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RECENTS ADVANCES IN THE CLINICAL TREATMENT OF CHRONIC CHAGAS' MYOCARDITIS

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The clinical treatment of chronic Chagas' myocarditis (CCM) is oriented toward the two major complications of this cardiopathy: 1) congestive heart failure (CHF); 2) cardiac arrhythmias (Prata, Andrade & Guimarães, 1974).

The major problem in the treatment of the CHF of CCM is mainly dependent of the severe inflammatory and/or fibrotic myocardial lesions which make these patients very sensitive to digitalis and compensation difficult. Even very low oral doses of digitalis like 0.125 mg of Digoxin every day may ensue the appearence of complex ventricular arrhythmias, ventricular bigeminal rhythm being the most common. The limited amount of digitalis these patients may tolerate make the use of diuretics the basic tool for their treatment. However, high doses of a potent diuretic like furosemide leads to hypokalemia giving origin or worsening pre-existing ventricular arrhythmias.

The introduction of vasodilators for the treatment of CHF was of real benefit for the compensation of these patients. It became easier to bring these patients from functional class IV to class II when these drugs were associated with oral doses of digitalis as low as 0.125 mg of Digoxin every day or every other day and daily oral doses of 40 to 80 mg of furosemide. In patients with severe peripheral edema and ascites, intravenous digoxin and furosemide may be initially necessary. This new therapeutic approach shorten significantly the hospitalization time (4 to 5 weeks to 2 to 3 weeks) bringing the cost of treatment down.

Presently, the most used oral vasodilator at the University of Bahia Hospital is prazosin, an alpha-1 blocker with a slight predominant peripheral venous action. It leads to a simultaneous decrease in pre-load and after-load, what reduces ventricular diameter and facilitates ventricular ejection, respectively; both actions also decrease myocardial oxygen consumption what may further enhances ventricular function. The usual initial dose of prazosin is of 0.5 mg every six hours, increasing progressively every two days until a satisfactory response is obtained; the average daily maintenance dose has been around 6 to 8 mg but doses as high as 15 to 20 mg daily may be occasionally necessary. It should be pointed out that the initial hypotensive reaction sometimes observed in the treatment of arterial hypertension with this drug (Stanaszck et al., 1983), has not been observed in these cases of CHF. However, it is important to monitor blood pressure response to increasing doses of prazosin, both supine and standing; systolic blood pressure below 100 mmHg should be avoided in order to assure proper myocardial perfusion. Due to the high cost of prazosin, isosorbide dinitrate (40 mg t.i.d.. orally) has been employed as an alternative vasodilator after hospital discharge also with a satisfactory response. It should be emphasized that any other oral vasodilator available may be helpful for the treatment of the CHF of CCM provided it doesn't show a negative inotropic effect. Then further experience with drugs like captopril, enalapril, indoramine and hydralazine would be desirable.

Treatment with oral vasodilators must be started as soon as possible after patient admission, simultaneously with diuretics, digitalis, a low sodium diet (2 g of NaCl per day) and bed rest.

For patients in cardiogenic shock, the intravenous infusion of nitroprusside for 24 to 72 hours associated with digitalis and diuretics may be lifesaving.

In patients who need doses of furosemide higher than 80 mg per day, a better diuretic response can be obtained by the simultaneous use of a distal tubule diuretic like hydrochlorotiazide (50 mg) and an aldosterone inhibitor like spironolactone (50 to 100 mg). The use of this latter drug is also convenient by its potassium sparing property.

Sometimes, refractoriness of CHF in CCM is secondary to recurrent pulmonary embolism, a common complication in this condition (Rocha & Andrade, 1955). So, in patients with severe systemic venous congestion it is advisable the use of I.V. heparin (a loading dose of 10.000 U followed by 5.000 U or more, every 6 to 4 hours) in order to prolong the coagulation time beyond twenty minutes until a satisfactory degree of cardiac compensation is reached. In the great majority of these patients oral anticoagulation after hospital discharge, despite indicated, is not advisable due to their very low social and cultural conditions.

Even with these therapeutics interventions there is no proof of increased survival once these patients went in advance CHF. Indeed, at this stage, response to treatment tended to be limited by the severity of myocardial lesions and of chambers dilation. A better outlook, however, may be possible, in the future, if the patient with a dilated heart is identified and treated with digitalis and vasodilators before clinical manifestations of heart failure appears.

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Brady and tachyarrhythmias and ventricular premature beats (VPBs) are common in patients with CCM, not necessarily associated with CHF and may occur in the absence of cardiomegaly (Prata, Andrade & Guimarães, 1974). Complex VPBs (bigeminal, multiforms, couplets and salvos) occur in 60 to 80% of those patients with VPBs in the standard 12 lead ECG at rest (Maguire et al., 1981).

Because sudden cardiac death is a common cause of mortality in this disease adequate antiarrhythmic treatment is of paramount importance.

The choice of an antiarrhythmic drug for patients with CCM is a difficult task because of the frequent association of a low myocardial contractile reserve with a sick sinus node and/or AV nodal-His-bundle conduction defects (Prata, Andrade & Guimarães, 1974).

With the advents of drugs like amiodarone, disopyramide, mexiletine, propaphenon and verapamil the outlook of these patients markedly improved. Since these drugs may present side-effects leading to its temporary or permanent withdraw it is desirable to test the patient response to more than one of them, if possible to all five. A satisfactory suppressive effect has been observed with all these drugs, with a significant decrease in the number of VPBs and disappearence of couplets or salvos what constitutes the ultimate goal of antiarrhythmic therapy in order to prevent sudden cardiac death.

Clinical experience is greater with amiodarone and mexiletine, specially the former one, because in their usual therapeutic doses they don't show either a negative inotropic or a significant depressant dromotropic effect (Almeida, Guimarães & Maguire, 1983; Santana, Guimarães & Maguire, 1982). On the other hand experience with disopyramide, propaphenon and verapamil is very limited (Albanesi Filho et al., 1979; da Silva et al., 1981; Vichi et al., 1977); these drugs possesse a strong negative inotropic and dromotropic action, their use being avoided in patients with cardiomegaly and/or A-V conduction disturbances. Except for mexiletine, all these drugs may cause severe bradychardia, eventually requiring permanent pecemaker implantation. Indeed, mexiletine seems to be the safest antiarrhythmic medication for the chagasic patient but its long-term use is limited by frequent gastrointestinal intolerance. In addition, its effective antiarrhythmic action lasts only 8:00h making its regular use imperative for a full protection of the patient. For the low social class patients who frequently take these drugs irregularly this is a very important point. In this regard amiodarone is the drug of choice because of its cumulative effect with a very low disappearence rate.

Amiodarone has been used in an average loading oral dose of 600 mg a day for 10 days, followed by a maintenance dose of 400 mg once daily; loading doses as high as 1200 mg may be eventually needed and maintenance doses may vary from 200 to 800 mg per day (Almeida, Guimarães & Maguire, 1983). In severe forms of ventricular arrhythmias, when a prompt antiarrhythmic effect is needed a drug with a faster beginning of action like mexiletine must be associated to amiodarone; subsequently it may be withdraw or maintained what may allow lower maintenance doses of both drugs. The prolonged use of amiodarone may be associated with vision loss due to crystals deposition in the cornea and crystalin, with hypo or hyperthyroidism and with pneumonitis (Fogoros et al., 1983). These side-effects are usually reversible with drug withdraw (Almeida, Guimarães & Maguire, 1983; Fogoros et al., 1983).

Average therapeutic doses of disopyramide are 100 mg every 6 hs (Albanesi Filho et al., 1979), mexiletine 200 mg every 8 hs (Santana, Guimarães & Maguire, 1982), propaphenon 300 mg every 8 hs (da Silva et al., 1981) and verapamil 80 mg every 8 hs (Vichi et al., 1977).

Proper antiarrhythmic treatment of chagasic patients will require an adequate diagnosis and drug response evaluation. Whenever possible, their work-up must include an exercise stress test and a 24:00 h E.C.G. monitoring before and after drug therapy. Nevertheless, when these facilities are not available, the disappearence of VPBs in the standard 12 leads E.C.G. (Maguire et al., 1981), and of symptoms like bouts of palpitation and/or syncope or pre-syncope may be used as clues for a good antiarrhythmic drug effect.

Symptomatic patients with a sick sinus node and severe bradychardia or patients with third degree A-V block require permanent pacemaker implantation. Thereafter, the outlook of patients with third degree A-V block and without cardiomegaly definitively improved; on the other hand, in patients with severe cardiomegaly (CTR $\geqslant$ 60%) a progressively downhill course may be frequently observed after pacemaker implantation (Esteves et al., 1975). In these severely dilated hearts the deleterious influence of a faster heart rate with a consequent increase in oxygen consumption and the beneficial effect of a properly timed atrial contraction through the implantation of a sequential pacemaker needs evaluation.

As mentioned before, pacemaker implantation may also be required by patients who develop severe bradychardia or advanced A-V block while on antiarrhythmic therapy.

In spite of all these advances for the clinical treatment of patients with CCM, once severe myocardial lesions become established the patient is condened to chronic disability and premature death. In order to avoid this stage of the disease primary prevention must be, of course, the ultimate goal. Once, however, the individual become infected, a better understanding of the pathogenesis of the chronic myocarditis may lead to therapeutic measures that can stop the disease before the advanced and irreversible stage of difuse myocardial involvement is reached.

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