RENAL HANDLING OF SALT AND WATER IN MYXEDEMA AND HYPOTHYROIDISM

THESIS

Submitted in Partial Fulfilment for the Master Degree in Internal Medicine

By

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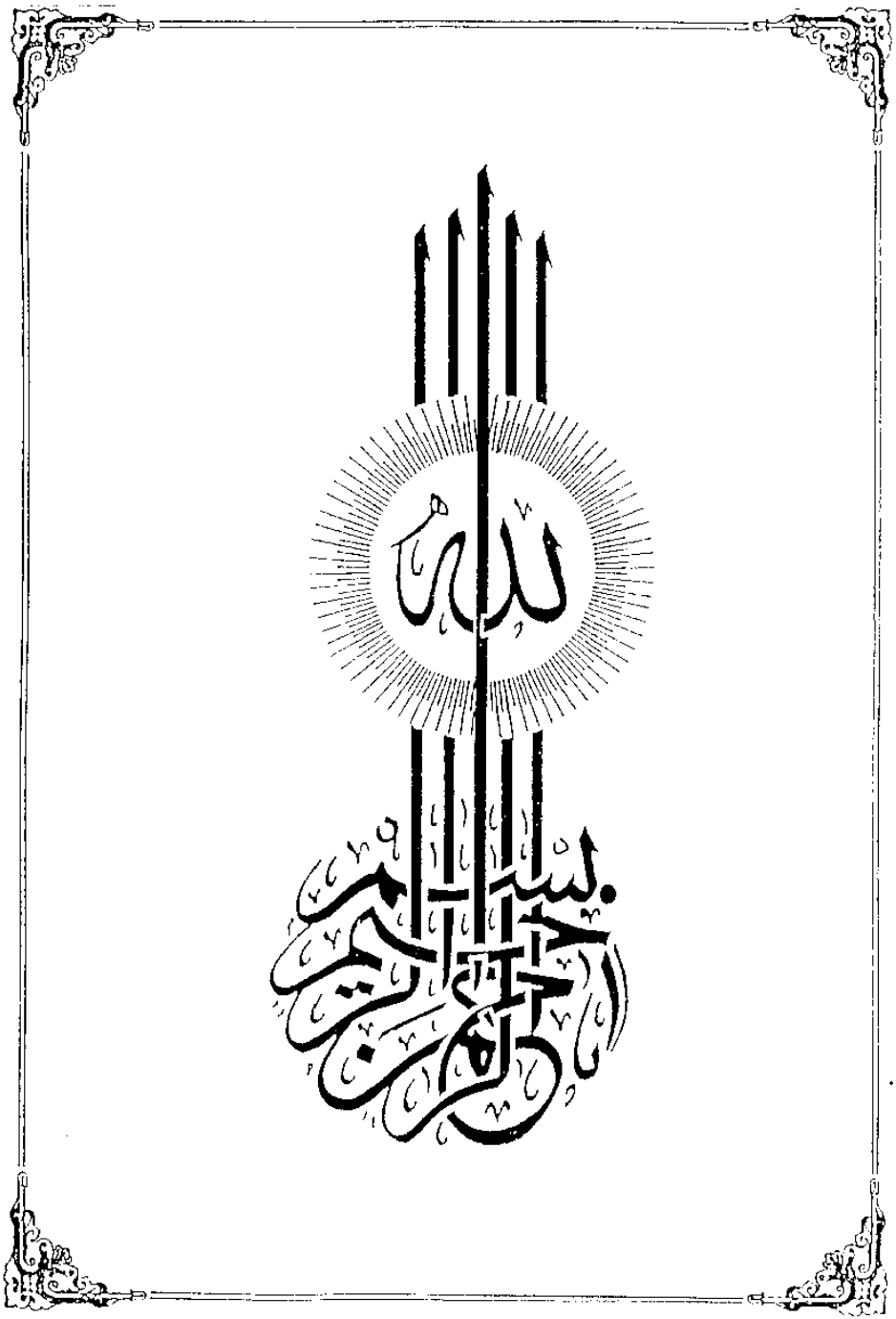
DEDICATED

To

Fifi, my wife

Who

Gave too much and received too little.



C O N T E N T S

A C K N O W L E D G M E N T S

It is with much pleasure and deep stisfaction that I acknowledge the gracious support of my great teacher Dr. Wahyed El-Saed.

Special gratitude is due to Dr. Mahmoud Abdel-Fatah for his helpful criticism and revision of this study, and Dr. Mohamed Alla El-din Hamed for evaluating and referring the patients.

For her sustained support and meticulous attention to detail, I express my deepest gratitude and appreciation to Dr. Sawsan Hosni.

In addition, I am grateful to Dr. Maha Abdel-Kader for her help with the statistical analysis of data.

Lastly, there are people who have taught me much over the years and from whom I continue to learn. I acknowlege their contribution, and will alwayes be grateful to them.

INTRODUCTION AND AIM OF WORK

I N T R O D U C T I O N

Hypothyroidism is associated with significant changes in renal hemodynamics and the renal handling of salt and water (Derubertis F.R. et al., 1971)[1].

These changes include a diminished glomerular filtration rate, decreased effective renal plasma flow and lowered tubular excretory capacity (Michael U.F. et al., 1972)[2].

Renal capacity to excrete free water as well as the renal ability to dilute and concentrate urine in response to changes in plasma osmolality are impaired (Di Scala V.A. and Kinney M.D., 1971)[3].

Dilutional hyponatremia is a frequent finding in the more severe cases of myxedema (Goldberg M. and Reivich M., 1962)[4].

A number of studies on the mechanism of impaired water excretion and hyponatremia associated with hypothyroidism and myxedema have been made with no consistent finding.

Inappropriate secretion of antidiuretic hormone is suggested by some authors (Skowsky W.R. and Kikuchi T.A., 1978)[5], others stated that the hyponatremea is related to decrease volume delivery to the distal

diluting segment of the nephron (Derubertis F.R., et al., 1971)[1], still others suggested a resetting of the osmolar regulatory mechanism (Di Scala V.A. and Kinney M.J. 1971)[3].

AIM OF THE WORK

The aim of the present work is to evaluate the response of patients with primary myxedema and hypothyroidism to standarized oral water load so as to provide further insight into the effects of this disorder on renal solute and water transport.

LITERATURE REVIEW

F O R E W O R D

The basic physiology of the renal handling of salt and water and the regulation of plasma osmolality as well as the structural features of the renal architecture and microcirculation are fundamental for understanding the renal effects of thyroid hormone deficiency.

However, any attempt to include such physiologic or anatomic basic principles in this study will ultimately make it unnecessarly lengthy and exhaustive and will limit the space available for discussion of the more recent and extensive views of the kidney changes in myxedema and hypothyroidism.

In the discussion that follows, we will selectively review several important aspects of renal structure and function in states of hypothyroidism and myxedema, with emphasis on human studies whenever possible.

Nevertheless, in some instances reference will be made to basic physiologic or anatomic information pertinent to the point in view.

This approach, in our opinion, will help to avoid much repetition and will enables ones thought to go uninterrupted over the whole subject.

CHAPTER (1)

THE THYROID HORMONES AND THE KIDNEY

GRADES OF HYPOTHYROIDISM

It was widely accepted during the early years of this century that hypothyroidism was an "all or none" phenomenon. Nevertheless, the advent of more precise diagnostic techniques, which enable different aspects of thyroid function to be measured, have shown that hypothyroidism is a graded phenomenon (Evered D.C. et al., 1973)[6].

The laboratory techniques available for assessing thyroid function fall into three groups, and the use of each group of technique allows different aspects of impaired thyroid function to be defined. The three groups of techniques are:-

1. Tests of thyroid function, including direct and indirect measurements of circulating thyroid hormone concentration and measurement of thyroid radioiodine uptake before and after administration of thyroid stimulating hormone (T S H).
2. Tests of peripheral tissue function, including measurement of the duration of the ankle tendon reflex, measurement of serum lipid concentrations, and inspection of the standard 12- lead electrocardiogram.

3. Tests of hypothalamic - pituitary function, including measurement of the basal serum T S H concentration and the rise in concentration after adminstration of thyrotrophin - releasing hormone (T R H).

A classification of the various grades of hypothyroidism has been proposed by Evered D.C. et al., 1973, on the basis of the clinical and laboratory features of hypothyroidism:

Firstly, patients with overt hypothyroidism, had obvious clinical features of hypothyroidism and abnormal results from routine tests of thyroid function. In the more severe cases of this group, the full - blown myxedema results, with thickened features, enlarged tongue, hoarseness, nonpitting edema, and extreme mental and physical lethargy.

Secondly, those with mild hypothyroidism, had a minor and non-specific symptoms e.g. tiredness, constipation, dryness of skin and hair loss, but the routine measurements of circulating thyroid hormone concentration generally lay within the normal range, although they were significantly lower than those seen in normal subjects. The serum concentration of

T S H is raised in this group and their symptoms resolve with treatment.

Thirdly, patients with subclinical hypothyroidism are asymptomatic, have a raised serum T S H concentration, but all other measurements of thyroid function are indistinguishable from those recorded in normal subjects. In this group a reduction of thyroid activity has been compensated by an increase T S H output to maintain an euthyroid state.

Lastly, subjects with circulating thyroid antibodies, normal indices of thyroid function, and a normal serum T S H concentration were indistinguishable biochemically from normal subjects. The natural history of these subjects is unknown.

Although the terms hypothyroidism and myxedema are not synonymous, they are used in this study as a general definition of the hypothyriod state with disregard to clinical severity, except when otherwise indicated.