COMPARATIVE STUDY BETWEEN

AMIODARONE - VERAPAMIL - PROPRANOLOL

IN THE CONTROL OF VENTRICULAR RATE

IN PATIENTS WITH CHRONIC RHEUMATIC ATRIAL FIBRILLATION

THESIS

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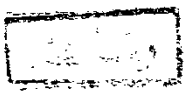

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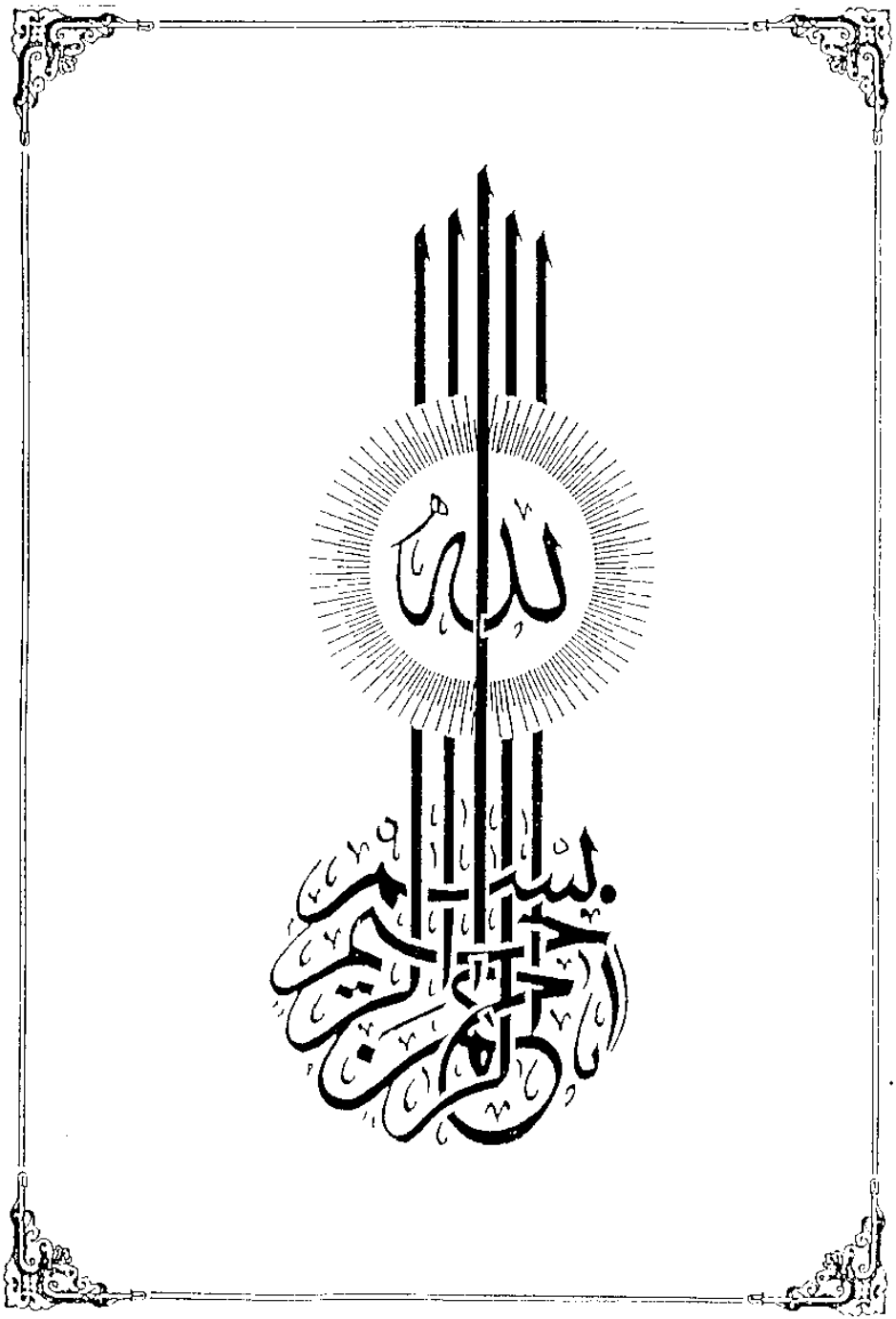

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INTRODUCTION & AIM OF THE WORK

The long-term treatment of atrial fibrillation should mainly directed to slow the ventricular rate.

Digoxin is the most commonly used cardiac glycosides and is considered the drug of choice in the long-term treatment of atrial fibrillation.

Frequently, Digoxin alone is not enough to control the rapid ventricular rate. In haemodynamically stable patients, Amiodarone, propranolol or Verapamil may be given orally in combination with Digoxin to control the ventricular rate more effectively.

The aim of our study is to compare the effects of Verapamil, Propranolol and Amiodarone in digitalised patients with chronic rheumatic atrial fibrillation.

CHAPTER I: REVIEW OF LITERATURE

A. Chronic Rheumatic Heart Disease

CHRONIC RHEUMATIC HEART DISEASE

The clinical features of rheumatic fever and the subsequent chronic rheumatic heart disease and its complications have a great geographic variation, with a high frequency in certain parts of the world including Africa, Asia and the economically underprivileged areas.

(Reference 22)

The course of the disease can be malignant and accelerated so that a well established mitral valve disease occurs in childhood, the mitral valve is involved in about 85% of cases, the aortic valve in 54%, the tricuspid and Pulmonary valves are less than 5% of cases.

In 1972. Gordis and Markwitz reported that the rheumatic valvular disease occurs in the following order of frequency:

1) Mitral valve insufficiency (M.I.)
2) Dominant M.I. with mitral stenosis (M.S.)
3) Aortic insufficiency (A.I.) with mitral valve disease.
4) Isolated aortic valve disease.
5) Dominant M.S. with or without M.I.
6) Tricuspid valve disease with insufficiency secondary to pulmonary hypertension due to left-sided valvular lesion.
7) Tricuspid stenosis usually associated with mitral and aortic valve disease.
8) Pulmonary valve insufficiency secondary to pulmonary hypertension due to left sided lesion.

(Reference 22)

In the process of healing of the rheumatic myocardial lesions, varying degrees of interstitial fibrosis results.

Subacute or chronic carditis may modify the course of the disease by intensifying the myocardial dilatation which has resulted from the haemodynamic effects of the valvular lesions.

Acute rheumatic carditis may heal with a few residual effects, as a minor degrees of fibrosis in the valvular endocardium, vascularization of the valve leaflets, thickening of the cordae tendineae and small myocardial perivascular scars.

(Reference 22)

Those lesions may not progress or lead to abnormal haemodynamic effects, but the valves are still susceptible to endo-carditis and it is very much possible that episodes of subclinical carditis can occur with the resultant chronic rheumatic heart disease, as many adults with rheumatic heart disease deny any earlier acute episodes.

(Reference 22)

Chronic rheumatic heart disease with mitral valve insufficiency is the commonest lesion found in children and adolescents, but an associated organic M.S. is difficult to exclude in the majority of cases. The healing process with the resultant fibosis of the valve leaflets, contracture and valvular shortening is the common sequence so that the leaflets can not coapt. The left atrial enlargement also will lead to a further separation initiating a vicious cycle with increase in the degree of M.I.

(Reference 11)

A secondary M.I. also may result from a left ventricular enlargement due to aortic valve disease due to the displacement of the papillary muscles and elongation of the chordae tendineae which accompanies the left ventricular dilatation.

(Reference 11)

The left atrium is always enlarged in patients with M.I. and generally larger than in patients with M.S., but the maximum atrial volume is a poor guide to the severity of M.I. On the other hand, the change in atrial volume during cardia cycle is increased in M.I. and it is related to the severity of the insufficiency.

This large cyclic change in atrial volume does not depend on atrial contraction, as it occurs passively early in diastole, only a small increment of atrial emptying that results from atrial contraction is lost when atrial fibrillation (A.F.) develops.

(Reference 11)

The left-ventricular systole in M.I. patients will result in blood regurgitation into the left atrium. In cases of moderate to sever M.I. the regurgitant flow will lead to increase in the pressure and volume of left atrium, this will be transmitted to the pulmonary circulation with increase in both pulmonary venous and atrial pressures with increase in the pulmonary vascular resistance and the resultant pulmonary hypertension with right ventricular hypertrophy and dilatation.

(Reference 11)

A secondary tricuspid insufficiency and sometimes pulmonary valve insufficiency might occur.

Atrial fibrillation occurs in long-standing disease specially patients with large and hypertensive left atria. Intermittent premature atrial or ventricular contractions may occur for many months and precede the establishment of A.F. with rapid ventricular response that may herald the onset of heart failure.

(Reference 11)

Isolated M.S. is not so common in rheumatic patients as many years must elapse before narrowing of the valve orifice to level sufficient to produce symptoms. But cases of severe rheumatic M.S. have been reported specially in the children under 10 years, and frequently these patients may deny previous history of acute rheumatic fever.

(Reference 54)

In M.S. the left atrium is increased in volume and the atrial wall become hypertrophied yet the maximum volume of the left atrium is found to be not related to the severity of the stenosis.

the majority of patients with M.S. develop A.F. due to the left atrial dilatation and hypertrophy.

The A.F. here according to Ryan-etal has three deleterious effects:-

1) Reduce the left ventricular filling.

2) Increase the heart rate with decrease in the diastolic portion of the cardiac cycle.

3) Stagnation of blood in the dilated left atrium with increase in the left atrial pressure may result in development of left atrial thrombi, hence, the control of ventricular rate plus the anticoagulant therapy are the major therapeutic measures in this disease.

(Reference 54)

Fustar-etal in 1985 identified 8% of patients with dilated cardiomypathy who have had a history of acute rheumatic fever. Hence, it is classified as a late sequel to a previous acute rheumatic attack, 20% of those patients had A.F. which is the most common supra-ventricular arrhythmia that can occur in those patients, they were actually ill with dyspnea and other manifestations of haemodynamic compromise.

(Reference 17)

B. Atrial Fibrillation

EARLY THEORIES OF ATRIAL FIBRILLATION

In 1827, Robert Adams was probably the first to recognise A.F. and mark it as a sign of M.S. Fifty years later while the rheumatic heart diseases was so common in England, George Balfour wrote: "Extremely irregular action of the heart is almost pathognomic of M.S."

In 1904, Mackenzie was very much conceived the atria to be immobile and paralysed in cases of A.F., allowing the cardiac rhythm to originate in the A.V. node, this is because his polygraph could record no jugular pulsations in patients with A.F.

(Reference 37)

In the same year, H.E. Hering called the arrhythmia "Pulses irregulars perpetus", and he demonstrated the electrocardiogram (ECG) of two patients with A.F. and declared the atrial activity to be invisible.

Rothenberger, in 1909, was the first to use the term "Fibrillation of the Auricles" and in the same year Thomas Lewis published a brief paper titled "Auricular Fibrillation, a Common Clinical Condition" and he was the first to label the "F" waves and he also emphasised that digitals slowed the ventricular rate effectively.

(Reference 37)

In 1913, Braxton Hicks first recognised that A.F. could occur transiently or permanently in normal hearts.

(Reference 37)

Many trials were done to clarify the mechanism of A.F., Engelman, in 1894, had theorised that A.F. was caused by multiple foci in the atria.

(Reference 37)

In 1948, David Scherf injected aconitine into the head of sinus node to induce A.F. that could be reverted by local cooling, he also was convinced that a high frequency heterotopic foci were responsible for A.F. not a circus movement.

Prinzmetal, in 1951, has used a high speed cinematography to see the fibrillation and no circus movement was found.

(Reference 37)

However, in a computer simulation, Moe and Co-workers succeeded in producing fibrillation in a mathematics two-dimensional area or in a closed surface without holes. In this model, multiple circulating wavefronts were shown to occur during fibrillation, reentry occurred over numerous loops of varying size and position, wandering over the excitable surface like eddies in a turbulent pool.

This made it clear that the most likely mechanism underlying fibrillation is the presence of multiple circus movement.

A very important outcome of this study shows that the crucial factor for induction and termination of fibrillation is the dimension of the heart relative to the dimension of the smallest possible circuit in the myocardium.

If the heart is large or the dimension of a functionally determined circuit is small, many circuits can exist in the heart and chances for spontaneous termination of fibrillation is low.

On the other hand, if the heart is small or the dimension of the leading circuit is large, the heart can accommodate only a limited numbers of circuits and so the possibility of conversion of fibrillation is great.

According to that concept, interventions that either decrease the dimension of the heart or increase the dimension of a functionally determined circuit by drugs that increasing the refactory period or conduction velocity, will decrease the chance for induction of fibrillation or may terminate it.

(Reference 44,45)

During atrial fibrillation, atrial activity is chaotic and uncoordinated. On the electrocardiogram, the completely irregular atrial activation is recorded in the form of small waves that constantly vary in amptlitude and configuration. It is usually impossible to count accurately the number of atrial responses from the ordinary ECG but it has been estimated to vary between 400-650 beat/min. The ventricular rhythm during A.F. is completely irregular, but what is meant by a controlled ventricular rate in A.F.?

This was a title of a recent study published by John M. Rawles in 1990, the conclusion of this study is that the reduction of rapid ventricular rate in A.F. result in a longer diastolic filling period and higher left ventricular stroke volume, but this is offset by reduced contractility and fewer beats per minute and the net effect on cardiac output is uncertain.

The sequences of stroke distances were measured by Doppler ultrasound in 60 resting patients with A.F. to determine the relation between ventricular rate and cardiac output (C.O.P.).