BASIC CONCEPTS OF THERAPY WITH AMIODARONE

ESSAY

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BY

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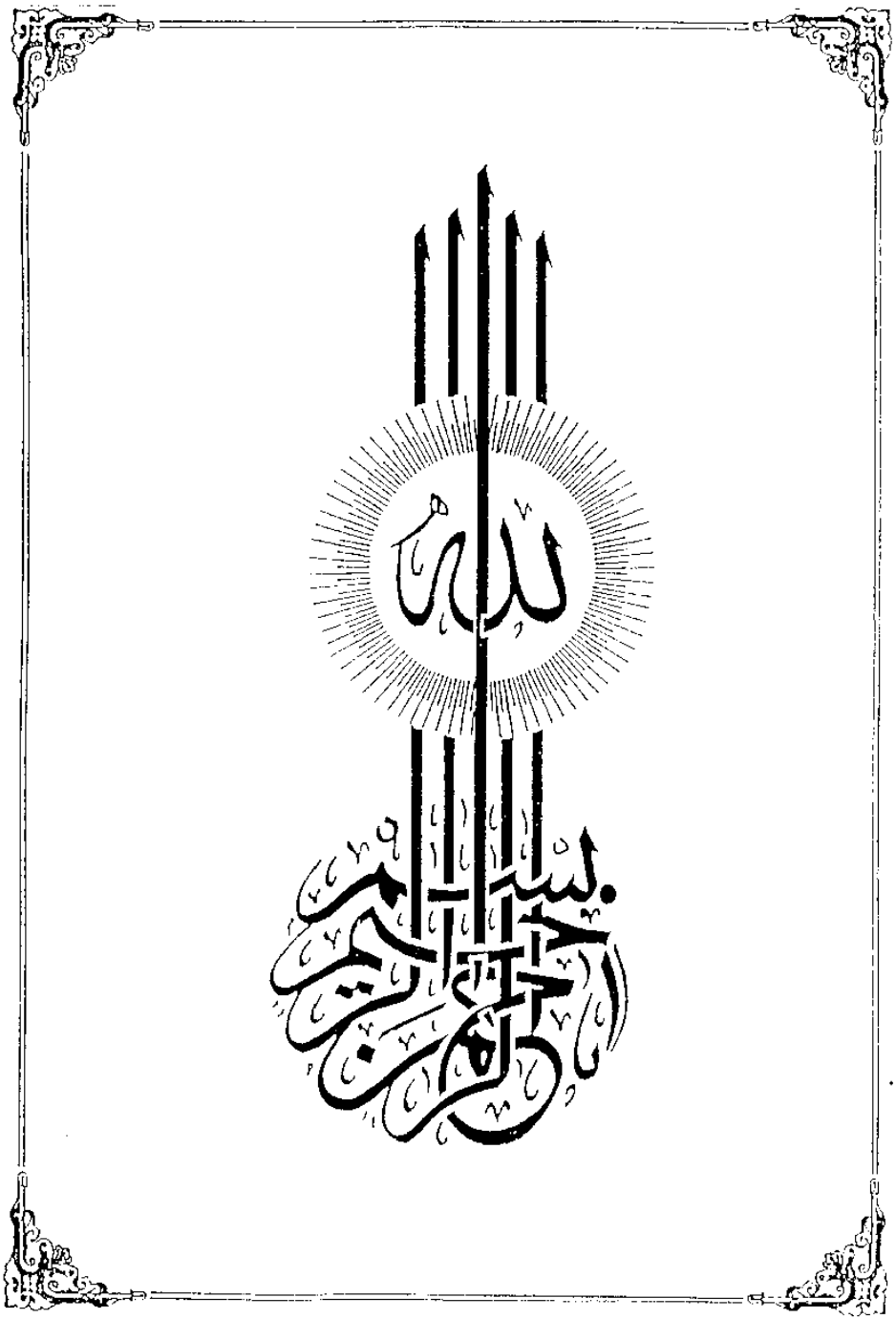

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Gamal Shoeb

TO THE MEMORY OF MY FATHER

"For mere living is not a good, but living well. Accordingly, the wise man will live as long as he ought, not as long as he can ... . It is not a question of dying earlier or later, but of dying well or ill. And dying well means escape from the danger of living ill".

Seneca, (1976)

INTRODUCTION

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Unfortunately, the incidence of mortality was increasing in the last years, due to arrhythmias in cardiac patients. For prophylaxis and treatment of those fatal arrhythmia, many trials were done to select an appropriate drug to avoid this dangerous event. One of the most recent drugs, discovered for treatment of arrythmias is amiodarone, which is classified under group III antiarrythmic drug.

In this review, a trial to collect and arrange the data in regards, the pharmacokinetic, dosing regimens chemical structure, heamodynamic action, electro-physiologic action, indications, contraindication complications, side effects and drug interactions. This will be of a great help to use this drug on a wide scale for different types of arrythmias, as a trustable and safe drug, with less complication and side effects than other antiarrhythmic drugs.

The aim of this review is to enlighten the reader about the basic concepts of therapy with Amiodarone in belief that this drug is near to be the ideal antiarrhythmic drug.

CLASSIFICATION OF ANTIARRHYTHMIC DRUGS

ANTI-ARRHYTHMIC AGENTS

Anti-arrhythmic agents may be divided broadly into those that act on both ventricular and supra ventricular arrhythmias, such as quindine, those that act mainly on ventricular arrhythmias, such as lignocaine and those that act on supraventricular arrhythmias such as verapamil (Reynolds, 1982).

According to their different properties and modes of action anti-arrhythmic agents have been classified into different classes (Elizari et al., 1980a):-

Class 1: Membrane stabilizing agents:-

A. Quindine and quinidine - like agents (major effect) is inhibition of fast Na^+ channel): include quinidine, procainamide disopyramide, Lorcainide, encainide.

B. Lignocaine and Lignocaine- like agents (complex effects including some fast channel inhibition) : include lignocaine, phenytoin, mexilletine and tocainide.

C. Other membrane stabilizing agents: aprindine.

Class 2: Includes agents that reduce sympathetic activity either acting presynaptically or by competi-

tion. This class corresponds to beta receptor blocking agent : Includes propranolol and all other B-Blockers.

Class 3: Includes agents that prolong the duration of the cardiac action potential, such as amiodarone and bretylium.

Class 4: Includes drugs that interfere with calcium conductance such as verapamil.

Based on the hypothesis that anilidine restricts the flow of current through anion - selective channels, anilidine was considered as the prototype of a fifth class of anti-arrhythmic agents (Miller and Vaughan, 1981).

Many of the drugs classified in the above manner may have more than one type of anti-arrhythmic action. Thus, high doses of quinidine can have a class III action. Propranolol and some of the other beta adrenoceptor blocking agents also have class I action: amiodarone and bretylium also have class II action and in addition, amiodarone also has class I action (Reynolds, 1982).

Antiarrhythmic drugs may be divided into three groups according to their effects on atrioventicular conduction tissue:-

Class 1: This group includes compounds such as digoxin, B adrenergic blocking agents and verapamil. These drugs depress atrioventricular conduction, increase the A - H interval and increase the refractory period of the A - V node. These drugs may be expected to prolong ventricular response to atrial tachycardia (Touboul, 1980).

Class 2: These act mainly on the Hiss Purkinje system, and require separation into two groups.

- Group 2 a drugs: essentially increase the H - V interval and therefore reduce the velocity of conduction in the Hiss-purkinje system. The refractory periods of the Hiss-purkinje are usually increased, as it has been demonstrated with quinidine, procainamide and disopyramide. These drugs are mainly of value in controlling ventricular tachyarrhythmias but have much broader additional effects on the refractory periods of the atrium and on the accessory pathways. The drugs in this group are generally effective in treatment of atrial tachyarrhythmias and tachycardia associated with the wolff - parkinson - white syndrome (Touboul, 1980).

Group 2 b drugs: have an effect on the Hiss-purkinje system but do not prolong the H - V interval. There is no slowing of conduction in the Hiss - purkinje system.

The Hiss - purkinje refractory periods are decreased with Lidocaine, diphenyl hydantoin and mixeletine, and are increased with bretylium tosylate. The effectiveness of such drugs is essentially limited to ventricular tachyarrhythmias (Touboul, 1980).

Class 3: Includes drugs such as amiodarone, which possess both types of effects:

- Depression of the A - V node and increase in the A - H interval and intranodal refractory periods; justifying its use in treatment of artrial tachyarrhythmias and reciprocal tachycardia (Touboul, 1980).
- Effect on the Hiss - Prukinje : amiodarone increases the refractory periods of the atrium, ventricle and accessory pathways; it is thus useful in controlling atrial and ventricular tachyarrhythmias and also tachycardias in the Wolff-Parkinson white syndrome (Touboul, 1980).

Ideal Properties of an anti-arrhythmic drug:

1. Broad spectrum of therapeutic activity with a low toxicity profile.
2. Few side effects.
3. Effective in the presence of arrhythmias produced by slow response due to calcium.
4. Good heamodynamic effects.
5. Administration both intravenously and per mouth.
6. Few drug interactions, additive or synergistic activity with other antiarrhythmic drugs, so that minimum quantities of several drugs may be given.
7. Minimal effect upon normal electrophysiology.
8. Long duration of action so as to obtain stabilised control of the arrhythmia. (Drefus and Ogawa, 1977)

CHEMISTRY