Magnesium Deficiency and Ventricular Arrhythmias in Digitalised Patients

Thesis

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the Master Degree in *Cardiology*

By

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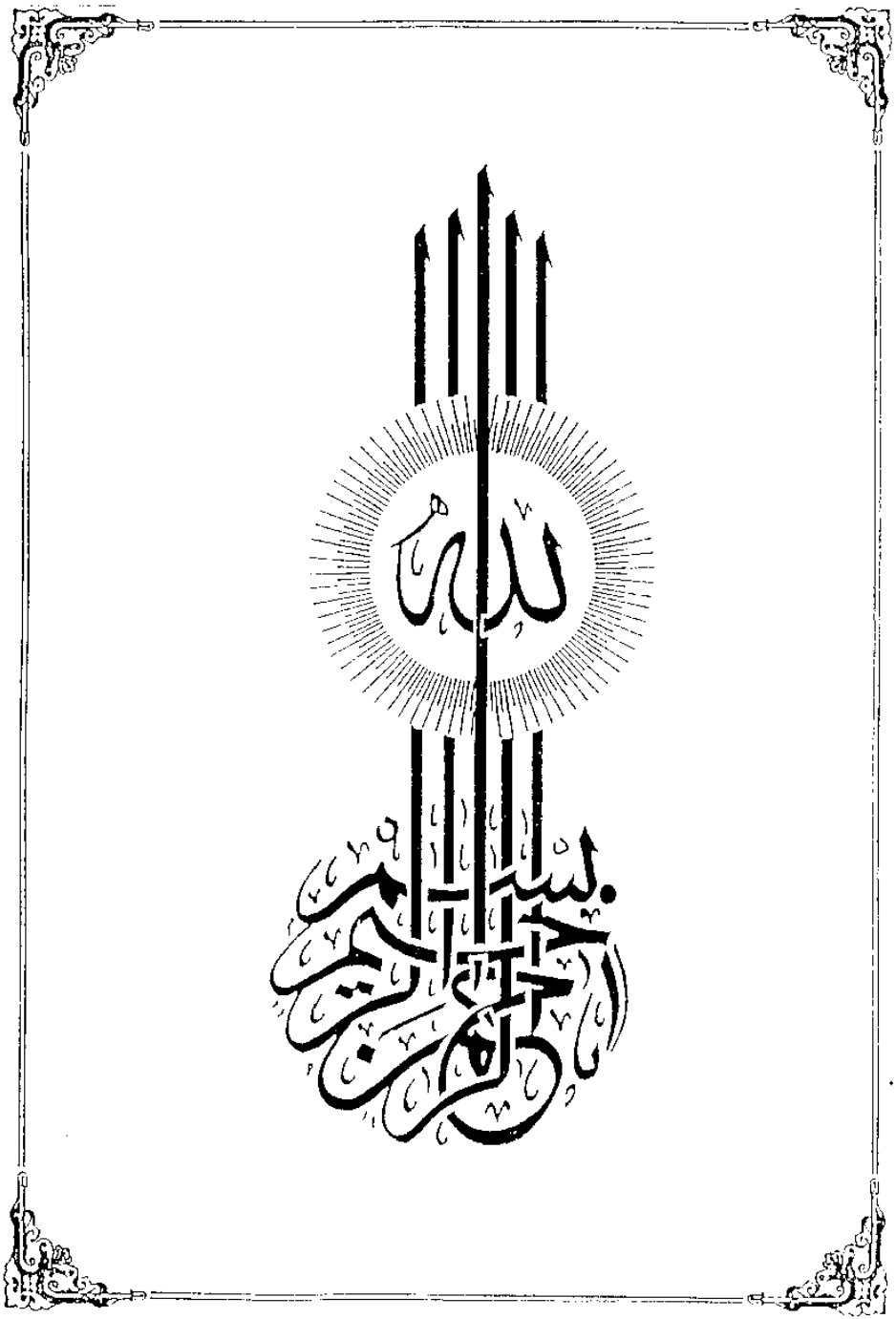

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INTRODUCTION AND AIM OF THE WORK

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Magnesium is the fourth most plentiful cation in the body, The cardiac muscle has a high concentration of magnesium and higher concentration is found in the ventricles than in the atria. Digitalis is one of the commonly used drugs in the treatment of cardiac failure, its pharmacological effects are related to its action on the membrane Na-K dependant adenosine triphosphatase.

Magnesium is an important metallocoenzyme for many enzymatic reactions. Magnesium is directly involved in the regulation of potassium as there is evidence that the membrane Na-K dependant adenosine triphosphatase (ATPase) requires magnesium to maintain the potassium level inside the cell.

Both digitalis and magnesium are related to the enzyme adenosine triphosphatase (ATPase) of the cardiac muscle.

So the objective of this thesis is to study the relationship between serum magnesium and the incidence of development of ventricular dysrhythmias in digitalised patients prospectively.

REVIEW OF LITERATURE

ELECTROPHYSIOLOGY OF ARRHYTHMIA

Cardiac impulse initiated through development of an action potential in the sino nodal cells (Rosen et al., 1987)

Due to asymmetric distribution of sodium and potassium ions with high intracellular potassium and low intracellular sodium; which produced by the continued action of the ionic sodium pump that causes electronic-chemical gradient for sodium and potassium; Thus resulting in keeping the resting cell membrane potential (-90 mv) (Abott 1966).

The cardiac action potential in its sequential depolarization and repolarization has conventionally been divided into 5 phases: (Fig. 1).

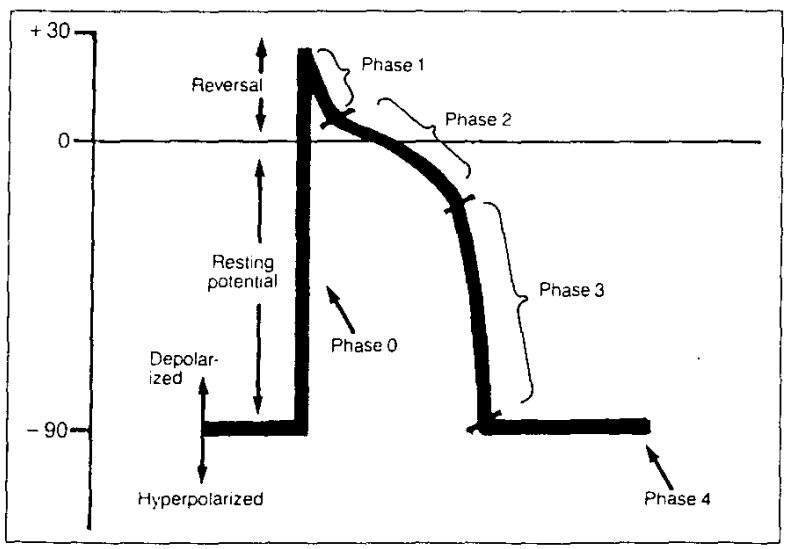

Figure 1. *Phases of a typical action potential.*

Phase 0:

Rapid depolarization from -90 mv to about +25 mv due to sudden influx of Na^{+}.

High magnesium concentration decreases the upstroke velocity of phase 0. (Cooksey 1977).

Phase 1:

This is short phase and represents early repolarization when the electrical potential falls to about 0. It is due to transient inward CI^{-}current (Katz 1975).

Phase 2:

The plateau phase of repolarization, corresponding to the ST segment of the ECG and lasting about 150 m.sec. It is due to slow influx of Ca^{++}. Low magnesium increases the plateau of phase 2 (Cooksey 1977). **(Fig. 2 & 3).**

Phase 3:

This is short lasting about 50 m.sec. It corresponds to the T wave and ends with the membrane potential returning to resting potential. During most of phase 3, the cell is unable to respond to any stimulus, no matter how strong (absolute refractory period). **(Fig. 2 & 3).**

In the last part of phase 3, as the membrane potential approaches the threshold value the cardiac cell is now only relatively inexcitable (the relative refractory period), and will respond to strong stimulus either by propagation from

neighbouring cell or from early spontaneous depolarization of the succeeding phase. In phase 3 K^+ ions move out of the cell (Helfant 1986).

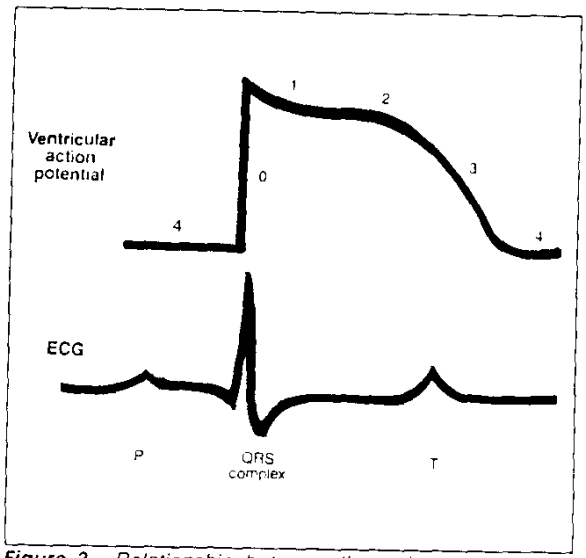

Figure 2. Relationship between the action potential of a ventricular myocardial cell and a superimposed electrocardiogram.

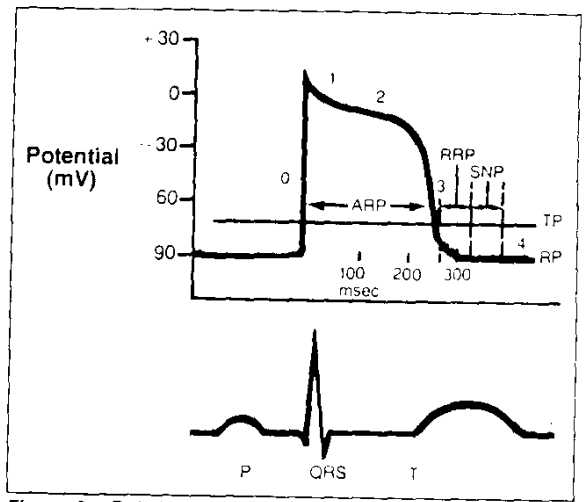

Figure 3. Relationships between the refractory periods with respect to the action potential. ARP = absolute refractory period; RRP = relative refractory period; SNP = supernormal refractory period; TP = threshold potential; RP = resting potential.

Phase 4:

The action potential gradually returns to a resting value of -90 mv in all but the specialized automatic cells, in which the voltage raises to or towards threshold of -75 mv (rising phase 4 diastolic depolarization).(West 1974).(Fig.4)

At the beginning of phase 4 there is active extrusion of Na^+ by sodium pump. Energy is supplied by magnesium dependant ATP. (Stephenson 1974).

Because the upward slope of phase 4 in the sinoatrial node is normally steeper than any part of the specialized conductive system, threshold potential is reached first at this site, making the sinoatrial node the pacemaker of the heart and the initiator of the sequence of events leading to cardiac contraction (Davies 1971).

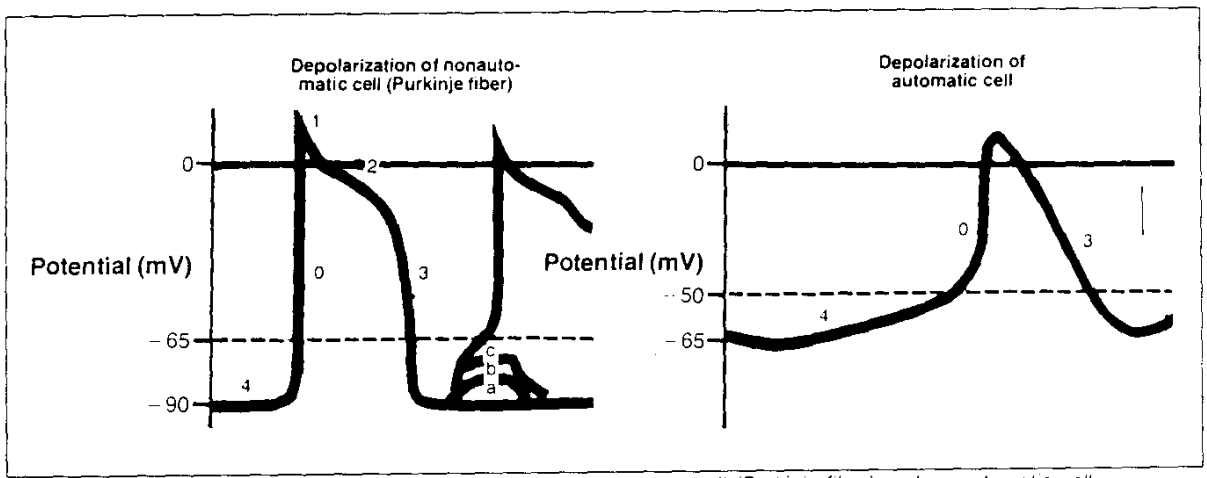

Figure 4. Relationship between the depolarization of a nonautomatic cell (Purkinje fiber) and an automatic cell.

SPECIALIZED CELLS PROPERTIES

These include automaticiły, excitability, conductivity, refractoriness and capacity of reentry:

A. Automaticity:

Certain specialized tissues of the heart principally the SA node, A-V junction and Purkinje fibers possess the ability to initiate the cardiac impulse spontaneously. This property is termed automaticity.

*** Factors increasing automaticity:**

1. Increased stretch of automatic fibers, (Singer et al.,1967).
2. Exogenous catecholamines and sympathetic stimulation.
3. Low extracellular potassium concentration increases the slope of stage 4 depolarization.
4. The direct action of digitalis in therapeutic concentration causes enhanced automaticity in Purkinje fibers. (Hoffman and Singer 1964).

*** Factors decreasing automaticily:**

Automaticity is decreased by the reverse of the factors just described. In addition certain antiarrhythmic drugs decrease automaticity of pacemaker fibers. Hypermagnesemia causes AV block (Cooksey 1977).

B. Excitability:

It is that property of living tissue which permits it to respond when stimulated.

*** Factors increasing excitability:**

1. Increased sympathetic tone (Pristla 1969).
2. Hypopotassemia, hypomagnesemia and hypercalcemia (Watanabe

1965).

3. Sympathomimetics (Schmidt 1960), propranolol (Davies 1968).

*** Factors decreasing excitability:**

Excitability is decreased whenever the membrane potential cells falls below the usual resting value -90 mv.

The antiarrhythmic drugs quinidine , lidocaine and procainamide decrease excitability.

c. conductivity:

Is the ability of a tissue composed of a series of cells to propagate an impulse (Singer 1955).

Conductivity is enhanced by:

(1) Elevation in transmembrane potential by sympathomimetics , hypokalemia , diphenylhydantoin and propranolol (Davis 1968) .

(2) Enhancement of cell response by calcium (Posey 1967).

Conductivity is decreased by organic heart diseases, digitalis, quinidine, procainamide & high doses of beta-blocking agents and potassium (Singer 1967).

D. Refractoriness:

Refractoriness is the property by which cardiac cells fail to respond to an oncoming stimulus because repolarization is incomplete and the voltage of the interior of the cell has not become sufficiently negative to initiate or propagate an action potential (Davies 1971). It is related

to excitability in that the cell is totally unexcitable when the voltage is less negative than threshold and no stimulus, no matter how strong, can evoke a propagated response. This is the absolute refractory period. As the voltage of cell becomes more negative at the end of phase 3, the resting membrane potential may not have reached its normal value of -90 mv but may be sufficiently negative that a powerful stimulus can evoke a response even though it may not be sufficiently strong to be fully propagated and may depolarize neighbouring cells. Shortly after this relative refractory period and before the normal resting maximum diastolic potential has been reached, there is a short "Super-normal" phase corresponding to down stroke of the T wave, during which time a smaller than usual current can induce a propagated response. The supernormal or vulnerable phase is responsible for the so-called R on T phenomenon, in which a ventricular premature beat falling on the descending limb of the T wave may induce repetitive ventricular ectopic discharge including ventricular fibrillation (Berns 1976).

E. Capacity of reentry:

*** Mechanism of arrhythmias:**

Reentry is not a property of cardiac cells per se but is thought to be the mechanism by which arrhythmia can develop in any portion of the heart. An automatic cell, by increasing the slope of phase 4 depolarization and increasing its automaticity can become the pacemaker of the heart. Through