ANTI-ARRHYTHMIC TREATEMENT AND ELDERLY – WHERE ARE WE NOW?

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Rezumat:

Fibrilatia atriala (FA), o tulburare de ritm de importanta majora, frecvent intalnita in practica medicala, este responsabila de cresterea morbiditatii si mortalitatii in populatia generala. In prezent, in SUA sunt diagnosticati cu FA 2.3 milioane de indivizi, preconizandu-se ca acest numar va creste la 5.6 milioane in anul 2050. Prevalenta FA se dubleaza la fiecare zece ani, ajungand la 9% la indivizii din grupa de varsta 80-89 de ani, avand astfel proportii epidemice (1). Riscul de a dezvolta un accident vascular cerebral in randul populatiei cu FA este de 1.5% la indivizii cu varsta cuprinsa in intervalul 50-59 de ani, si creste la 23.5% la indivizii cuprinsi in intervalul de varsta de 89-89 de ani (2,3). Cu toate ca diagnosticul de fibrilatie atriala nu ridica de obicei probleme, tratamentul adecvat insa, o face. Scopul acestei lucrari este de a discuta strategia terapeutica a fibrilatiei atriale in cadrul pacientilor varstnici, prevenind astfel trombembolismul.

Abstract:

Atrial fibrillation (AF), a common and serious cardiac rhythm disturbance, is responsible for substantial morbidity and mortality in the population. Currently about 2.3 million people in the US are diagnosed with AF and, based of the US census, this number is expected to rise to 5.6 million by 2050. It doubles in prevalence with each decade of age, reaching almost 9% at age 80–89 years. It has increased in prevalence over the calendar decades, reaching 'epidemic' proportions (1). The risk of stroke increases from 1.5% in patients with atrial fibrillation from 50–59 years of age to up to 23.5% for such patients aged 80–89 years (2, 3). Although the diagnosis of atrial fibrillation is usually straightforward, effective treatment is not. We aimed to discuss how rhythm control of atrial fibrillation can best be achieved in elderly patients, the controversy over the rhythm versus rate control, and prevention of thromboembolism.

Introduction

Atrial fibrillation is the commonest cardiac arrhythmia. It is associated with serious morbidity, mortality and significant health services utilization. It has been conclusively shown that patients with non-valvular atrial fibrillation have five times the risk of stroke over the general population with an absolute risk of 2–6% per year in those without a previous stroke and 12–13% in those who have had a previous cerebrovascular. Although thought not to be life threatening, its presence increases mortality by up to twofold (4, 5). The most important morbidity and mortality associated with atrial fibrillation result from stroke. The attributable risk of stroke increased from 1.5% for patients with atrial fibrillation aged 50–59 years to 23.5% for those aged 80–89 years. It is also associated with congestive heart failure. These result in a significant increase in the cost of health care in the community. Moreover, ischemic stroke secondary to atrial fibrillation carries about twice the risk of death in comparison with stroke from other causes (6, 7). Despite the high prevalence of atrial fibrillation and the increased morbidity and mortality associated with it, its treatment strategy remains less well defined. The present treatment of atrial fibrillation is based on four main principles: restoration of sinus rhythm, rate control, maintenance of sinus rhythm, prevention of thromboembolism (8, 9, 10). We studied the therapeutical options we had in treating atrial fibrillation in elderly patients and their evolution one year after their first admittance in our department.

Methods and results

A retrospective study of 1439 patients > 65 years admitted in our clinic in the last 18 months for cardiovascular diseases was conducted. 562 patients (39.05%) had atrial fibrillation as one of

the main diagnosis. There were no significant differences regarding the distribution according to gender (55% were women and 45% were men) or background (45% were from urban zone and 55% were from rural areas). The distribution according to age is represented in Table 1:

Age (years)	Patients with atrial fibrillation (%)
65 – 69	29.18
70 – 74	28.47
75 – 80	26.7
> 80	15.65

Table 1: Distribution of atrial fibrillation according to the age of patients

There were no significant differences regarding the distribution of atrial fibrillation according to the age of the patients.

Complete evaluation (clinical examination, ECG and echocardiography) divided our patients into two groups: Group A = 45 patients (8%) who were converted to sinus rhythm and Group B = 517 patients (92%) who did not have indication for conversion. The main indications for conversion to sinus rhythm in Group A were: onset of atrial fibrillation less than 1 year, normal dimensions of left atrium, high risk of embolism and persistence after correct treatment of the cause (e.g. hyperthyroidism, electrolyte imbalance).

The patients from Group B had no indication for conversion to sinus rhythm due to the following circumstances: 320 patients (62%) had atrial fibrillation older than 1 year associated with dilatative cardiomyopathy and heart failure (62%), 93 patients (18%) had hypertension associated with heart failure and recurrent atrial fibrillation, 52 patients (10%) had enlarged left atrium (> 55 mm) due to varied causes and 52 patients (10%) had counter-indications for anticoagulant therapy (e.g. recent stroke, peptic ulcer, recent surgery).

The main therapeutical goal in patients from Group B was controlling the ventricular rate at < 80 beats/minute with digoxin alone in 20 patients (4%) and with different associations of drugs such as: digoxin + α and β blockers (carvedilol) in 208 patients (41%) (especially in those with associated heart failure), digoxin + selective β-blockers (metoprolol) in 174 patients (33%), especially those with associated hypertension, amiodarone in 60 patients (11%), especially in those with recurrent atrial fibrillation and digoxin + diltiazem in 35 patients (7%), especially in those with myocardial ischemia. 20 patients (4%) did not need any rate control treatment as they had concomitant atrio-ventricular nodal disease and a convenient ventricular rate. In 59 patients (10.5%) the rate control treatment was followed by spontaneous conversion to sinus rhythm but we did not switch to other anti-arrhythmic drug in order to maintain sinus rhythm but continued the same treatment as before restoration.

The patients from Group A were reverted to sinus rhythm, 35 patients (78%) were reverted pharmacologically – subgroup 1 - and 10 patients (22%) had

electrical cardioversion – subgroup 2. Subgroup 1 received different antiarrhythmic drugs: 59% received amiodarone, 30% received propafenone and 11% received β-blockers. From the patients in subgroup 1 only 33 patients (73.33%) preserved sinus rhythm, most of them after treatment with amiodarone (90%). Unfortunately, 10 patients (33%) had negative side-effects after amiodarone: hypo/hyperthyroidism, pulmonary dysfunction and ocular disturbances which forced us to change amiodarone with another anti-arrhythmic drug, usually propafenone. Sub-group 2 was electrically converted to sinus rhythm and 8 patients (80%) maintained normal rhythm 1 year after conversion. We recommend amiodarone or propafenone for prophylaxis of recurrences, both drugs being well tolerated. The patients from both sub-groups that did not succeed to convert to sinus rhythm had the same therapy as patients from Group B.

Prevention of thromboembolism was another main goal of our treatment and anticoagulation therapy was considered for all our patients as guidelines recommend vitamin K antagonists (VKA) medications as the first line antithrombotic treatment for all patients with atrial fibrillation who have at least one risk factor for thromboembolism (Table 2).

Low-risk factors	Medium-risk factors	High-risk factors
Feminine gender	75 + years of age	Previous episodes of cerebral embolism
Hyperthyroidism	Hypertension	Mitral or aortic valve disease
Coronary artery disease	Congestive heart failure	Cardiac valve repair
	Left ventricular dysfunction by echocardiography (ejection fraction < 35%)	Post-valvuloplasty
	Diabetes mellitus	

Table 2: Risk factors for thromboembolism in patients with atrial fibrillation

The anticoagulant therapy was based on this classification of risk factors as presented in Table 3:

Risk factor	Treatment recommended	Number of patients	% patients
No risk factor	Aspirin OR Ticlopidine OR Clopidogrel	284	50.5%
1 medium-risk factor	Aspirin OR Acenocoumarol	195	34.6%
> 1 medium-risk factors OR any of the high-risk factors	Acenocoumarol	83	14.9%

Table 3: Anticoagulant treatment in patients with atrial fibrillation

Treatment with acenocoumarol was controlled by measuring twice a month INR values that should remain in the therapeutic range (between 2 and 3). A large number of our patients (all 195 patients with 1 medium-risk factor) that should have received VKA drugs remained on Aspirin due to difficulties in monitoring VKA treatment.

Discussions

AF is associated with a 50% to 90% increase in all cause mortality, principally due to excess risk of death from cardiovascular complications (including heart failure) and stroke. Being age-related, it is the 'new epidemic' of cardiovascular disease afflicting ageing societies. In the elderly, it is a particularly important risk factor for stroke, since both the incidence of stroke and the prevalence of AF rise with age, and is an important aggravating factor in the evolution of congestive heart failure (12).

AF accounts for more than 35% of all hospital admissions for cardiac arrhythmias in the United States (1). Our study reported that more than 1/3 (39.05%) of patients 65 + years of age admitted in our Geriatric Department in the last 18 months had atrial fibrillation. The prevalence of this arrhythmia was equally distributed according to gender, background and the age of the patients.

Restoration of sinus rhythm in AF patients confers many benefits to patients, including: symptom relief, improved exercise tolerance and haemodynamic function, avoidance of stroke and the inconvenience and risks of long-term anticoagulation, and the prevention of tachycardia-induced cardiomyopathy (9, 13, 14, 15, 16). In this respect, our goal was to evaluate which of our patients benefited from rhythm control versus rate control and anticoagulant versus antiaggregant therapy in order to prevent stroke and pulmonary embolism.

The evaluation of our patients was based on personal history, complete clinical, biochemical and imagistic examination which allowed us to assess the best therapeutical approach for each patient.

Unfortunately, many of our patients (92%) were unable to benefit from restoration to sinus rhythm, mostly because their arrhythmia was older than 1 year and was associated with severe co-morbidities such as hypertension, advanced cardiomyopathy and congestive heart failure. A rather small number (8%) were reverted to sinus rhythm, the majority preferred pharmacological cardioversion (78% - subgroup 1) and only a small number (22% - subgroup 2) required electrical cardioversion. We initiated antiarrhythmic treatment for both situations, in the first case (sub-group 1) in order to induce and maintain conversion and in the second (sub-group 2) in order to prevent relapses. Almost all the patients considered that pharmaceutical conversion is the best option even after receiving all the information about the advantages offered by the electrical conversion.

Antiarrhythmic drugs currently recommended were amiodarone (59%), propafenone (30%) and β-blockers (11%) and the most effective proved to be amiodarone – 90% of the patients treated with this drug preserved sinus rhythm after 1 year. We prefer amiodarone in elderly persons as many other authors (17, 18, 19) because it is easy to administer (once a day), induces no rebound if stopped accidentally and least but definitively not last, is cheap which is an important issue for elderly. The risk for side-effects is well monitored every 3 months by checking

4

thyroid, lung and eye function and we registered a rather high number of patients who experimented side effects (33% after 1 year) and needed replacement of therapy.

The large majority of our patients benefited from treatment to control ventricular rate without aiming to attain sinus rhythm by the administration of digoxin, β-blockers or nondihydropyridine calcium channel antagonists. Heart rate was considered controlled when it was 60–80 b/min at rest and 90–115 b/min during moderate exercise (six minutes walk test) and we noticed that there was a linear relationship between resting heart rate and life expectancy. A small number of patients had a convenient ventricular heart rate and required no antiarrhythmic treatment. An interesting item was that 10.5% of these patients reverted spontaneously to sinus rhythm once their ventricular rate decreased to normal range. We did not change for antiarrhythmic drugs and they preserved sinus rhythm after 3 months of treatment. It was important that we adjust drugs' doses according to creatinine clearance, especially for digoxin.

Our observations concluded that the rate control approach did not confer inferior quality of life compared with rhythm control therapy. Moreover, while administering rate control treatment it is still possible to spontaneously convert to sinus rhythm. It looks like the best approach in treating atrial fibrillation in elderly is to decrease ventricular rate and prevent embolism while evaluating if the patient has conditions for rhythm control therapy and not initiate per primam antiarrhythmic treatment. These conclusions are in agreement with recent studies who demonstrated no advantage in establishing and maintaining sinus rhythm with currently available therapies (14, 15, 16). If symptoms associated with rate control are not an issue, the focus of patient management should be redirected to optimizing the means of rate control, and more universal and better long-term thromboembolic prophylaxis (20, 21, 22).

In order to prevent embolic complications (especially stroke and pulmonary embolism) we initiated anticoagulant therapy in all patients with atrial fibrillation who have at least one risk factor for thromboembolism and had no major contraindications for VKA treatment. Unfortunately only a small part of our patients (14.9%) remained on anticoagulants, mostly because of difficulties in monitoring VKA treatment, the vast majority (85.1%) being on Aspirin or clopidogrel. Improving the medical services which would allow our patients to monitor anticoagulant therapy should one of our top priorities.

Conclusions

In our experience, the particularities of treatment in atrial fibrillation in elderly patients consist in:

- a smaller percentage of patients are able to benefit from rhythm control therapy due to late addressability to physician and severity of co-morbidities
- most of the patients would choose pharmacological conversion to sinusal rhythm versus electrical conversion and would be exposed from important side effects of antiarrhythmic drugs
- amiodarone was the drug of choice and the most effective antiarrhythmic option even if it had the most frequent side effects
- we preferred to lower the ventricular rate than to initiate conversion; this way gave us time to fully evaluate the patient and

5

decide the best therapeutic option according to echocardiographic parameters
- we tried to initiate anticoagulant treatment in all our patients with 1 risk factor for embolism but succeeded in a saddening low percentage due to difficulties in monitoring INR.

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