THE ROLE OF ALPHA ADRENOCEPTOR BLOCKERS IN THE TREATMENT OF BENIGN PROSTATIC HYPERPLASIA

THESIS
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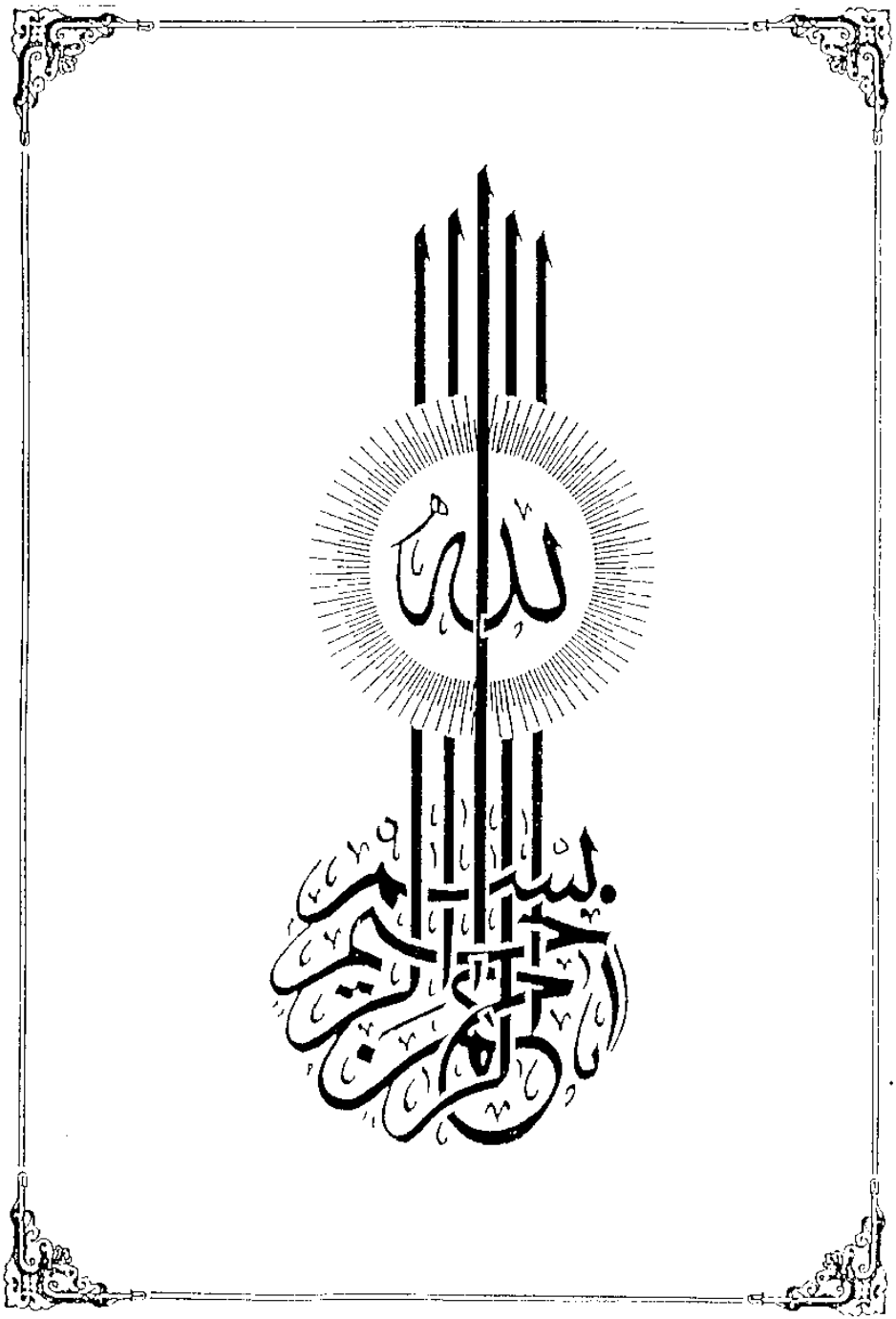

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INTRODUCTION

ANATOMY OF THE PROSTATE

INTRODUCTION

The definitive treatment for urinary outflow obstruction caus by B.P.H. is surgical removal of the obstructing tissue, but f many years attempts have been made to find an effective n operative treatment for B.P.H. Those efforts have generally be directed towards decreasing the size of the enlarged prostra often by means of hormonal therapy. However, despite t numerous studies on a variety of substances it was concluded tl to date no such therapy has established itself unequivocally effective.

Recently an entirely new pharmacological approach in help those patients with B.P.H. arose as the result of acade studies on the adrenergic receptor content of the prostrate. awareness that the prostate and the prostatic capsule in B.P both contain relatively large quantities of smooth muscle t have a high alpha receptor content has arisen the concept t symptomatic relief might be obtained in patients with B.P.H. the use of an appropriate alpha adrenoceptor blocking agent.

Although the prostate is considered to be a glandular organ it also contains a relatively large amount of fibromuscular stroma. The stereometric studies of Bartsch et al, 1979 has demonstrated that the fibromuscular stroma constitutes about 45 percent of the volume density of the normal prostate while this value is increased to 60 percent in the hyperplastic gland.

One of the typical features of B.P.H. is the variability in the severity of the patient's symptoms. It is well known that these may change rapidly so that, for instance, a patient with severe trouble one week may have relatively mild symptoms that barely trouble him the next week. It is also well recognized that certain factors such as cold, psychological tension and the administration of sympathomimetic drugs are liable to exacerbate the symptoms, whereas warmth and a relaxed state ameliorate them. As long as the prostatic obstruction was thought of only as a purely mechanical problem caused by the inert bulk of prostatic tissue, it was difficult to explain these variations.

However, once the importance of the muscular tissue in the prostate and its capsule together with its adrenergic receptor content was appreciated, the explanation became clear. This was formulated by Caine M., 1977 that there are two components in

B.P.H. obstruction which have been termed mechanical and dynamic. The former is that caused by the physical presence of obstructing prostatic tissue. This is present all the time, and apart from the possibility of a gradual increase over months or years, it is otherwise unchanging. Superimposed on this is the dynamic component related to the tone of the smooth muscle in the prostate and in particular, the prostatic capsule. In as much as the prostate gland is surrounded by a capsule, increases in capsular tone will increase the tendency of the prostate to compress the prostatic urethra. This tone is dependent on the degree of the sympathetic stimulation in the body acting via the alpha adrenoceptors. Thus, variations in the dynamic component produced by variations in the degree of sympathetic activity will be manifested by alteration in the prostatic obstruction over and above that produced by the mechanical component. "Caine M. et al 1988". These correspond well to the exacerbating factors mentioned above, which are known to increase the sympathetic activity in the body either intrinsically or extrinsically.

From this concept developed the logical idea that by blocking the alpha receptors one could expect virtually to abolish the dynamic component leaving the patient with the degree of obstruction produced by the mechanical component alone. Thus, one could hope

to obtain relief of patients' symptoms in accordance with the degree that the dynamic component contributed to them. Thus, it can be appreciated why an entirely new approach to helping these patients was proposed. It is in no sense a cure, for the basic underlying problem remains, but it is a treatment designed to relief the patients' symptoms. What then is the justification for considering such a palliative approach when an operation could be expected to cure the patient? The clue to this lies in the realization that the condition is not inevitably progressive. In approximately half of the patients having reached a certain stage, the prostatic obstruction no longer increases, but remains static for an indefinite period of time. "A.J. Bell, et al 1981". Some of these patients require an operation because the degree of obstruction may already endanger their health, but a considerable proportion of them are not in any danger and if their suffering could be sufficiently relieved by other means they would not need to undergo an operation. This treatment was first proposed by Marco Caine who published his first results on 1976. Since then, a very large number of patients have received this treatment and several publications from different parts of the world appeared, but the majority of them were concerned with the use of phenoxybenzamine. Despite its effectiveness, however, recent concern over the carcinogenic effect of phenoxybenzamine

in rodents has prompted the search for a satisfactory alternative. "Caine M. et al 1986".

In this thesis, prazosin, a selective alpha, adrenoceptor blocking agent will be used and its effectiveness in relieving the condition in B.P.H. will be tested.

ANATOMY OF THE PROSTATE GLAND

GENERAL DESCRIPTION

- The prostate gland is a composite structure which includes glandular elements and a stroma of collagenous and muscle tissue. It is classically described as a compressed inverted cone surrounding the very beginning of the male urethra and is situated in the true pelvis behind the inferior border of the pubic symphysis and the pubic arch lying in front of the ampulla of the rectum.

_ The prostate gland is conical in shape and has a base, apex, anterior, posterior, and two inferolateral surfaces.

THE BASE

It is the superior surface which is continous with the neck of the urinary bladder at the vesicoprostatic junction which is marked by a slight circular groove filled with fat and areolar connective tissue.

The base is triangular in shape and is pierced by the prostatic urethre near to its anterior extent.

ANATOMY OF THE PROSTATE GLAND

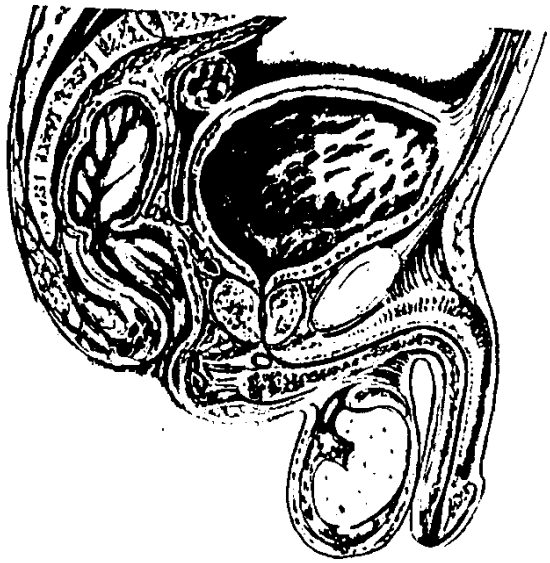

FIG. 1
Saggital section showing the position of the prostate in the pelvis and its relation to the symplysis pubis, the rectum, and the urinary bladder.

FROM GRANT'S ATLAS OF ANATOMY

FIG. 2
Coronal section showing the relations of the prostate to the muscles of the pelvic floor

FROM COLOUR ATLAS OF UROLOGY
R.W. LLOYD 1983

THE APEX

The apex of the prostate is directed inferiorly lying on the superior aspect of the superior fascia of the urogenital diaphragm which is itself continuous with the fascial sheath of the prostate.

THE ANTERIOR SURFACE

The anterior surface is relatively narrow and convex from side to side and extends from the apex to the base. It is about two centimeters behind the pubic symphysis separated from it by a rich plexus of veins and loose adipose tissue. Near its upper limit it is connected to the pubic bone on each side by the puboprostatic ligament. The urethra emerges through this surface a little above and in front of the apex of the gland.

THE POSTERIOR SURFACE

The posterior surface of the gland is flattened transversally and vertically is convex. It lies in front of the ampulla of the rectum separated from it by its own capsule and by Denonvilliers fascia. The upper border of the posterior surface is the vesico-prostatic junction. The two ejaculatory ducts enter this surface near to its upper border where they pass downwards and forwards to open in the prostatic urethra on either side of the verumontanum.

THE INFEROLATERAL SYSTEM

The inferolateral surfaces are prominent and somewhat convex, and are related to the anterior part of the levator ani-muscles which are separated from the gland by a rich plexus of veins embeded in fibrous tissue forming the lateral part of the prostatic sheath.

DIMENSIONS

The normal prostate reaches 20 plus or minus 6 gm in men between 21-30 years old and this weight remains essentially constant with increasing age unless B.P.H. develops, "Berry S.J. et al, 1984." It measures about 3.5 cm transversely at its base and about 2.5 cm in its vertical and anteroposterior diameters.

FASCIAL INVESTMENT, LIGAMENTS, AND ATTACHMENTS OF THE PROSTATE

THE PROSTATIC CAPSULE PROPER

The prostate gland has a fibromuscular stroma directly continuous with the fibromuscular element of the gland itself which, in turn, is directly continuous with the muscular element of the smooth musculature of the bladder neck . This fibromuscular stroma condenses on the periphery of the gland to form the prostatic capsule proper which is thin but firm capsule directly adherent to the prostatic tissue.