FETAL AND MATERNAL PROLACTIN IN PREGNANCY INDUCED HYPERTENSION

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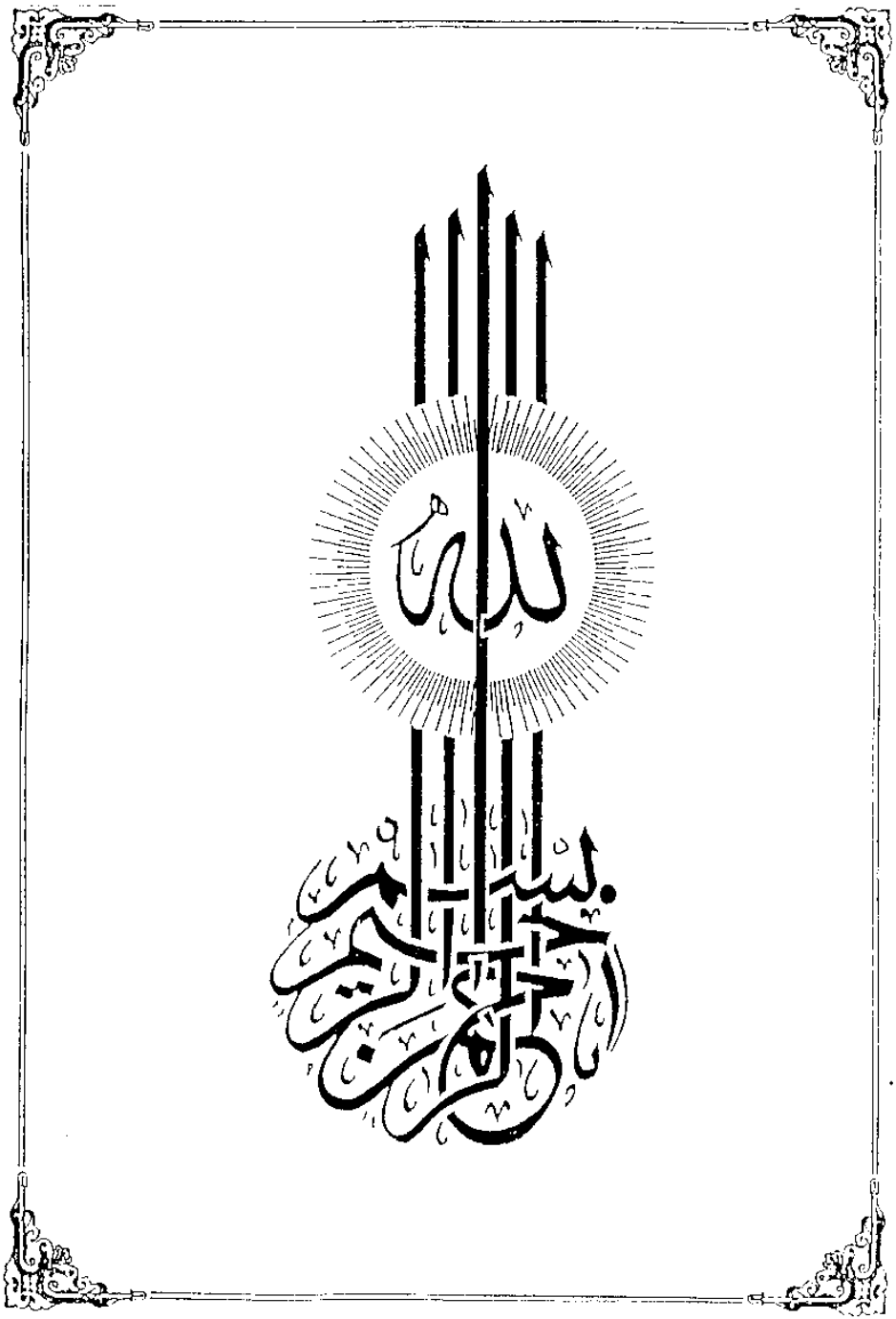

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Introduction

INTRODUCTION

The basic objectives of an obstetrician managing a case of pregnancy-induced hypertension (PIH) are the prevention and improving maternal and fetal outcome.

The preventive measures are dependent on the knowledge of the underlying etiology of the disease.

The condition of preeclampsia-eclampsia has fascinated many clinicians and scientists, even since ancient times and a vast literature has accumulated on the subject.

Over the past century such a large number of hypotheses have been produced to try to explain the cause of preeclampsia-eclampsia, that Zweifel, 1916, termed it "the disease of theories".

Many hormones produced by the placenta have been suggested as etiological factors in PIH, but non has so far been clearly proven, although they probably play a secondary role in producing some of the observed changes.

It has been suggested that prolactin (PRL) plays a role in the pathogenesis of hypertensive states of pregnancy by affecting osmoregulation (Horrobin et al,1971).

Reports on maternal serum prolactin concentrations in hypertensive pregnancy are conflicting.

The relation between TSH and PRL secretion is well known since thyrotropin-releasing hormone (TRH) stimulates the secretion of both hormones from the anterior pituitary gland.(Hershman et al, 1973).

On the basis of the above mentioned data, we are stimulated to study PRL and TSH concentrations in maternal serum, fetal serum and amniotic fluid in PIH and normal pregnancy aiming to throw a beam of light on the pathogenesis of this curious disease specific for pregnant women.

Aim of the work

AIM OF THE WORK

The aim of this work is to study the levels of PRL hormone and TSH in maternal serum, fetal serum and amniotic fluid in normal pregnant women and in pregnancy-induced hypertension (PIH).

The possible relationships between the pathogenesis, clinical course and fetal outcome of PIH and these hormones will be speculated.

Review of literature

HISTORICAL REMARKS ABOUT PROLACTIN

The first indication that the adenohypophysis was involved in mammary function came in 1928 from studies by Stricker and Gueter (Nicoll 1974). They reported that the injection of crude pituitary extract induced lactation in pseudopregnant rabbits, which have well developed mammary gland.

Riddle and Braucher 1931, reported that crude pituitary extracts stimulated the production of milk by the crop sac of pigeons. It was later established that the same adenohypophysial principle was responsible for the crop milk production and for mammary secretion (Lyons 1937; Riddle and Bates 1939).

The gonadotropic action of prolactin was established by Astwood (1941) and by Evans and his colleagues, (1941) when they demonstrated that the effectiveness of crude pituitary extracts in maintaining functional corpora lutea in rats was attributable to the prolactin contained therein. This finding gave origin to an additional synonym for prolactin, namely luteotropin.

Prolactin (PRL) as a distinct pituitary hormone in animals was initially identified as a result of its ability to initiate milk secretion in the pseudopregnant rabbit. This effect is the biologic response that led to its discovery and early designation as a lactogenic hormone (Nicoll, 1974).

Human prolactin has been chemically isolated as separate pituitary hormone by Hwang et al, 1971.

PHYSIOLOGY OF PROLACTIN HORMONE

Chemical Structure:

It is a single chain polypeptide of molecular weight about 20.000. The entire linear sequence of 198 aminoacids has been identified (Shome and Parlow, 1977).

Although it is a distinctly separate hormone, prolactin bears some structural resemblance to human growth hormone (hGH) and human placental lactogen (hPL), and shares some of the same biologic properties. Although GH and hPL demonstrate substantial lactogenic activities, yet the lactogenic potential of PRL is significantly greater than that of GH or hPL (Chang 1978).

Prolactin Secretion:

Prolactin is secreted by the lactotropic cells which coexist with G H-producing cells in the lateral wing of the anterior pituitary gland (Chang 1978).

Histologic examination by light microscopy demonstrated that the lactotropic cells contain acidophilic granules that can be differentiated from those of somatotropic cells by the uptake of carmosine or erythrocin stains (Chang,1978).

Electron microscopy and immunohistochemical staining techniques indicated that the prolactin -secreting cells possess distinct morphologic features; lamellar pattern of the rough endoplasmic reticulum, large secretory granules (400-900μm in diameter), and polymorphism of their secretory granules (Hopkins et al., 1973).

In the lactotropic cells, prolactin is synthesized within the cisternas of the rough endoplasmic reticulum and packaged by the Golgi apparatus into small membrane-bound proganules, 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).

Molecular Actions:

Most studies indicate that prolactin acts on specific receptors which are located on the outer membrane of the target cells (Fraser 1979). It is well known that the target organ for PRL is the mammary gland during pregnancy and lactation; however, a number of other organs are affected by this hormone (Hamosh & Hamosh, 1977). Zinder et al.,(1974) have shown that the adipose tissue becomes a target organ for PRL during late pregnancy and lactation. In addition to the mammary gland, PRL binds specifically to a number of other tissues such as liver, adrenal cortex and kidney (Posner et al.,1974).

Physiologic Serum Levels in Non-pregnant State :

Prolactin levels prior to menarche in the female and puberty in males are comparable and at a low level (Chang 1978).

In prepubertal children, prolactin levels are low, ranging between 2-12ng/mL. (Archer 1977).

During puberty, prolactin levels are not significantly altered in boys, whereas a steady incremental change occurs in girls, which persist until adult prolactin concentrations are attained (Friesen et al.,1972). This increase in the circulating prolactin has been observed to correlate closely with menarche, and therefore

is attributed to the ovarian production of estrogen (Archer 1977).

RIA of prolactin in blood of women during the menstrual cycle indicated that the plasma levels of the hormone change with different stages of the cycle (Robyn et al., 1973).

During the early follicular phase plasma prolactin concentrations are low, but they increase slowly as the time of ovulation approaches. One day prior to the midcycle increases in LH and FSH, plasma prolactin levels increase abruptly then decline coincident with the decreases in FSH and LH. During the luteal phase, plasma prolactin levels increase again and remain elevated until the end of the cycle. (Nicoll, 1974). However, other groups of investigators have found no changes in plasma prolactin levels during the menstrual cycle of women (McNeilly et al.,1973; Zarate et al., 1973; Friesen et al., 1972).

As the women ages, there is a progressive decline in prolactin concentration which begins after the age of 40 years. This decrease is associated with the menopause and the resultant decline in circulating estrogen (Friesen et al., 1972 & Robyn et al., 1977). There is diminished prolactin response to TRH, suggesting diminished prolactin stores and possibly a reduced number of lactotrops secondary to estrogen deprivation(Chang, 1978).

Control of prolactin production:

Current investigative efforts indicate that prolactin secretion is regulated primarily by hypothalamic inhibitory factor called prolactin-inhibitory factor (PIF) (Meites and Clemens, 1972).

A review by L'Hermite et al., (1978) cited studies indicating that dopamine and norepinephrine, when injected into the third ventricle of rats, lower serum prolactin levels.

Control of prolactin release appears to be largely inhibitory in nature although prolactin-releasing activity has also been demonstrated in several animal species, furthermore thyrotropin-releasing hormone (TRH) in pharmacologic amounts has been shown to stimulate prolactin secretion in human (Meites and Clemens,1972).

Serotonin has also been implicated in mediating prolactin release (Zacur et al., 1976).

Factors affecting the Secretion of Human Prolactin:

(1, moderate increase; 1^{+}, marked increase; 1^{++} very marked increase; N, no change; D, moderate decrease; D^{+}, marked decrease).

FACTOR	CHANGE IN PRL LEVEL
* Sleep	1+
* Nursing	1++
* Breast stimulation in non lactating	1
* Stress	1+
* Hypoglycemia	1
* Sternuous exercise	1
* Sexual intercourse in women	1
* Pregnancy	1++
* Estrogens	1
* Hypothyroidism	1
* TRH	1+
* Phenothiazines	1+
* Opiates	1
* Glucose	N
* Somatostatin	N
* L dopa	D+
* Apomorphine	D+
* Bromocriptin & related ergot derivatives	D+

(Ganong ,1983; modified from Frantz A. 1978).

Dopamine is the major biogenic amine controlling basal secretion of prolactin (Meites, 1973; Birge et al.,1970).

Biological Activities of PRL:

The physiologic role of hPRL in both males and females is obscure, despite the fact that not less than 85 biological actions of PRL have been proposed (Saxena 1977).

Prolactin and breast development :

There is a small rise in prolactin level in girls during breast development (Thorner et al., 1977).

PRL is a lactogenic hormone and it also appears to induce mammotropic stimulation, at least in experimental animals (Sulman, 1970). Its role in normal pubertal breast development of the human female is only theoretic as there are no data in humans to support or deny its potential mammotropic role (Jacobs, 1974).

Moreover, serum PRL levels in pubertal males with unilateral or bilateral gynecomastia have not been reported to be elevated (Jacobs, 1974 and Nicoll, 1974). However, Archer, 1980 had suggested that a combined effect of estrogen and prolactin on the breast tissue accounts for breast development that is recognised as thelarche.

Prolactin and lactogenesis:

The principal physiologic role of PRL is initiation and maintenance of lactation (lactogenesis) and this is the only well documented effect or PRL in the human (Saxena, 1977 and Archer, 1980).

Prolactin can induce milk formation when added to explants of mammary glands from pregnant mice in vitro (Williams, 1974).

The action of prolactin on the corp sac of pigeons and doves is a facinating facet of comparative endocrinology. Following