = 0.74$, $P < 0.001$) ; ④施太可组有 2 例(6 .7 %) 出现轻度副作用 ,包括无力 、头晕 、耳鸣 ,均能耐受 ,无 1 例出现尖端扭转型室速 。结论 :低剂量索他洛尔(80 ~ 160 mg/ d) 治疗国人老年房颤的疗效确切 ,副作用少 ,无明显的致心率失常作用 。

关键词 索他洛尔 ;心律失常 ;老年人 ;临床试验

Sotalol is one of anti - arrhythmia medications which has property of both class Ⅱ and class Ⅲ. It[1] has been proven to be efficient in managing atrial fibrillation. The ESVEM investigator[2] and James AR[3] also showd the efficacy and safety of sotalol in treatment of cardiac arrhythmia. Harold L[4] reported that sotalol did not improve the mortality in patients after myocardial infarction. In thoughts of chinese patients are more sensitive to sotalol than west patients, especially in the elderly patients. This clinical trial is aided to evaluated the efficacy and safety of low - dose sotalol in managing atrial fibrillation of chinese elderly patients.

Data and method

Subjective: All the 60 patients aged > 65 years admitted from 10.97 to 5.2000 were documented atrial fibrillation with EKG or Holter, paroxysmal atrial fibrillation happened more than once a day and persistent atrial fibrillation lasted less than 6 months.

Exclusion criteria: ① patients with congenital or acquired longQT syndrome; ② patients with low blood pressure (SBP < 100 mmHg); ③patients with bradycardia(HR < 60); ④patients with SSS and Ⅱ or Ⅲ degree AVB without artificial cardiac pacemaker; ⑤patients with acute myocardiac infarction or unstable angina; ⑥ patients with impaired liver and renal function; ⑦patients with CHF (EF < 40 %); ⑧patients were allergic with β receptor blocker; ⑨ patients with diabete without being controled or severe COPD.

Total 60 patients were randomized into group A using sotalol and group B using amiodarone, In group A 30 patients aged 65 ~ 87 years(mean age 74.5 ±8.3 years), in this group(male 23, female 7), 24 patients with coronary heart disease, 3 patients with hypertensive heart diease, one patient with congenital heart disease, one patient with isolated atrial fibrillation, one patient with ischemick heart disease; In group B 30 patients aged 65 ~ 89 years(mean age 73.8 ±7.4 years), in this group(male 24, female 6), 22 patients with coronary heart disease, 3 patients with hypertensive heart disease, 3 patients with isolated atrial fibrillation, 2 patients with ischemic heart disease. There were no significant differences in baseline clinical characteristics between two groups.

Methods: Total 60 patients entered the randomized study. among whieh, 30 patients received sotalol and 30 patients received amiodarone. Patients randomized to sotalol began with 80 mg/d, after first and second week, the dosage was added 40 mg/d for those who had not reached the responsible criteria, patients randomized to amiodarone began with 200 mg/d, meanwhile 100 mg/d would be added for those who had not reached the responsible criteria until the dosage reached 400 mg/d. Holter monitoring was used to assess the arrhythmias. During 3 months of the treatment, at first 3 weeks, the patients should be monitored by EKG and blood preasure every day, and be examined by DCG and UCG every week. After reaching the criteria, the dosage would be reduced gradually to 80 mg/d(group A) and 200 mg/d(group B), the DCG and UCG had been takend every month. If the maximum dosage had been used for 2 weeks and the patients still had not reached the responsible criteria, we would discontinued the treatment.

Confirmed criteria: ① Efficient standard was atrial fibrillation disappeared; ② No reaching the efficient standard was the invalid standard; ③ According the Morganroth standard we can confirm the proarrhythmia caused by sotalol or amiodarone.

Data nalysis: All data were analyzed in Microsoft Excel, ordinal data were reported as mean ± SD, $P \leqslant 0.05$ was considered significantly, $QTc = QT/\sqrt{R-R}$.

Results

Therapeutic effect: One patient of group B discontinued the treatment because he appeared thyroid dysfunction, and others finished the course all. 19 patients(63.3 %) in group A reached to the responsible criteria, and 18 patients(62.1 %) in group B also reached to the responsible criteria($P > 0.05$). The relationship between the dosage and efficacy showed at Tab 1.

Tab. 1 The dosage and efficacy rate of group A and group B

Time	Group A/ $n = 30$			Group B/ $n = 29$		
	Dosage/ mg·d^{-1}	Efficacy n/ %	Percentage of total	Dosage/ mg·d^{-1}	Efficacy n/ %	Percentage of total
1st week	80	8(26.70)	42.10	200	3(10.30)	16.70
2nd week	120	7(23.30)	36.80	300	12(41.40)	66.70
3rd week	160	4(13.30)	21.10	400	3(10.30)	16.70
Total		19(63.30)			18(62.10)	

After first week treatment, the efficacy rate of sotalol was 26.7 % and amiodarone was 10.3 %, $P < 0.01$; two weeks later, the effficacy rate were 50 % and 51.7 %, $P > 0.05$

The change of BP, HR, QTc of two groups: In the group A, the BP and HR were declined obviously at the end of first week($P < 0.01$), but the declinement had not continued during following treatment. The QTc was prolonged after first week($P < 0.05$), but it had not the prolonged trend too. In the group B, the BP and HR also declined during the first week, but it had no statistical signification, two week later, HR declined obviously($P < 0.01$), but Bp had not the declining trend. The QTc was pronlonged obviously after first week($P < 0.01$) and second week($P < 0.01$), but after third week, this trend did not continous.

Tab .2 The change of BP , HR , QTc of two groups

Time	Group A				Group B			
	SBp	DBp	HR	QTc	SBp	DBp	HR	QTc
Before treatment	125 .65 ±16 .53	80 .52 ±8 .12	78 .56 ±8 .25	0 .38 ±0 .03	126 .85 ±80	81 .34 ±0 .80	8 .85 ±82	0 .38 ±0 .04
First week	115 .20 ±14 .20 *2	78 .20 ±7 .60	71 .23 ±7 .50 *2	0 .40 ±0 .04 *1	125 .80 ±16 .95	80 .48 ±3 .40	6 .55 ±20	0 .41 ±0 .03 *2
Second week	113 .40 ±13 .10 *1	76 .77 ±7 .60 *1	68 .14 ±9 .10 *1	0 .40 ±0 .03 *1	129 .45 ±16 .83	89 .85 ±8 .42	81 .62 ±6 .90 *1	0 .42 ±0 .04 *1
Third week	114 .23 ±13 .85 *1	76 .80 ±7 .60 *1	66 .85 ±4 .30 *1	0 .41 ±0 .03 *1	123 .23 ±15 .28	89 .40 ±8 .20	0 .53 ±8 .38 *1	0 .42 ±0 .04 *1

Compare with Before treatment : *1 $P < 0.01$, *2 $P < 0.05$

The UCG change :

Tab . 3 The UCG before and after treatment

Time	Group A			Group B		
	LA	CO	EF	LA	CO	EF
Before treatment	3 .85 ±0 .86	6 .45 ±1 .25	0 .63 ±0 .07	3 .76 ±0 .82	6 .63 ±1 .32	0 .64 ±0 .06
Two weeks later	3 .86 ±0 .83	6 .85 ±1 .0	0 .62 ±0 .08	3 .7 ±0 .810	6 .48 ±1 .28	0 .63 ±0 .08
Three months later	3 .82 ±0 .68	6 .5 ±1 .13	0 .6 ±0 .06	3 .78 ±0 .74	6 .82 ±1 .42	0 .62 ±0 .08

There were no significant differences in UCG in group A and B at the course of treatment .

Relativity: The relativity between the efficacy rate vs the average heart rate decreasing and the efficacy rate vs the QTc interval prolonged . Analyse those two relativities respectively , the first relativity modulus in group A was $r = -0.85$ ($P < 0.001$) and in group B was $r = -0.81$ ($P < 0.001$) , the second relativity modulus in group A was $r = 0.74$ ($P < 0.001$) and in group B was $r = 0.76$ ($P < 0.001$) , the above relativities were remarkable .

Side - effects :2 patients(6 .7 %) of group A were suffered from dizzy and fatigue , the symptom was relieved after patients taking appropriate solution , this phenomena never happened later . In group B , a patient discontinued treatment because of throid dysfunction six weeks later . No torsades de points emerged in two groups .

Discussion

Atrial fibrillation is the most common lasting arrhythmia in the elders and the occurrence is increasing with the age , In some data of elderly patients , the occurrence of atrial fibrillation was 15 %[5] , It can cause the rhythm of atrial and ventricle absonant , and decrease the cardiac output of left ventricle . The above phenomena is more severe in the elderly patients[5] .

We found that the total efficacy rate of low - dosage (80 ~ 160 mg/ d) sotalol in the elderly patients with atrial fibrillation was 63 .3 % and that of amiodarone(200 ~ 400 mg/ d) was 62 .1 % , $P > 0.05$. We also found that the efficacy rate was 26 .8 % after first week of sotalol , but amiodarone was 10 .3 % , $P < 0.05$. So we think the efficacy rates of two groups were similar , but the effect of sotalol got rapaidly than that of amiodarone .

Meanwhile , Tab . 2 show that Bp and HR in sotalol group decreased rapaidly after first week , but there were not a decreasing trend . It tells us that we should notice the change of Bp and HR during the first week , and it is necessary to adjust the drug dosage if the patients take the anti - hypertension drugs . The results of UCG show that the sotalol was safe in elderly patients , the main side - effects of sotalol is similar to those of other β receptor blockers , Daniel JM[6] reported that the side - effects of sotalal was 4 . 3 % . Tt appeared in early period , especially in three days early , but Torsade de point often emerges under large dosage(320 mg/ d) . We use low - dose sotalol in treating Chinese elderly patients with atrial fibrillation , and found no proarrhythmia happened .

In conclusion , low - dose sotalol(80 ~ 160 mg/ d) is effective and safe on Chinese elderly patients with atrial fibrillation , which is similar to amiodarone , but the effect of sotalol appeared early than that of amiodarone . Anyway , it is necessary to notice the change of HR and BP in early three days . Of course , further study is needed .

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