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POSTMYOCARDIAL INFARCTION HYPOMAGNESAEMIA AS A RISK FACTOR

THESIS

Submitted In Partial Fulfilment For
The M. Sc. Degree In Internal Medicine

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بسم الله الرحمن الرحيم

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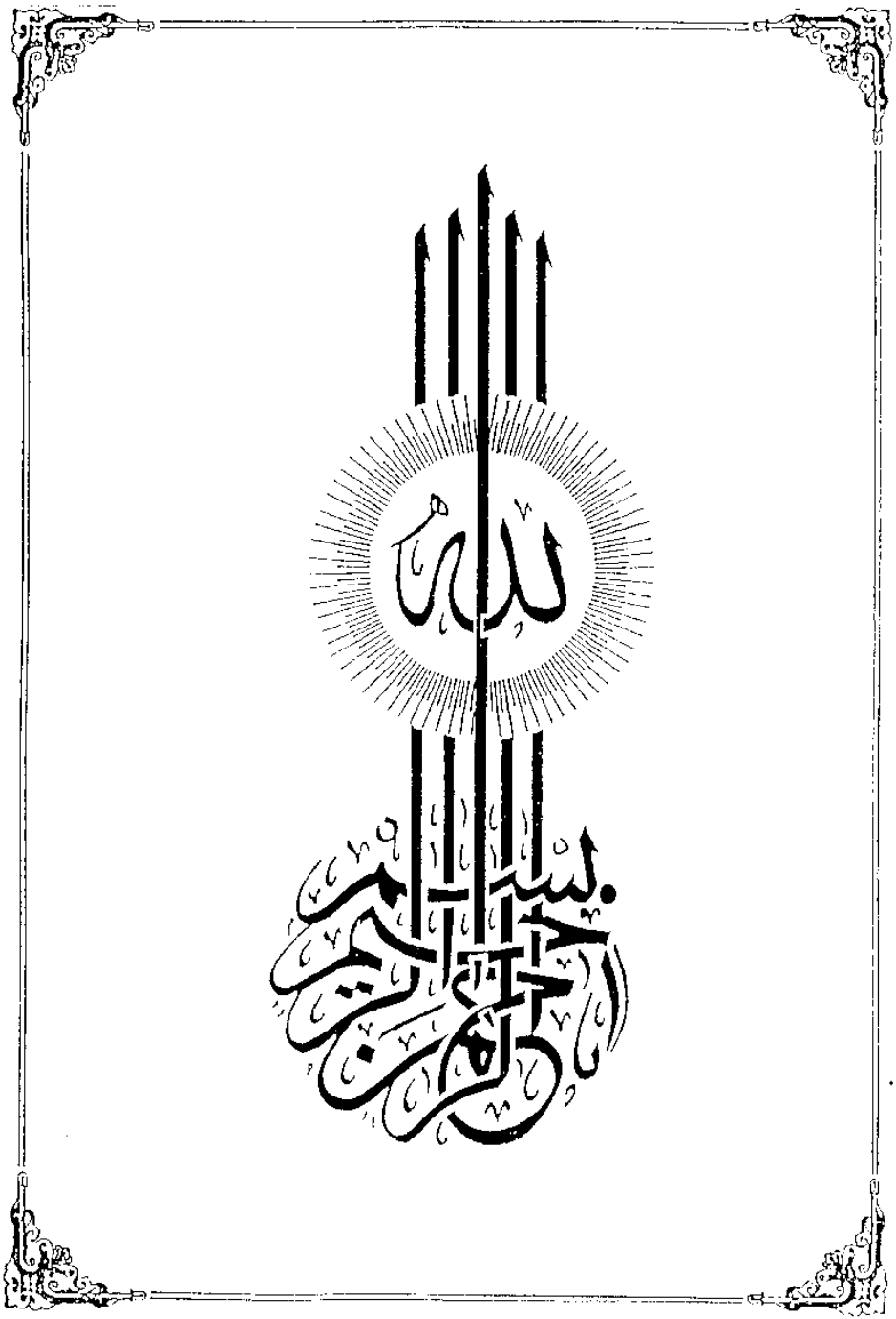

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INTRODUCTION AND AIM OF THE WORK

Magnesium plays a great role in cardiac diseases . In animals study, a reduced magnesium level leads to cardiac arrhythmias , coronary artery spasm and increased frequency of catecholamine-induced myocardial necrosis . In man, hypomagnesaemia is associated with a high frequency of cardiac arrhythmia, symptoms of cardiac insufficiency and sudden ischaemic heart death .

The aim of the present work is to assess the degree of post infarctional hypomagnesaemia and its relationship to some of the arrhythmias related to acute myocardial infarction .

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REVIEW OF LITERATURE

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REVIEW OF LITERATURE

Physiology of Magnesium

(A) Normal Distribution and Turnover of Magnesium in Man:

* Body Content :

The magnesium content of the human body ranges between 22.7 and 35.0 mEq/kg wet weight of tissue (Widdowson, 1951) . Extrapolations from tissue analysis perfumed on victims of accidental death indicate that the body content of magnesium for a man weighing 70 kg would be of the order of 2000 mEq (24 gm) (Schroeder, 1969) .

80 % of total magnesium in bone and muscle .

60 % are present in bone (at a concentration of about 90 mEq/kg wet weight) .

40 % of total magnesium is distributed equally between muscle and non-muscular soft tissues .

About 1 % of total body magnesium is extracellular.

The levels of magnesium in serum of healthy people on the average at 1.7 mEq/Liter and varying less than 15 % from this mean value (Wacker and Parisi, 1968).

About $\frac{1}{3}$ of extracellular magnesium is bound non-specifically to plasma proteins. The remaining $\frac{2}{3}$ (65 %) of extracellular magnesium is diffusible or ionized and appears to be the biologically active component.

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* Secretion :

The secretion from bile and from pancreatic juices is followed by almost complete reabsorption. Parotid saliva contains about 0.3 mEq/Liter (Lear and Gron 1968) and pancreatic juice contains about 0.1 mEq/Liter of magnesium . The concentration of magnesium in other secretions varies considerably . The observation that hypomagnesaemia can occur in patients suffering from large losses of intestinal fluids suggests that intestinal juices contain enough magnesium to deplete the serum, when magnesium is not reabsorbed by the colon . Further investigations may show that the cells of the intestinal mucosa, like those in the kidney and elsewhere in the body, may depend, in part, upon metabolic activity for the uptake and release of calcium and magnesium .

* Excretion :

Most of that portion of the magnesium that is absorbed into the body is excreted by the kidney . Fecal magnesium represents largely the unabsorbed fraction . In subjects on a normal diet, $\frac{1}{3}$ or less of the ingested magnesium (5 - 17 mEq) is excreted by the kidney . The maximal renal capacity for

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excretion is not known but it is probably quite high, perhaps greater than 164 mEq / day (Wacker and Parisi, 1968) . The diffusible magnesium in plasma is filtered by the glomeruli and is reabsorbed by the renal tubules, probably by an active process . There is some evidence that magnesium may be secreted by the renal tubules (Forster and Berglund, 1956) . Both the mercurial and the thiazide diuretics increase excretion of magnesium, calcium, potassium and sodium. Magnesium excretion also occurs in sweat (Consolazio, 1963) . Under extreme conditions, sweat can account for 25 % of the magnesium lost daily; this factor would be important when the intake of magnesium is low.

* Magnesium conservation on a low-magnesium diet :

Any protein-bound magnesium that is filtered is returned to the circulation via lymph . The excretion of magnesium may be greater than normal in renal diseases associated with heavy proteinuria .
In spite of the probability of diets being low in magnesium under certain circumstances, magnesium deficiency does not occur in human beings with healthy kidneys . The explanation for this clinical observation appears to be that renal mechanisms are efficient enough to conserve all but about 1 mEq of magnesium per day. Fecal losses are minimal (Barnes et al. 1958) .

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* Abnormal magnesium levels in the blood :

Values less than 1.1 mEq/Liter have been obtained in patients with congestive heart failure, cirrhosis or renal failure after hemodialysis .

All values higher than 2.0 mEq/Liter were found in patients with renal failure before therapy (Aikawa 1958 - 1959) .

(B) Plasma Clearance and Tissue Uptake of Magnesium :

* Early studies :

Smith et al. (1939) studied the excretion of magnesium in dogs after the intravenous administration of magnesium sulfate and concluded that the magnesium distributed itself throughout the extracellular fluid during the first 3 - 4 hours . During subsequent hours, some of the ion appeared to be segregated from the extracellular fluid and was not excreted .

* Tracer studies in human beings :

The introduction of the radioactivity isotope of ^{28}Mg for clinical studies, in 1957, made possible determination of the " exchangeable " pool in human subjects . The clearance curves in general showed

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a rapid phase during the first 4 hours, a subsequent more gradual decline up to about 14 hours, and a slow exponential slope thereafter . Biopsies of tissues contained concentrations of ^{28}Mg in liver, appendix, fat, skin and subcutaneous connective tissue that could not be attributed solely to the extracellular components of these tissues . The maximal distribution of radioactivity at the end of infusion over the right upper quadrant of the abdomen . This finding suggests initial concentration of magnesium in the liver . At 18 hours, the specific activity in bile was equal to that of serum . This equilibration of the infused ^{28}Mg had occured earlier in bile than in any other tissue or fluid available for study (Aikawa et al., 1960) . The infused material had equilibrated with the stable magnesium in a rather labile pool and that further exchange was occurring very slowly in a less labile pool . The size of this labile pool in normal subjects ranged between 135 and 397 mEq (2.6 - 5.3 mEq/kg of body weight) . Since the body content of magnesium is estimated to be 30 mEq / kg , it appears that less than 16 % of the total body content of magnesium is measured by the ^{28}Mg exchange technique. During starvation, the renal excretion of magnesium amounts to 61.7 mEq/kg of weight loss(Aikawa et al.,1959).

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(C) Gastrointestinal Absorption :

* Daily absorption in man :

In normal individuals on regular diets, the average daily absorption of magnesium from the gastrointestinal tract is 0.14 mEq/kg, an amount approximately 40 % of the size of the extracellular pool (Wallach et al., 1966) .

* Factors affecting absorption :

No single factor appears to play a dominant role in the absorption of magnesium as does vitamin D in the absorption of calcium (Aikawa , 1959)
On ordinary diet containing 20 mEq of magnesium , 44 % of ingested magnesium was absorbed per day .
On a low-magnesium diet (1.9 mEq/day), 76 % was absorbed .
On a high-magnesium diet (47 mEq / day), absorption was decreased to 24 % .
Absorption begins within an hour of ingestion and continues at a steady rate for 2 - 8 hours; it is minimal after 12 hours (Graham et al., 1960) .

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* Site of absorption :

Evidence from a variety of animals suggests that the small intestine is the main site of magnesium absorption . Absorption from large intestine is negligible in the rabbit . There appears to be an interrelationship between the absorption of magnesium and calcium in the proximal part of small intestine in the rat (Alcock and Mac Intyre, 1962) . The suggestion has been made that there is a common mechanism for transporting calcium and magnesium across the intestinal wall (Mac Intyre, 1960) . The ionic magnesium concentration in the digest at the absorption site must be the main factor controlling the amount absorbed in a given time (Smith and Mc Allan, 1966) .

(D) Renal Excretion :

* Control of body content :

The kidney is the major excretory pathway for magnesium , once it is absorbed into the body (Mendel and benedict, 1909) . The mean daily excretion of magnesium in the urine of normal men on unrestricted diet was 13.3 ± 3.5 mEq (Wacker and Vallee, 1958).

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