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MEDICAL TREATMENT OF RECURRENT ATRIAL TACHYARRHYTHMIAS

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Summary. *Recurrent and symptomatic atrial tachyarrhythmias require the necessity of an efficient and low risk medical therapy.*
The relation between dose, ECG surface parameters, left atrium size and clinical efficiency of Propafenone, Quinidine and Amiodarone has been studied on 215 patients with recurrent atrial arrhythmias. The average age was 62.7±11.3 years and as a fundamental disease they have: valvular disease – 23 patients, heart surgery – 5 patients, coronary heart disease – 168 patients, the preexcitation syndrome – 11 patients, other cardiopathy – 3 patients, apparent healthy heart – 2 patients.
The clinical and ECG monitoring has been done daily for the first seven days and then monthly.
Propafenone in an average dose of 542±141 mg/day administrated on 93 patients was efficient in 62.8 % of cases for 6 months, 32% for 9 months, 5.68% of patients required increasing of the dose, 8.33% presented side effects (digestive intolerance, transaminase elevation, weakness, visual disorders and ECG alterations: 33% PR prolongation with 93±7 and QT prolongation with 75±5.
Amiodarone administrated on 91 cases in an average dose of 245±108.7 mg/day was efficient at 93.4% of cases for 6 months, 85% for 9 months, with severe side effects at 4 patients (9.52%).
Quinidine has controlled the rhythm disorders at 87.5% of patients for 6 months and at 64.5% of patients for 9 months, its administration has been reduced for intolerance and QTc prolongation at 10.52% of cases at the beginning of therapy.
We haven't found any correlation between the drug efficiency and left atrium size ($p>0.05$).
The drug control of recurrent atrial tachyarrythmias as an alternative to surgical and ablation therapy is possible but is time limited at Propafenone (increased side effects through metabolism features) and is also limited by the side effects of the other two antiarrhythmic drugs..

Key words: *Atrial tachyarrythmias, treatment, antiarrythmic drugs*

Introduction

Atrial tachyarrhythmias such as atrial fibrillation (AF), atrial flutter (AFL) and supraventricular tachycardia (SVT) may occur in various underlying diseases, including valvular cardiopathies, cardiac ischaemic disease, dilated myocardiopathies and hyperthyroidism. They may also be observed in the absence of any detectable underlying heart disease or thyroid dysfunction. Treatments aimed restoring sinus rhythm seem, at best, to minimize the two major risks of atrial tachyarrhythmias: thromboembolic events and heart failure, and should be optimally proposed to most patients. Electrical transthoracic cardioversion remains the reference treatment but needs general anesthesia and prolonged anticoagulation before it can be performed (1).

Antiarrhythmic drugs can be used to control the ventricular response, to restore sinus rhythm (chemical cardioversion) or to maintain sinus rhythm after cardioversion (2). Effective maintenance of normal sinus rhythm using antiarrhythmic therapy reduces the risk of embolization.

The recurrent and symptomatic AF requires the necessity of an efficient, low medical therapy risk as an alternative of ablative and surgical therapy, which are difficult to access to (3).

Several controlled trials have been performed assessing the efficacy and safety of the antiarrhythmic agents in the maintenance of sinus rhythm.

The purpose of this study was to investigate the efficacy of 3 antiarrhythmic drugs: Propafenone, Amiodarone and Quinidine in prophylaxis of atrial tachyarrhythmias.

Methods

The clinical casuistry was composed of 215 patients (122 male and 93 female) with an average age of 62.7±11.3 years, being observed over the past 3 years in

the 2nd Department of Internal Medicine, the City Hospital Timişoara.

We started the antiarrhythmic therapy in the following chronic rhythm disorders:

- atrial fibrillation (AF) – 121 patients
- atrial flutter (AFL) – 41 patients
- supraventricular tachycardia (SVT) – 53 patients

The basic pathology was represented by: 23 patients with valvular prosthesis disease, 5 patients with interventions for other cardiopathies, 168 patients with coronary heart disease, 3 patients with dilated cardiomyopathy, 2 patients with apparent healthy heart and 11 patients with preexcitation syndrome.

We divided the patients into 3 groups: the A group included 121 patients with AF, the B group included 41 patients with AFL and the C group included 53 patients with SVT.

They were treated with propafenone with an average dose of 542±161mg/day, with quinidine with an average dose of 612±49.9mg/day and with amiodarone with an average dose of 245±108.7mg/day (Table 1).

Table 1. Treatment of patients with propafenone, quinidine and amiodarone

	Group A AF	Group B AFL	Group C SVT
Propafenone 542±161mg/day	60	10	23
Quinidine 612±49.9mg/day	19	2	10
Amiodarone 245±108.7mg/day	42	29	20
Total	121	41	53

The follow-up was daily for the first seven days and then monthly for a period of 10.5±3.7 months for propafenone, 16.5±9.9 months for quinidine and 26.7±17.5 months for amiodarone; 10 patients were Holter monitored.

We studied the dose efficiency, ECG surface parameters (QRS, QT, QTc, PR and RR in D2 or V2) and left atrium size, the efficiency and the side effects of medical treatment of AF versus the other supraventricular arrythmias.

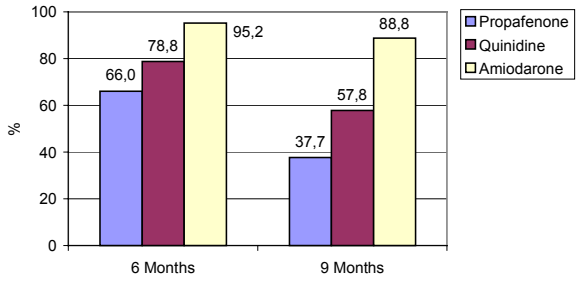
Results

We observed the time-efficiency of the medical treatment of AF:at 6 months, 49 patients (62.8%) treated with Propafenone (35 patients (66%) with AF) was restored at sinus rhythm comparative with Quinidine: 28 patients (87.5%) (15 patients (78.9%) with AF) and Amiodarone 85 patients (93.4%) (40 patients (95.2%) with AF), At 9 months 25 patients (32%) treated with Propafenone was restored at sinus rhythm (20 patients (37.7%) with AF) comparative with Quinidine: 20 patients (64.5%) (11 patients (57.81%) with AF) and Amiodarone: 77 patients (85%) (37 patients (88.8%) with AF) (Table 2).

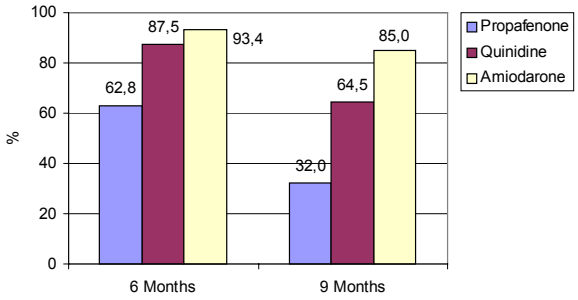
Table 2. The prolonged efficiency of the treatment (AF)

	6 Months	9 Months
Propafenone	AF 35 (66%) Total 49 (62.8%)	AF 20 (37.7 %) Total 25 (32%)
Quinidine	AF 15 (78.9%) Total 28 (87.5%)	AF 11 (57.8%) Total 20 (64.5 %)
Amiodarone	AF 40 (95.2%) Total 85 (93.4%)	AF 37 (88.8%) Total 77 (85%)

Treatment efficiency for AF



Tretmant efficiency for total arrhythmias



Major and minor side effects occurred at 24.76% of patients treated with propafenone (5 patients (8.33%) with AF) comparative to quinidine: 4 patients (6.45%) and amiodarone: 6 patients (6.59%).

The side effects of AF prophylaxis with Propafenone were:

- Major-PR prolongation with 40%-at 2 patients (3.8%)
  - Sinusal arrest > 2" -at 1 patient (1.6%)
  - total a-v block-at 1 patient (1.6%)
  - neurological dysfunction - at 1 patient (1.6 %)
- Minor-PR (93±7) and QT (75±5) prolongation at 19 patients (33%)
  - digestive disorders - at 1 patient (1.6%)
  - transaminase elevation at 1 patient (1.6%)
  - Atrial flutter occurred at 3 patients (5.7%)

We haven't found any correlation between the drug efficiency and left atrium size ($p > 0.05$).

The prophylaxis with propafenone for recurrent AF required dose elevation with 210±82.1mg/day at 5.68% of patients, at 3.2±3 months.

In the recurrent supraventricular arrhythmias controlled with propafenone, we observed: SVT prophylaxis required higher dose (562.25±150mg/day) versus

AF (491±108.6mg/day). The AF versus SVT recurrences were less frequent (p=0.04).

The major side effects of AF prophylaxis with amiodarone occurred at 4 patients (9.52%): pulmonary toxicity at 2 patients, hypothyroidism at 1 patient and liver enzymes elevation at 1 patient, comparative with quinidine: 2 patients (10.52 %) intolerance at 1 patient and QTc prolongation at 1 patient.

Discussion

In short-term therapy the first goal in the treatment of AF is to reduce and control the ventricular rate, to control the symptoms of arrhythmia, to reduce the risk of systemic embolization. Often is necessary treatment with digoxin, beta-blocking and calcium-channel-blocking agents (4). In long term therapy the main objective is induction and maintenance of sinus rhythm and to control the ventricular response rate, preventing thromboembolism with oral anticoagulation agents.

We consider that basic pathology of all studied patients had an important influence of the therapy response:

- In apparent healthy heart in which supraventricular arrhythmias were due to increased vagal tone the appropriate drugs used were propafenone and amiodarone and to increased sympathetic tone was quinidine (5).
- Studies performed on postoperative cases (cardiac surgery) treated with amiodarone and propafenone showed that they are equally efficient (6).
- In old patients with WPW-syndrome with left ventricular dysfunction amiodarone is used because it does not reduce ventricular contractility if it is orally given and it also has a decreased proarrhythmic action (7).

Propafenone prevent AFL and AF relapses without major side effects, but has negative inotropic effects (1,2,5). The side effects percentage for propafenone, which is higher in our casuistry than the literature data, could be explained by the metabolism feature: the pharmacodynamic profile of these drugs being dependent not only of the dose but also of the metabolism Brisoquine phenotype (Bryton). Effective therapy with quinidine may be limited by proarrhythmic properties (ventricular tachycardia, torsades de pointes) and sudden death (8). Amiodarone has no negative inotropic effects, but long term side effects could be relevant (pulmonary toxicity, hypothyroidism, liver enzymes elevation).

Early proarrhythmia can occur in different situations (overdose or suspending drug therapy and most often in coronary heart disease) and later proarrhythmia is often produced by quinidine. Amiodarone is still in study (9). Both class I and class III antiarrhythmic agents are associated with the risk of potentially lethal proarrhythmia, mediated either by arrhythmogenic early depolarization for drugs that delay repolarization (class IA or class III) or by blocking sodium channels and favoring reentry (class IA and class IC) (10, 11). Although quinidine increases the proportion of patients maintaining sinus rhythm after cardioversion of AF it also significantly increase the mortality rate (4). The mortality rates of amiodarone-treated patients in several available studies average 0.4% lower than that of a class I (12).

Conclusions

- Propafenone controls AF recurrences in a percentage of 66% for 6 months and in 37.7% for 9 months comparative with quinidine (78.9% for 6 months and 57.8% for 9 months) and amiodarone (95.2% for 6 months and 88.8% for 9 months).
- The efficiency of propafenone decreases in time: 5.6% of patients required dose elevation with 210±82.1mg/day at 3.2±3 months.
- The major side effects have similar incidence comparative between drugs but they are not so serious for propafenone. No malignant proarrhythmias have been diagnosed.
- The medical control represents an alternative to surgical and ablation therapy. It is time limited at propafenone and limited by the side effects at quinidine and amiodarone.

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TERAPIJA REKURENTNE ATRIJALNE TAHIARITMIJE

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Kratak sadržaj: *Povratna i simptomatska atrijalna tahiaritmija zahteva bolničko lečenje zbog efikasnosti i smanjenim rizikom.*
Relacija između doza, površnih parametara EKG-a, veličine levog atrijuma na jednoj strani i kliničke efikasnosti Propafenona, Hinidina i Amjodarona na drugoj, ispitivana je kod 215 pacijenata sa povratnom atrijalnom aritmijom. Prosečno godište pacijenta je 62,7±11,3 godina. Kao fundamentalna bolest preovlađivala je valvularna bolest (kod 23 pacijenata), operacija srca (5 pacijenata), koronarno oboljenje srca (168 pacijenata), ostale kardiopatije (3 pacijenta), izgled zdravog srca (2 pacijenta). Kliničko i EKG snimanje rađeno je jednom dnevno u prvih 7 dana a kasnije jednom mesečno.
Propafenon, u prosečnoj dozi 542±141mg/dan primenjen je na 93 pacijenta, efikasan u 62,6% slučajeva (za period od 6 meseci); 32% (9 meseci); kod 5,68% bila je neophodna veća doza; 8,33% pacijenata je imalo neželjene efekte (kontraindikacije) – poremećaj digestivnog trakta, transaminazna elevacija, slabost, poremećaj vida i promene EKG-a (33% PR prolongacije sa 93±7; QT prolongacije sa 75±5).
Amjodaron, primenjen u 91 slučaja, u prosečnoj dozi od 245±108,7mg/dan je bio efikasan u 93,4% slučajeva (period od 6 meseci); 85% slučajeva (za 9 meseci) sa jakim neželjenim efektima kod 4 pacijenta (9,52%).
Hinidin je kontrolisao poremećaje ritma u 87,5% pacijenata za 6 meseci i 64,5% pacijenata za 9 meseci, primena smanjena zbog neželjenih efekata i QTs prolongacije u 10,52% slučajeva na početku terapije.
Nismo otkrili nikakvu korelaciju između efikasnosti lekova i veličine levog atrijuma ($p > 0,05$). Kontrola lekova kod povratne tahiaritmije je moguća alternativa za operacionu i ablativnu terapiju, ali je ograničena vremenski kod propafenona (pojačana kontraindikacija u osobinama metabolizma). Takođe postoji ograničenje zbog neželjenih efekata kod drugih dvaju lekova.

Ključne reči: *Atrijalna tahiaritmija, terapija, antiaritmici*

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