AIN SHAMS UNIVERSITY
Faculty of Medicine
Department of Obstetrics & Gynecology

ORAL AND VAGINAL LISURIDE IN THE TREATMENT OF HYPERPROLACTINEMIA

A Thesis

Submitted in Partial Fulfillment of
Master Degree in
Obstetrics and Gynecology

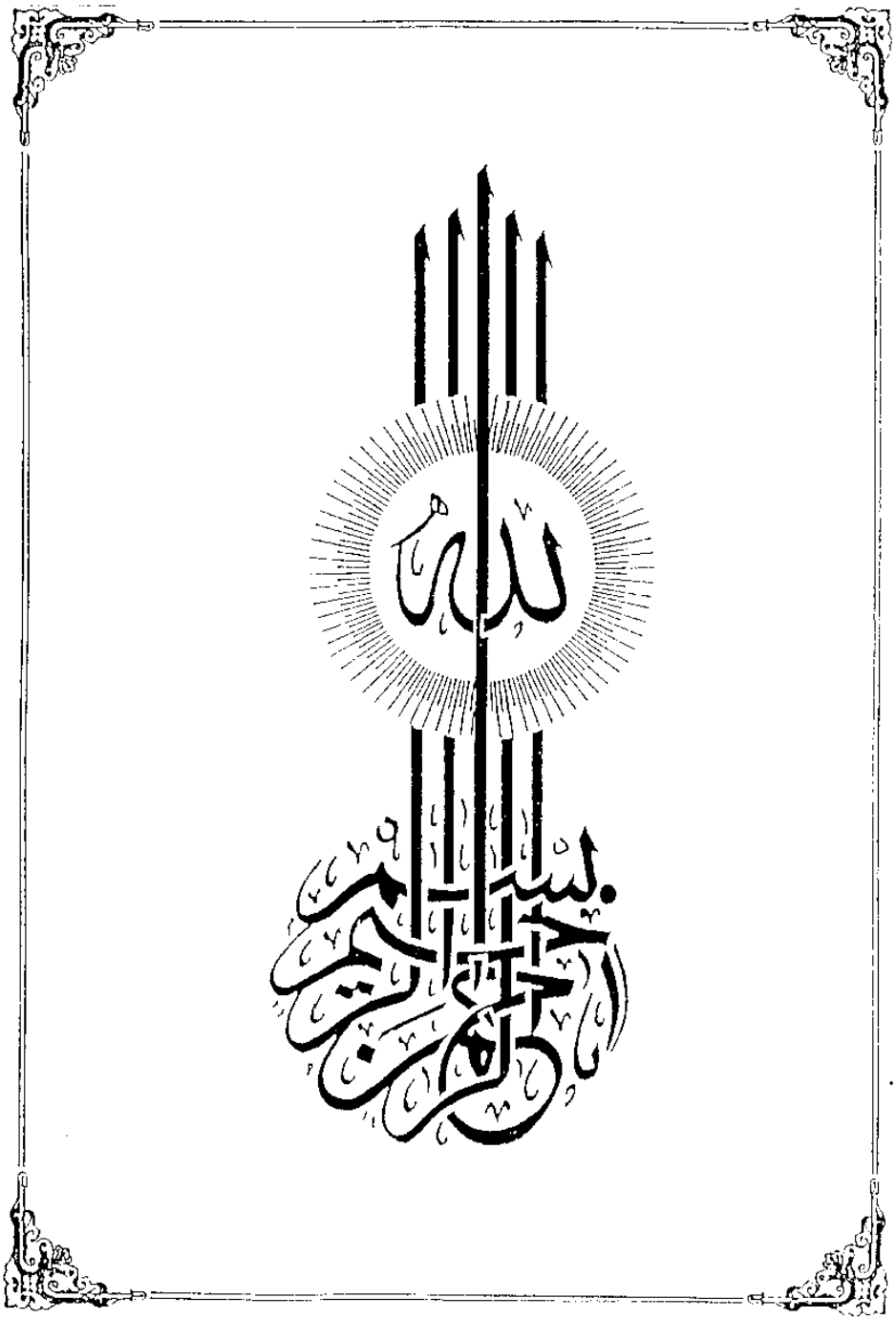
By
Naglaa Ahmed Shehata
M.B.,B.Ch.

Supervised by

Prof. Dr. Ibrahim El-Mitwally Samaha
Professor of Obstetrics and Gynecology
Faculty of Medicine
Ain Shams University

Prof. Dr. Gamal Abdel-Salam Wafa
Professor of Obstetrics and Gynecology
Faculty of Medicine
Ain Shams University

1995



Acknowledgement

I wish to express my sincere appreciation and deepest gratitude to Prof. Dr. Ibrahim El-Mitwally Samaha, Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his precious guidance comments valuable suggestions and criticism. His valuable assistance during the preparation of this thesis will remain a valued memory.

I am also deeply indebted to Prof. Dr. Gamal Abdel-Salam Wafa, Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University for his keen supervision and cardial support during the preparation of this thesis will remain a valued memory.

Last but not least, I am very grateful to every one who helped me by any means during the course of this work.

Naglaa Ahmed

LIST OF ABBREVIATIONS

ACTH	Adrenocorticotropine hormone
AII	Angiotensin II
Ca	Calcium
DA	Dopamine
DHA	Dehydroepiandrosterine
DHAS	dehydroepiandrosterine sulphate
DHT	Dihydrotestosterone
ELISA	Enzyme linked immunosorbant assay
FSH	Follicular stimulation hormone
G-PRL	Glycosylated prolactin
GnRH	Gonadotrophin releasing hormone
hCS	human chorionic somato memmotropin
LH	Luteinizing hormone
PIF	Prolactin inhibiting factor
PIP	Phosphatidyl inositol biphosphate
PLC	Phospholipase
PRF	Prolactin releasing factor
PRL	Prolactin
RIA	Radioimmunoassay
SHBG	Sex hormone binding globulin
T	Testosterone
TRH	Thyrotropin releasing hormone
TSH	Thyroid stimulating hormone

CONTENTS

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INTRODUCTION

Prolactin is a protein hormone of the anterior pituitary gland. It has many physiological actions in the body including development of the breast, milk production, maintenance of hypothalamic - pituitary ovarian axis *(Leon Speroff, 1989).*

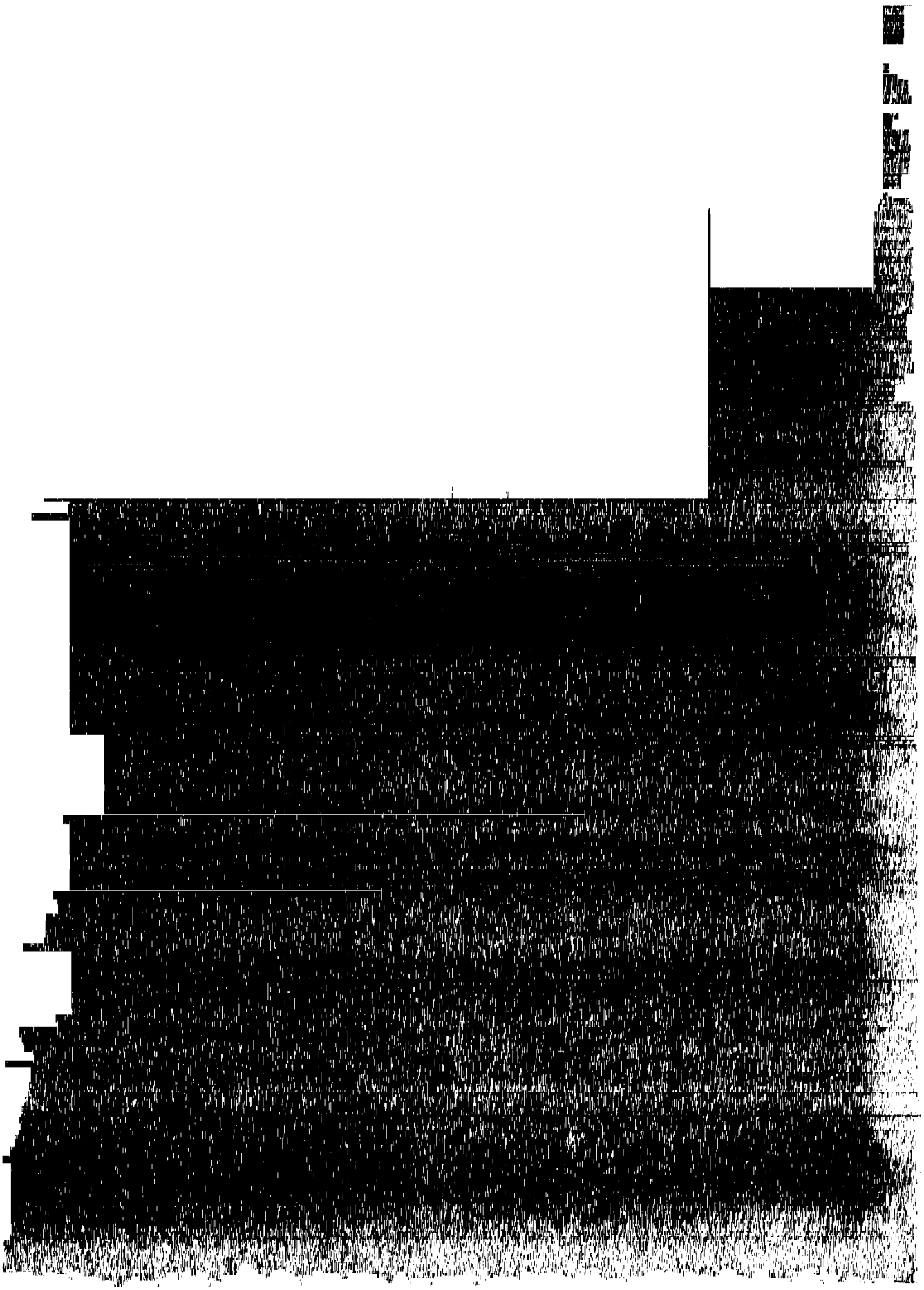
Hyperprolactinemia is either physiological or pathological, it is usually treated with bromocriptine but with side effects in half or more of patients *(Ginsburg, 1992).*

Oral bromocriptine is a standard treatment for hyperprolactinemia but it has marked gastrointestinal side effects so many studies on vaginal bromocriptine have been done and it is an effective treatment vaginally without gastrointestinal side effects *(Oscar et al. 1989 and Ginsburg et al., 1992).*

Lisuride is semisynthetic ergot derivative (Dopergin) very effective in reducing prolactin level in hyperprolactinemia with dose lower than that of bromocriptine and less side effects *(Rynolds et al., 1981 and Horowiski et al., 1978).*

AIM OF THE WORK

The aim of this work is to study the therapeutic effect of oral versus vaginal lisuride (Dopergin) in the treatment of hyperprolactinemia.



NORMAL PROLACTIN

A. Structure:

Human prolactin is a polypeptide hormone secreted by the anterior pituitary gland.

It contains 198 aminoacids and three disulphide bridges.

It has a structural similarity to human chorionic smatomamotropin and growth hormone *(Ganong, 1975).*

Prolactin gene structure

The prolactin gene is positioned on human chromosome No. (6) *(Owerbach et al., 1981),* which is also the locus of human leukocyte antigen (HLA) *(Farid et al., 1981).* The significance of this association, if any, is currently unknown. The gene for human prolactin was cloned in 1981. A remarkable sequence homology, up to 92 per cent between human growth hormone and human placental lactogen *(Miller et al., 1983)* and 42 per cent between human prolactin and human growth hormone *(Seburg et al., 1982 and Truong et al., 1984),* has been observed. Additional members of the prolactin gene family have been described; the human decidual prolactin *(Truong et al., 1984).*

Prolactin is synthesized in the ribosomes and endoplasmic reticulum of the lactotrops, concentrated in Golgi

apparatus and stored in the form of granules in the cytoplasm, ready to be released. During the secretory process these granules are released from the cells either single granules or in small groups by exocytosis and during the process of exocytosis, the individual cell membrane fuses with the membrane surrounding the hormone granules *(Vila-procile et al., 1973).*

THE NORMAL LEVEL OF PROLACTIN

Archer, (1980) recorded some prolactin levels as follows:

In normal female

The normal prolactin level is 5-20 ng/ml and also *Kletzky et al. (1986)* recorded that the normal prolactin level in female is up to 20 ng/ml in follicular phase and up to 30 ng/ml in luteal phase.

During sleep

There is up to 50% increase in prolactin level during sleep.

Under stress and breast manipulation 40 ng/ml.

During pregnancy

First trimester 30-50 ng/ml.

2nd trimester 100 ng/ml.

3rd trimester 200 ng/ml.

Post partum about 200 ng/ml.

Level in normal male

Prepubertal boys 8.4 ng/ml.

Pubertal boys 11.6 ng/ml.

Adult males 13.9 ng/ml.

Green Span and Forshan (1983) suggested that prolactin is cleared by the liver 75% and kidneys 25% and its half time of disappearance from the plasma is about 50 minutes. *Schmide et al., (1975)* suggested that the half life of prolactin was estimated to be about 14 minutes.

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 *(Ben-David et al., 1982).*

Short et al. (1984), 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 non glycosylated monomer with a molecular weight of 23,000 and forms 80-85% of circulating radio-immunoassyable prolactin (RIA-PRL) and has highy receptor binding activity 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 has 1/4 bioactivity of little and the third type is a polymer "Big, Big" prolactin (M-W 100.000) which forms 0-5% of remaining (RIA-PRL) activity.

These heterogenous forms of PRL have been found in both normal and hyperprolactinemic states, and the "big" and "big-big" forms apparently have lower receptor-binding properties. Normal fertility is maintained in patients with hyperprolactinemia composed mainly of "big-big" PRL *(Walker et al., 1980)*. However, circulating "big" PRL in human plasma appears to be able to convert to "little" PRL by reduction of its disulfide bonds. Glycosylated forms of hPRL are less immunoreactive than "little" PRL.