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Medical treatment of cardiac arrhythmias in Chagas' heart disease

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There are no controlled clinical trials evaluating drug therapy in patients with ventricular arrhythmias and chronic chagasic cardiomyopathy. Empirical treatment with disopyramide (400-1,000mg/d), phenytoin (4-6mg/d), mexiletine (600-1,200mg/d), propafenone (900mg/d), amiodarone (loading: 1,000mg/d, 10-14 days; maintenance 200-600mg/d), and sotalol (320mg/d) had efficacy and tolerance ranging from 18% to 90% with heterogeneous criteria for efficacy definition. Further studies with homogenous criteria are required to determine which is the most appropriate drug therapy for patients with chronic chagasic cardiomyopathy and ventricular arrhythmias.

UNITERMS: Chronic chagasic cardiomyopathy. Cardiac arrhythmia. Antiarrhythmic drugs.

INTRODUCTION

The objectives of the treatment of cardiac arrhythmias are relief of symptoms and prevention of sudden cardiac death. The therapeutic algorithms are born from controlled clinical studies, where

efficacy and tolerance of these drugs are conveniently tested in human beings. These information do not have the mistakes originated from clinical reasoning.

The results of controlled clinical trials have important influence in scientific community, sometimes demonstrating that decisions guided only by clinical intuition can be dangerous to the patients. A well-known example occurred during the CAST study. It was demonstrated that patients treated with class IC antiarrhythmic drugs, which are potent antiarrhythmic agents for ventricular arrhythmias, had two to threefold increase in the number of deaths when compared with those who received placebo (28).

The majority of these studies derived from patients with ischemic cardiomyopathy after myocardial infarction. Unfortunately, there are few relevant studies in our country

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evaluating patients with Chagas' disease when the use of an antiarrhythmic drug is to be considered.

CLASS I ANTIARRHYTHMIC DRUGS

Group IA drugs: Only procainamide, quinidine and disopyramide are commercially available in Brazil. There are no adequate studies evaluating the use of such drugs in Chagas' disease.

Slow-release procainamide is not available in Brazil. Given intravenously, it is useful during an episode of sustained ventricular tachycardia. A total dose of 20mg/Kg is administered at an infusion rate of 50mg/min.

Quinidine, is commercially available in 200 mg tablets for oral administration every 6 hour, in doses of 800-1,600mg/day. It reduces premature ventricular beats in 36-70% of the patients.

Disopyramide is commercially available in 100 and 250mg. Drug discontinuation is mandatory in 9% of the patients due to symptomatic bradyarrhythmias(1,22). Worsening of congestive heart failure, a condition very common in chagasic cardiomyopathy, limits its use in patients with ventricular dysfunction (19).

Group IB drugs: Lidocaine, mexiletine, and phenytoin are commercially available in our country. When intravenous administration is imperative and the ventricular arrhythmia is not responsive to procainamide, lidocaine can be used. The loading dose is 1-2mg/kg and the maintenance dose ranges from 20 to 60mcg/kg/min. Mexiletine is available in tablets of 200mg, and the daily doses ranges from 600 to 1,200mg divided in 3 times doses. Premature ventricular complex suppression was achieved in 32%-69% but 19% of these patients had side effects (14,15,27). Phenytoin is given orally, in doses of 4-6mg/kg/day (3 times daily) and efficacy was demonstrated in 18% of 11 patients tested (27).

Group IC Drugs: Flecainide and encainide were described as potent suppressers of premature ventricular beats (2). However, a subsequent multicentric trial showed that these drugs should not be administered in patients with poor left ventricular function (9,28). Propafenone, another IC drug, is utilized orally (900mg/day), 3 times daily with efficacy and tolerance in 41%-66% (5,20).

It is important to stress that metanalysis of controlled studies of group I drugs in patients with ischemic cardiomyopathy delineated an increase in mortality in patients treated with these drugs when compared with a placebo group (29). Their use in chagasic cardiomyopathy, is indicated only to relief symptoms in selected cases.

CLASS II ANTIARRHYTHMIC DRUGS

In spite of being the most effective drugs in preventing sudden cardiac death (29), the beta blocker have only moderate efficacy in controlling ventricular arrhythmias (39-56%). There are no clinical studies with these drugs in Chagas' disease: alterations in automatism, conduction and left ventricular dysfunction, will restrict the use of these drugs only for selected cases.

CLASS III ANTIARRHYTHMIC DRUGS

Experimental data and results of clinical studies changed the trends of using sodium channel blocker (class I drugs) to drugs that prolong the repolarization time (class III drugs). At the present time, there is not a drug with exclusive class III action in clinical use. Amiodarone, a drug with multiple actions, and sotalol, a non selective beta blocker, have potent class III action, and are included in this group.

Amiodarone has been empirically used in our country in all kinds of arrhythmias. Unfortunately there are no controlled studies evaluating efficacy of this drug in chagasic cardiomyopathy. In non-controlled studies, the number of premature ventricular beats decreased in 35-92% of the patients evaluated with few side effects (3,4,13,21). The doses utilized in the majority of studies varied from 600 to 1,200 mg for 14 days (loading phase), followed by a medium doses of 400mg (maintenance phase).

Patients with chronic chagasic cardiomyopathy and sustained ventricular tachycardia are at major risk for sudden death. In our experience, criteria of efficacy according to Holter monitoring was found in 52% of patients. When electrophysiologic study was used to assess efficacy, ventricular tachycardia was not reinducible in 18% of the patients (11). None of these methods was able to predict clinical efficacy of this drug. The worst prognosis during amiodarone therapy was observed in patients with congestive heart failure (6,24).

Sotalol, another class III antiarrhythmic drug, also has a beta-blocker action, had better efficacy and tolerance than class I drugs (16). This drug was recently reintroduced in our country, and we observed 67% efficacy in 14 patients with Chagas' disease and sustained ventricular tachycardia refractory to drug therapy (12). Like amiodarone, its use must be extremely cautious in patients with bradyarrhythmias.

Finally, it is important to stress that ventricular function is the most important clinical variable influencing the prognosis of patients with Chagas' disease and complex ventricular arrhythmias (17,18). Patients with refractory ventricular arrhythmias, specially sustained ventricular

tachycardias can be studied with the electrophysiological (7) techniques. Surgical (26) or catheter ablation (10) of an arrhythmogenic focus of ventricular tachycardia and implantation of a cardioverter-defibrillator can be indicated in patients refractory to all therapeutic options (8).

RESUMO

Apesar da grande importância da cardiopatia chagásica em nosso meio, não existem estudos clínicos controlados que avaliem adequadamente as opções terapêuticas nessa patologia. Foram testadas disopirâmida (400-1.000 mg/dia), difenilhidantoína (4-6 mg/kg/dia), mexiletina (600-1.200 mg/d), propafenona (900 mg/d), amiodarona (impregnação: 1.000 mg/dia/10-14 dias; manutenção: 200-600 mg/d) e sotalol (320 mg/dia) com níveis de eficácia e tolerância variando de 18 a 90% dependendo das definições empregadas. Estudos comparativos controlados poderão esclarecer futuramente as melhores estratégias farmacológicas para o tratamento dessa entidade nosológica.

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