PROGESTERONE RECEPTORS AND MONTHLY INJECTABLE CONTRACEPTIVES

A Thesis

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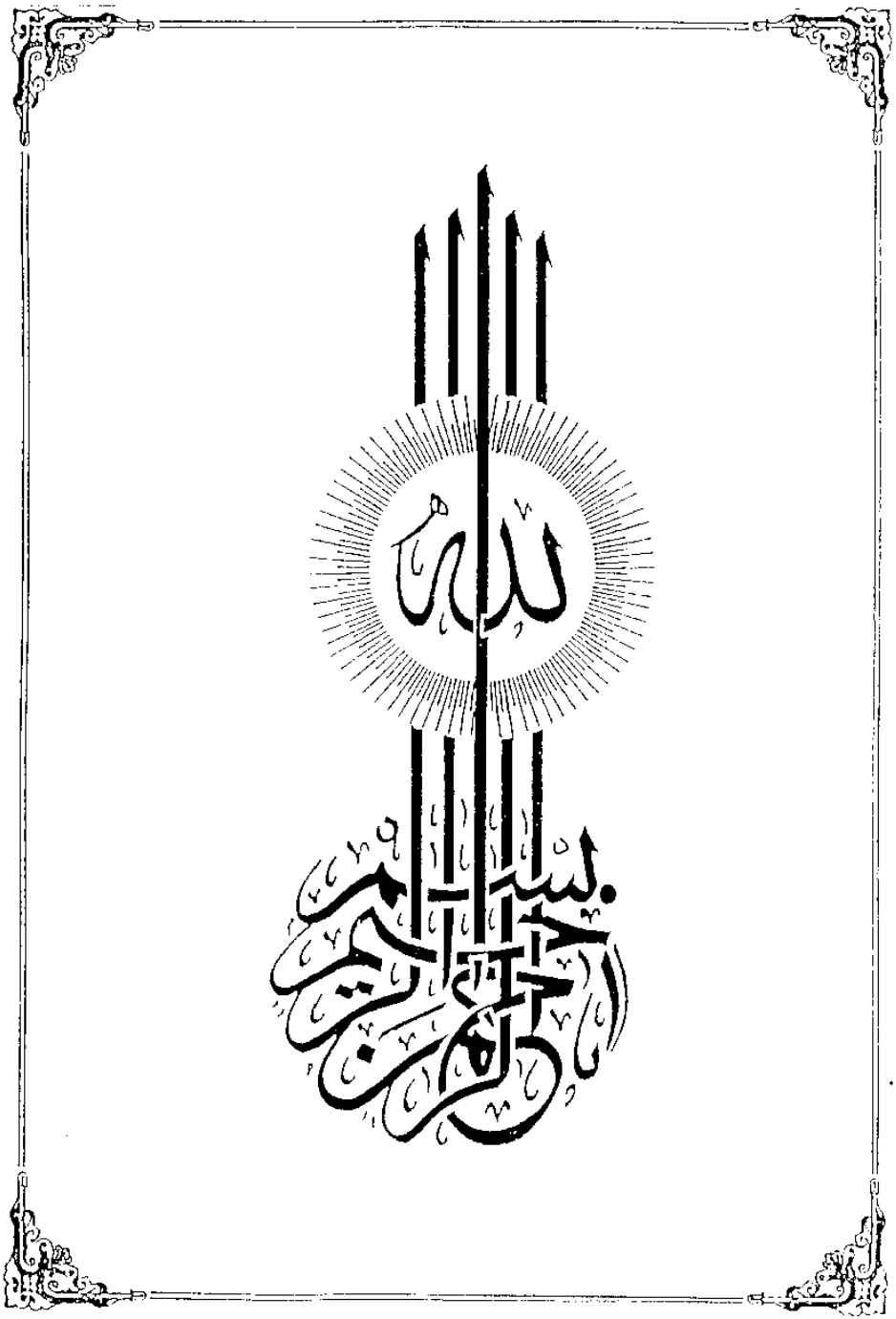

List of Tables

	Page
Table 1	84
Table 2	85
Table 3	86
Table 4	87
Table 5	88
Table 6	89
Table 7	90
Table 8	91

List of Figures

	Page
Figure 1	9
Figure 2	14
Figure 3	17

List of Abbreviations

PGR	Progesterone Receptor
PR	Progesterone Receptor
ER	Estrogen Receptor
SHR	Steroid Hormones Receptors
PGR. PRB	Progesterone Receptor Before
PGR. PRA	Progesterone Receptor After
CER	Cytoplasmic Estrogen Receptor
CPR	Cytoplasmic Progesterone Receptor
NER	Nuclear Estrogen Receptor
NPR	Nuclear Progesterone Receptor
HRP	Human Reproduction Program
E.CY	Estradiol Cypionate

Contents

	Page
Introduction	1 - 4
Aim of the Work	5
Receptors	6 - 15
Structure of Steroid Hormone Receptors (SHR)	16 - 18
Control of Receptor concentration	19 - 25
Distribution of SHR in Endometrium	26 - 28
Methods of Assay of Steroid hormone receptor	29 - 36
Injectable contraceptives	37 - 50
Pharmacokinetics and pharmacodynamics of the monthly injectables	51 - 59
Effects of the Monthly Injectable on the endometrium	60 - 64
Adverse reactions of the monthly injectables	65 - 69
Haemostatic Changes During Steroid Therapy	70 - 74
Subjects and Methods	75 - 83
Results	84 - 91
Discussion	92 - 99
Summary and Conclusion	100-103
References	104-134
Arabic Summary	1 - 4

INTRODUCTION

INTRODUCTION

Sex steroid hormones control the growth and differentiation of female reproductive organs.

Steroids are thought to produce most of their effects on cells by interacting with specific receptors which can be found in all hormone responsive tissues. It is always possible to detect receptors in samples of normal endometrium if sufficient tissues is available and the sample is transported to the laboratory and assayed correctly. Receptors concentration may be reported relative to tissue wet weight, protein or DNA content. Although protein content is the usual reference index, several authors have argued that expression of receptor content per unit DNA, is more correct when comparing receptor concentration among samples from different patients **(Bayard et al., 1978; Castagnetta et al., 1983).** Another possible source of variation in receptor content is the site of the biopsy within the uterine cavity. Several authors have reported a progressive decrease in cytoplasmic estrogen receptors (CER) and cytoplasmic progesterone receptors (CPR) content along the length of the organ from fundus to cervix **(Tsibris et al., 1981) and Robel et al., 1981). However, Bayard et al., (1978)** concluded that, although

variation occured between the fundus and the body of the uterus, no systematic trend could be observed and that the ratio of progesterone estrogen receptor content remained constant throughout the uterus. However, where possible, biopsies should be confirred to the mid region of the uterine cavity. Determining the receptor concentration in normal endometrium requires knowledge of the previous cycle, history, the basal body temperature, histological evaluation of the endometrium and serial measurements of plasma LH, estradiol and progesterone. Even so precise identification of the day of the cycle is difficult. For this reason, most authors prefer to divide the cycle into early proliferative, late proliferative, early secretory and late secretory phases. The (CER) levels reach a peak in late proliferative phase and then fall during the rest of the cycle **(Bayard et al., 1978; Levy et al., 1980).**

Similarly, nucleoestrogen receptor (NER) have been found to increase between the early and late proliferative phases and to fall thereafter **(Sotter et al., 1979; levy et al., 1980)**. This is consistent with the concept that estrogen stimulates synthesis of its own receptors, whereas progesterone supresses estrogen receptor synthesis **(Hunter et al., 1980).**

Within the past 25 years steroidal preparations have become available which allow the user contraceptive protection over extended periods of time, either because of their intinsic longacting properties eg., injectable preparations or, through the use of various delivery systems e.g. implants, intrauterine devices (IUD) or vaginal rings. Currently there are two injectable progestagen - only contraceptives used at all widely family planning programmes through the world. These are depot - medroxy progesterone acetate (DMPA) (IPPF Medical Bulletin Vol. 21 No. 2 April 1987) and norethisterone enanthate (NET-EN).

One of the major side - effects of progestagen only contraception is disruption of normal menstrual bleeding, giving rise to unpredicatable bleeding episodes as well as amenorrhea. The combination of a synthetic progestagen with an estrogen, however, appears to affect the endometrium in a similar way to that seen in combined oral contraceptives. Further more, although no systematic approach to treatment of prolonged and unpredictable progestagen induced bleeding has yet evolved, estrogens are often used satisfactorily for this purpose. **(Hall pE, 1983).** Thus investigators started to incorporate estrogen to reduce bleeding related problems. Because of concern about continued exposure of subjects to high levels of estrogen, long acting estrogen esters

were avoided and the resulting conbination products were therefore shorter acting than the existing progestagen - only preparations. In response to the demand from certain populations for safe, well investigated, once a monthly injectable contraceptive with high efficacy and giving minimal disruption of menstrual bleeding, the World Health Organization's special programrme of research in Human Reproduction devised a strategy for the development of once a month contraceptive. This involved, as an initial phase, the optimization of the dosage and progestagen: estrogen ratio of two combination form ulations based on (DMPA) and estradiol cypionate and (NET-EN) and estradiol valerate. **(Oriow MA et al., 1980).**

Studies on the pharmacokinetic profiles and pharmacodynamic effect of the estrogen alone and of various dosage combination of the progestagens and the estrogens have shown the optimal dosages progestagen estrogen ratio.

Cyclofem : 25 mg DMPA + 5 mg estradiol cypionate.

Mesigyna : 50 mg NET - EN + 5 mg estradial valerate.

(Aede A, et al., 1985).

AIM OF THE WORK

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The aim of this study is to compare PGR in Endometrium before and after administration of 2 preparations once monthly injectable contraceptives.

REVIEW OF LITERATURE