THE ROLE OF PROLACTIN IN THE GENESIS OF SEXUAL DYSFUNCTION IN URAEMIC MALE PATIENTS ON REGULAR HAEMODIALYSIS THERAPY AND THE EFFECT OF SIX WEEKS TREATMENT WITH BROMOCRIPTINE ON SUCH DYSFUNCTION

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1985

ACKNOWLEDGEMENT

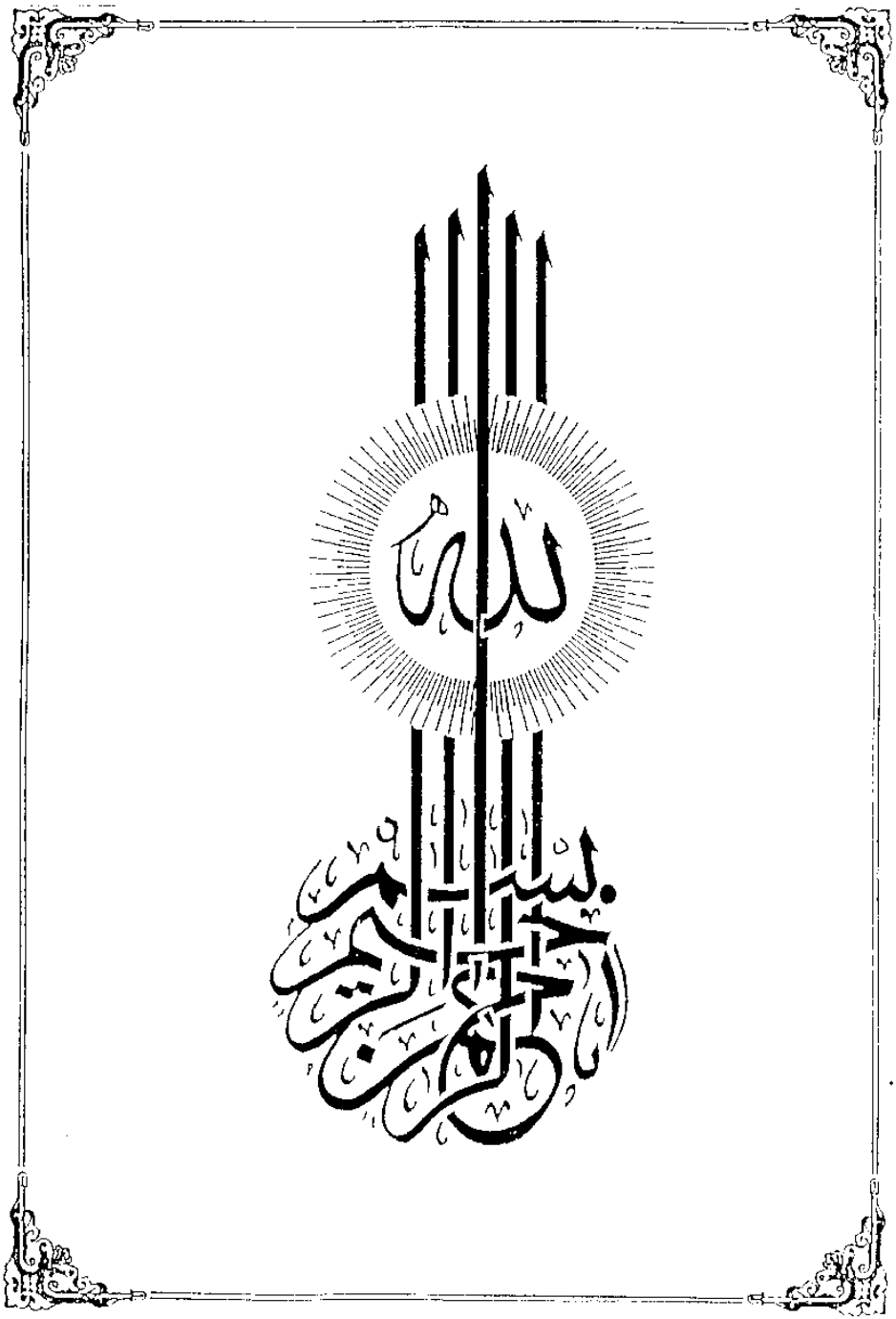
I wish to express my deepest gratitude to Prof. Dr. Mostafa Kamel Ismail for his help, guidance and the support he constantly offered through out the period of preparation of this thesis.

My special thanks and appreciation for Prof. Dr. Wahid El Said, who so willingly offered me his precious time and continuous advice to complete this work in a proper manner.

I would also like to thank Dr. Adel Afifi for the tremendous effort he has exerted and for his sincere concern in every single step taken to accomplish this thesis.

I would also like to express my gratitude to the Sandoz Pharmaceutical Scientific Division, and especially Dr. Medhat Adib for their efforts and fine work in supplying the necessary materials for the conduction of the double - blind study.

Last but not least, I would like to also thank all my colleagues, who helped me in the revision and organization of my work.



T A B L E O F C O N T E N T S

Introduction & Aim Of The Work

INTRODUCTION AND AIM OF THE WORK

Until the early 1960's chronic renal failure represented a terminal illness for which there was no treatment (Abram et al., 1975). The development of facilities for dialysis therapy has offered such patients an opportunity to return to a more useful life and often to productive work (Elstein et al., 1969). In this situation, the question of sexual potency became more relevant, especially to the patient who regards it as an important part of his return to a more normal life (Elstein et al., 1969).

Patients with chronic renal failure manifest a multitude of abnormalities in their sexual function (Massry et al., 1983). Dialysis may not improve these abnormalities and even frequently, some dialysis patients describe worsening of their sexual dysfunction after starting dialysis therapy (Procci et al., 1981).

The mechanisms responsible for the pathogenesis of sexual dysfunction in uraemia are not fully elucidated and several potential factors have been implicated. These factors include zinc deficiency, autonomic neuropathy, depression,

medication for hypertension as well as the state of chronic illness itself (Massry et al., 1983). Hormonal abnormalities in chronic renal failure have also been implicated. These abnormalities include hyperparathyroidism and abnormalities in the hypothalamic - pituitary gonadal axis including follicle-stimulating hormone, lutenizing hormone, testosterone and prolactin (Procci et al., 1981).

From this wide range of potential factors, abnormalities in the prolactin hormone was chosen as the main topic for this thesis.

The aim of this work is to:-

1. Find out the incidence of sexual dysfunction among uraemic males.
2. Find out the effect of dialysis on such dysfunction.
3. Measure the serum prolactin levels and find out the incidence of hyperprolactinaemia in those patients.
4. Note if there exists a correlation between hyperprolactinaemia and sexual dysfunction.
5. Evaluate the effect of a six week use of the drug bromocriptine on such sexual dysfunction using the double-blind technique.

6. Evaluate the serum prolactin levels after bromocriptine treatment and correlate the findings with the effect of the drug.

7. To record the side effects of this drug.

Review Of Literature

PHYSIOLOGY OF SEXUAL FUNCTION

According to several authors, sexual function in the male consists of five consecutive phases; libido, erection, ejaculation, orgasm and detumescence (Walsh and Wilson, 1980) (Braun, 1983) (Wenner and Braun, 1983).

Libido is the psychogenic preparatory phase which preceeds and accompanies erection (Braun, 1983). Its regulation is by psychic factors which are poorly understood and by testicular androgens (Walsh and Wilson, 1980). Castration causes a decline in libido that can be restored by treatment with testosterone (Walsh and Wilson, 1980).

Erection is primarily a neurological event that results in modification of the vascular supply of the penis causing it to become engorged with blood (Braun, 1983). The innervation mediating erection is mainly parasympathetic and to a lesser extent sympathetic (Wenner and Braun, 1983). The stimulus is either by tactile reflex or erotic psychic stimulation (Walsh and Wilson, 1980).

The tactile portion begins with fibres which originate from the paccinian corpuscles of the penis and pass via the pudendal nerve to S1 and S2 dorsal root ganglia. The efferent limb begins with parasympathetic preganglionic fibres from S2 to S4 dorsal root ganglia to synapse in the perivascular cavernous and prostatic plexuses. From there, post-ganglionic fibres pass to the blood vessels of the corpora cavernosa causing them to be engorged with blood and a state of erection occurs (Walsh and Wilson, 1980). The psychic portion begins with central impulses from the infundibular nucleus located in the floor of the third ventricle (Wenner and Braun, 1983). These impulses reach the genitalia via the sympathetic nervous system starting at the lateral columns of the spinal cord at the level of T12 and L1 at the so-called "Thoraco - Lumbar erection centre" and synapting in the pelvic and perivascular plexuses (Walsh and Wilson, 1980). Sympathetic innervation acts synergistically with the sacral parasympathetics to mediate erection initiated by psychic stimuli. In fact, patients with complete lower motor neuron lesion may have a psychogenic but not a reflex erection (Campese et al., 1982). On the other hand, sympathetic innervation is not mandatory for

erection. This is demonstrated by continued potency in most patients with bilateral complete sympathectomy (Walsh and Wilson, 1980).

The third phase, ejaculation, is under the control of the sympathetic nervous system and consists of two processes; seminal emission and true ejaculation. In emission, the lower segments of the sympathetic nervous system activate the contraction of the vas deferens, prostate and seminal vesicles, thus expelling their contents in the urethra. True ejaculation is brought about by the contraction of the striated muscles of the penis and perineum which are innervated by roots of S1 and S3. Retrograde ejaculation is prevented by partial bladder neck closure mediated by the sympathetic nerves (Wenner and Braun, 1983).

Orgasm is a cortical sensory phenomenon in which the rhythmic contraction of the penile muscles is perceived as pleasurable. It is purely psychic (Walsh and Wislon, 1980).

Detumescence is the phase during which blood flows away from the erectile tissue and the penis becomes flaccid (Braun, 1983). Its

mechanism and nervous supply is quite obscure and may be related to vasoconstriction of the arterioles supplying the erectile tissue (Walsh and Wilson, 1980). Following orgasm, there is a refractory period during which erection and ejaculation are inhibited. The length of this period varies with age, physical condition and psychic factors (Walsh and Wilson, 1980).

Sexual dysfunction is a derangement in one or more of these phases (Braun, 1983). However, the term impotence is sometimes used to define a dysfunction in one or more of the first four phases as loss of libido, inability to obtain or maintain an erection, absence of emission or inability to achieve orgasm (Wenner and Braun, 1983). Many subjects complain of more than one abnormality simultaneously. These complaints can be secondary to psychiatric disturbances or organic diseases (Walsh and Wilson, 1980).

A useful method for objective evaluation of sexual function and diagnosis of organic sexual dysfunction is the measurement of the nocturnal penile tumescence (NPT)(Campese et al., 1982). Studies done by several authors on normal subjects and uraemic males showed a significant

and direct relationship between nocturnal penile tumescence and the frequency of intercourse (Massry et al., 1980) (Procci et al., 1981) (Campese et al., 1982).

Nocturnal penile tumescence is the measurement of the penile erectile activity during rapid eye movement sleep at night (Massry et al., 1980). Measurement of nocturnal penile tumescence is recorded by using two mercury strain gauges attached to the tip and base of the penis connected with an electronic recorder. The subject wears the strain gauges throughout the night. Erection during sleep is sensed by the strain gauges and registered by a device as a deflection in a recorded graph. An erection is considered adequate when the change in penile circumference equals or exceeds 13 mms. The duration during which a change of this magnitude was maintained is calculated. Nocturnal penile tumescence in normal subjects ranges between 35 and 216 minutes per night with a mean of 85 $\pm$ 10.4 minutes (Procci et al., 1981) (Campese et al., 1982).

To eliminate personal stress experienced by the subjects during measurement, it was suggested

that nocturnal penile tumescence should be measured during at least two consecutive nights and the data obtained during the first night to be discarded (Karacan et al., 1978).