ROLE OF PROLACTIN HORMONE IN FEMALE INFERTILITY

Essay

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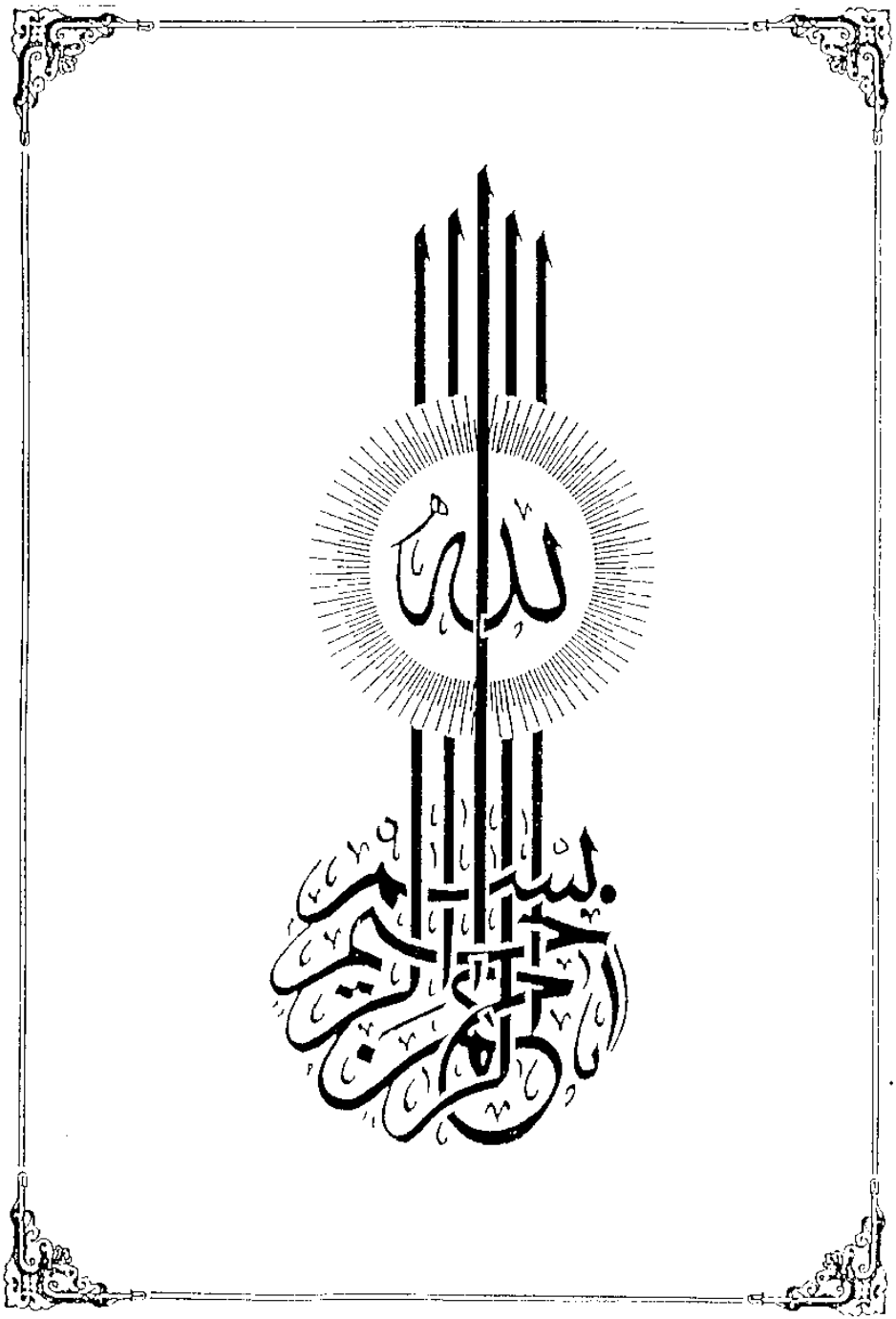

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INTRODUCTION

The development of radioimmunoassay and radioreceptorassay as a technique to determine minute amount of prolactin hormone in the serum and different body fluids had a remarkable repercussion on the gynaecolgical endocrinology and opened the door for different researches.

Prolactin is a polypeptide pituitary hormone, its chemical structure has been defined in man, it is composed of about 199 aminoacids and has a molecular weight of about 20,000 daltons. *(Shearman 1983)*.

Abnormally high levels of pituitary prolactin are now established as a cause of amenorrhoea, oligomenorrhoea, corpus luteum defects and infertility.

The mechanism by which hyperprolactinemia may interfere with gonadal function may be either:

- Suppression and or non-pulsatile secretion of pituitary gonadotropins.

- Lack of gonadal response to either endogenous or exogenous gonadotropins or combination of both *(Ben David & Schenker 1982)*.

Regardless of the mechanism, treatment which lowers the circulating levels of prolactin restores ovarian responsiveness

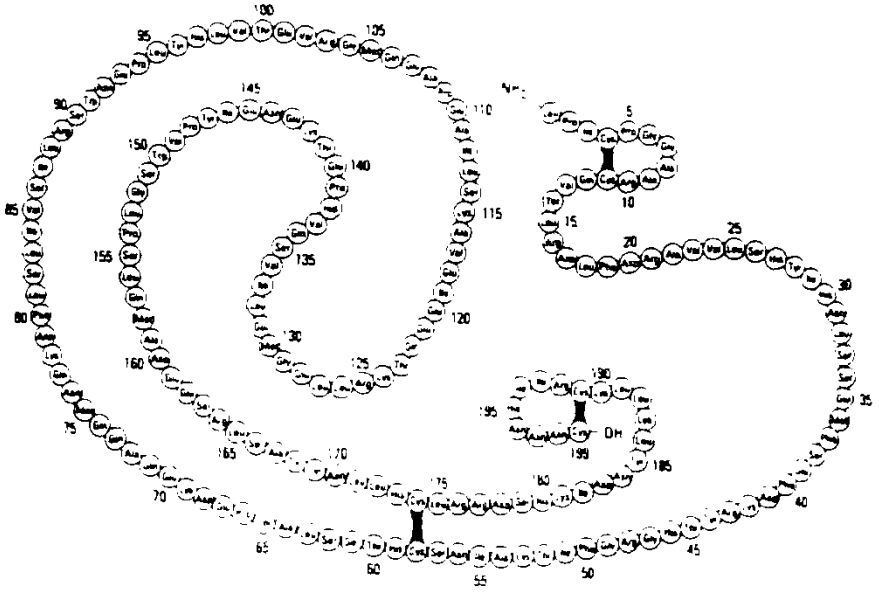
and menstrnal function. This is true whether the treatment consists of removal of a prolactin secreting tumor or suppression of pı olactin secretion *(Sperof et al 1989)*.

AIM OF THE WORK

Essay of full study of role of the serum prolactin level and female infertility whether hyperprolactinemia or normal levels.

Aetiology, diagnosis and management of these problems will be fully evaluated.

Review of Literature



HUMAN PROLACTIN HORMONE

PHYSIOLOGY OF PROLACTIN

BIOCHEMICAL STRUCTURE:

Human prolactin (PRL) is not a glycoprotein. It is an alcohol soluble polypeptide hormone made up of approximately 200 aminoacids and it contains 3 disulphide bridges within its structure. It has a relatively low molecular weight of 22.000. It is closely related structurally to growth hormone, but it differs from human growth hormone and human placental lactogen which contain only 2 disulphide bridges (*Friesen et al 1978*).

Prolactin is secreted by the lactotrophic pituitary cells containing esinophilic granules, which coexist with growth hormone producing cells in the lateral wing of the anterior pituitary gland (*Asch & Silverman 1982*).

Prolactin is synthesized within the cisternae of rough endoplasmic reticulum and packed by Golgi apparatus into small membrane bound pregranules which are used to form larger mature secretory granules. These granules lie in the cytoplasm until their contents are secreted by exocytosis resulting from fusion of the granule membrane with the surface membrane of the cell itself (*Chang 1978*).

Ben-David & Schenker (1982), found that human prolactin is composed of four isohormones, exhibit similar molecular weights, but differ from each other by their negative net charge.

Prolactin receptors are located in various tissues as mammary gland. liver. kidneys. Various human prolactin isohormones have a different affinities to binding sites of the different organs.

Soong et al (1982), have described three molecular weight variants of immunoreactive human prolactin in human sera or pituitary extracts. In normal serum, the predominant variant "Little" prolactin is probably monomer with a molecular weight of 23,000 and forms 80-85% of circulating radio-immunoassyable prolactin(RIA-PRL), the second one is dimer "Big" prolactin with a molecular weight of about 50,000 and forms about 9-20% of circulating (RIA-PRL) and the third type is a polymer "Big, Big" prolactin which forms 0-5% of remaining (RIA-PRL) activity.

Farkouh et al (1979), documented that by sensitive radioreceptorassay, decreased binding activity for the big, big and big variants of Prolactin, with radioreceptorassay RRA to Radioimmunoassay RIA ratio 25-50% those of "Little" prolactin in normal sera, suggesting the presence of RIA material that is not receptor active. The decreased RRA binding activity of the larger molecular weight variants indicates that these forms of prolactin may have a decreased biologic capacity compared to "Little" prolactin.

ASSAY METHODS OF PROLACTIN

Biological Methods:

Prolactin activity has classically been estimated by use of the pigeon crop sac test: many variations have been used ranging from the initial systemic crop weight method (*Riddle et al 1933*) to the sophisticated method depending on the local incorporation of ^{3}H-thymidine (*Ben-David 1967*). Assay methods in pigeons require rigid standardization since many factors have been shown to influence the response, such as the season of the year, the body weight of the birds, the strain and race of pigeon, the environmental temperature, and the volume of solution administered.

These methods remain quite useful to compare biological potencies of pituitary preparations of prolactin but are too insensitive and inconvenient to be applied to the routine assay of plasma samples (*L'Hermite 1976*).

Radioreceptor Assay:

The use of biologically active ^{125}I-ovine prolactin, as labelled by enzymatic radioiodination (*Frantz and Turkington 1972*), allows the hormone to be measured by its binding to specific membrane receptors for prolactin and other lactogenic hormones (*Frantz et al 1974*). The receptors can be prepared from rabbit or mouse mammary gland or from rabbit liver.

Biological lactogenic activity is quantified by the ability of samples to inhibit the binding of ^{125}I-ovine prolactin to these specific receptors. These assays cannot be regarded as being specific for prolactin measurement since they do not discriminate prolactin from growth hormone or chorionic somatomammotropin hCS (or hPL) *(L'Hermite 1976)*.

One advantage is, however, that they are not species-specific and can thus be used for identification and measurement of prolactin and placental lactogenic hormones secreted in various animal species *(Shiu et al 1973)*.

Radioimmunoassays (RIA):

Using partially purified human prolactin prepared from tissue cultures and antiserum to this material, *Bryant et al (1971)* developed the first radioimmunological procedure applicable to the detection of human prolactin in serum samples.

The lack of purified human prolactin prevented the development of an assay in which the materials used for immunization and for labelling were from the same animal species as that of the material to be measured *(L 'Hermite 1976)*.

In the development of radioimmunoassays, problems of extensive cross-reactivity and unavailability of purified material can sometimes be obviated by the use of heterologous systems in

which the hormones used for immunization and labelling are derived from different species *(L 'Hermite & Midgley 1971)*.

The subsequent isolation and purification of human prolactin *(Hwang et al 1972)* led to the development of homologous radioimmunoassays *(Friesen et al 1972)*.

Comparison of assay methods:

Differences between bioasssays and immunoassys are inherent in the definition of activities estimated by either procedure. The biological activity of prolactin is defined by the lactogenic effect of this hormone in several animal species. But other hormones such as growth hormone and human chorionic somatomamotropin also exhibit lactogenic effects in these bioassays, although their interference can be neutralised by pre-incubation with specific anti-growth hormone serum. Furthermore, human prolactin can exhibit biological activities in addition to the lactogenic effect. Alternations in the human growth hormone molecule as a result of proteolysis, can increase markedly its prolactin bioactivity and this may also contribute to differences between bioassay and immunoassay results *(L'Hermite 1976)*.

Radioimmunoassays are usually not directed against the entire molecule but rather to immunological sites, possibly of only a few amino acids, specific to this molecule. Degradation products, precursors or aggregated forms of the secreted