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RESEARCH ARTICLE

A Prospective Study on Due of Hormonal Supplements using in Gynecology Department

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ABSTRACT:

AIM AND OBJECTIVE: Aim of our study is to study the role of hormonal replacement therapy in gynecological problems. To study the effect of estrogen, progesterone hormones used in gynecological problems such as, dysfunctional uterine bleeding ,pregnancy, menopause, polycystic ovarian syndrome.
METHODS AND MATERIALS: 100 patients were included in this study, which includes prospective monitoring of different type of gynecological problems who under went for Hormonal Replacement therapy. The statistical test used in the study is Student t test. **RESULTS:** Out of 100 patients taking hormonal therapy most of them were pre and post Menopausal women, and also pregnancy status women were included in this study. Indications like DUB patients were more(21%),followed by Menopausal women(16%) and for these specific indications, specific hormonal therapy was given in which Mala N(25%) drug was commonly used, followed by progesterone(17%).

KEYWORDS: Estrogen, Progesterone, Gynecological problems, Hormonal replacement Therapy.

INTRODUCTION:

HRT(Hormone replacement therapy)typically refers as replacement of hormones,that are naturally available with synthetic and semisynthetic hormones. some HRTs like marketed progestins, are completely synthetic. others like conjugated equine estrogen(CEE) are semisynthetic and these are drived from animal sources. Bioidentical hormonal replacement therapy generally involves use of steroid hormones includes estrone sulfate, estropipate, 17-β estradiol, estriol, progestrone, testosterone and dehydro epiandrosterone (DHEA). Bioidentical hormones are derived from plant sources and are named as Bioidentical because it is found that they arethey are structurally similar to endogenous hormones, its not just hormone receptor binders.Bioidentical hormone replacement therapy otherwise refered as natural hormone replacement therapy.[1]

In Hormone replacement therapy(HRT) the estrogen is similar to natural ovarian production should not be confused with the potent ethinyl estradiol used in combined oral contraceptive regimens.the add of progesterone or micronised progesterone is essential if a women who still has uterus.and it is used to prevent endometrial hyperplacia and cancer.estradiol can be given orally(micronised estradiol, estradiol valerate estrone, estrol or conjugated equine estrogens), or can also be given transdermally ((17-βestradiol) commonly topical vaginal administration of estrogen is also used for relieving of local symptoms.various progesterones also be used in combination with estradiol, either in sequential cyclical regimen or as continuous therapy(CCT)progestogenes are mostly administered orally, and only two formulations being available transdermally.[2]

Hormonal therapy this has been shown that by inducing anovulation and amnorrhoea, GnRh agonists, leuprolide, histreline, and goeseriline can also provide significant relief of symptoms in various patients with out comorbid depression. in women with a history of, the treatment of indused menopause with estrogen or estrogen plus

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progestational agent can also induce recurrent symptoms of PMDD. this has been shown that it it supports the theory of an etiologic role forfemale gonadal hormones in PMDD. these medications can also induce menopausal symptoms such ashot flaushes, vaginal dryness, fatigue, irritability, cardiac problems, and osteopenia. Danazol (Danocrine), a weak androgen prescribed for patients with who has endometriosis, fibrocystic breast disease, and hereditary angioneurotic edema, can also be used to treat PMDD. The usual dosage is 100 mg twice a day. Such type of treatment can reduce symptoms.[3]

17-β-estradiol (E2):

is a lipophilic hormone with low molecular weight, and it occurs naturally. Cellular signaling of estrogen is mediated and classically binds to two soluble intracellular nuclear receptors, i.e estrogen receptor (ER) alpha, and ER beta. The isoform β is comparetively smaller than the isoform α, and the DNA-binding domains of both subtypes are highly conserved. After binds to the E2, ER forms a stable dimer that interacts with specific sequences known as estrogen response elements (EREs) and to initiate the transcription of target genes. Ligand- bound ERs can also interact with other transcription factors complexes and it influence the transcription of genes that do not harbor EREs. Third and fourth mechanisms of ERs regulatory actions are, respectively, non-genomic and the ligand independent pathway. Various rapid signalling events such as activation of kinases and phosphatases and also increases in ionfluxes through out membranes has been described.[4]

Progestins are effectively used to decrease excessive menstrual bleeding and the shorter course of oral progestin therapy can also be used for anovulatory uterine bleeding. Progestin therapy for menorrhagia necessary to be given for 21 days per month for effective treatment.The continuous progesterone release provided by the levonorgestrel-releasing intrauterine system and it reduces menorrhagia more effectively than oral progestins.[5]

COMBINATION OF ORAL CONTRACEPTIVE PILLS:

Most combinational OCPs contain ethinyl estradiol (20 to 50 mcg) and a synthetic progestin (e.g., norgestrel, norethindrone, levonorgestrel, desogestrel).These pills inhibit he ovulation in most women. They also used to helps in thickening of the cervical mucus, which impedes transport of sperm to the uterus. Progestin- only pills,also known as birth control pills, that contains only progestin.it also referred as "minipills",which inhibit ovulation about 50percent of women. their primary mechanism of action is thickening of the cervical mucus.this effect can occurs with in hours of taking a progestin-only pill can take and peaks about four hours after the pill is taken.[6]

Progestin only pills:

are very helpful in women who cannot use OCPs that contain estrogen and/or who do not want to take long term contraception.Breastfeeding women can also use this form of contraception with perfect use.only 0.5 percent of women got pregnency with in the first year of using progestin-only OCPs.

Contraceptive injections:

medroxyprogesterone acetate (Depo-provera) is an intramuscular progestin injection.the usual dose is (150 mg) which provides approximately 14 weeks of adequate contraceptive levels.ovulation is inhibited in most women,because of the high dose of progestin.[7]

Contraceptive implants:

levonorgestrel (norplant) is a contraceptive implant. it consist of six subdermal implants that release a constant low level of the progestin levonorgestrel over a five year period.0.05 mg to 0.08 mg per day for the first year and 0.03 mg per day for the remaining four years.by use of this OCPs ovulation is inhibited in most women.the implants also induce a thickened cervical mucus and cause endometrial changes that impede implantation.[8]

METHODS AND MATERIALS:

The present study was conducted in ESI hospital ,ayanavaram, chennai. It is government hospital consist of all departments i.e., general medicine, orthopaedics, surgery,gynecology, pediatrics and psychiatry.

This study is a prospective, single centered observational study and it includes 100 female patients who are having different gynecological problems such as DUB,PCOD, menopause, implantation, pregnancy, fibroid uterus.

The statstical analysis used for the study is student t test and the duration of the study is 10 months. This statsical analysis was done after all the data was obatained. the complete data was collected from the patients and it is documented in a case proforma.

The case proforma used in the study was consist of patient details(age, IPno, height, weight, family history, social history, past medical history),general examinations, lab investigations ,tests of the particular conditions.

INCLUSION CRITERIA:

- Female patients with polycystic ovarian syndrome, dysfunctional uterine bleeding, menopause, thyroid.
- Pregnant women

EXCLUSION CRITERIA:
Psychological patients.

RESULTS AND DISCUSSION:

Table 1 shows distribution pattern based on age

Age	No.of patients(n=100)	Percentage(%)
15-25	37	37%
26-35	29	29%
36-45	7	7%
>45	27	27%

Out of selected 100 patients 37 patients were in the age group of 15-25, 29patients were in the age group of 26-35,7 patients were in the age group of 36-45,and 27 patients were in the age group of above 45.according to this data 15-25 age group of people were mostly affected.

Table 2 shows distribution pattern based on Menopausal status

Groups	No.of patients	Percentage(%)
Pre menopausal	72	72%
Post menopausal	28	28%

Out of selected 100 patients premenopausal patients were 72 and post menopausal patients were 28

Table 3 shows distribution based on pregnancy status

Groups	No.of patients(n=32)	Percentage(%)
1st trimister	17	53.1%
2nd trimister	0	0%
3rd trimister	15	46.8%

Among 100 patients 1st trimister patients were 17,2nd trimister patients were none, and 3 rd trimister patients were 15. according to this data hormonal therapy was taken by mostly 1st trimister women.followed by 3rd trimister women.

Table 4 shows distribution based on comorbidities

Disease	No.of patients(n=63)	Percentage
Hypertension	11	17.5%
Diabetis	13	20.63%
Thyroidism	15	24%
Bronchial asthma	9	14.2%
COPD	5	8%
TB	4	6.3%
CAD	6	9.5%

Table 5 shows distribution based on concomitant drug use

Concomitant Drugs	Diagnosis	No.of patients(n=100)	Percentage%
Metformin	Diabetis	11	11%
Coversyl AM(Perindopril+Amlodipine)	Hypertension	13	13%
Levothyroxine	Thyroidism	15	15%
Salbutamol	Bronchialasthma	9	9%
Deriphylline(Theophylline+Etophylline)	COPD	5	5%
DirctlyObservedTherapy(DOTS)therapy(INH,RMP,PZA,EMB)	Tuberculosis	4	4%
Isosorbid dinitrite	CAD	6	6%

Table 4 and table 5 shows that gynecological problems associated with other diseases and concomitant drugs of diseases. Hypertension patients were 11, coversyl AM was taken by these patients, Diabetic patients were 13, Metformin was taken by these patients,thyroidism patients were15, Levothyroxine was taken by these patients. Bronchial asthma patents were 9, Salbutamol was taken by these patients,COPD patients were 5, Deriphylline was taken by these patients, TB patients were 4, DOTS therapy was taken by these patients and CAD patients were 6, Isosorbide dinitrite was taken by these patients.according to this data Thyroidism patients were more, followed by diabetis and hypertension patients.

Table6 shows distribution based on indications

Indications	No.of patients	Percentage(%)
DUB	21	21%
PCOS	11	11%
Implantation	15	15%
Menopausal	16	16%
Menorrhagia	7	7%
Contraceptives	8	8%
Fibroid uterus	7	7%
Induction of labour	15	15%

This collected data shows that among 100 patients 21patients have suffered with DUB, PCOS patients were 11, implantation patients were 15, menopausal patients were 16, menorrhagia patients were 7, contraceptive patients were 8, Fibroid uterus patients were 7, and who came for delivery(induction of labour) patients were 15.according to this data DUB patients were more.

Table 7 shows distribution based on Hormonal replacement therapy

Drugs	Dose	No.of patients	Percentage (%)
Progesterone	400mg(p/o)	17	17%
Estradiol	2mg(p/o)	12	12%
Mala N	1 tab(p/o)	25	25%
Mala D	1 tab(p/o)	16	16%
Levonorgestrel	36mg(p/o)	13	13%
Oxytocin	20U in 1000ml IV	12	12%

This study shows among 100 patients Progesteronewas taken by 17 patients, Estradiol was taken by12 patients, Mala-N was taken by25 patients, Mala-D was taken by 16 patients, Levonorgestrel was taken by 13 patients, and Oxytocin was taken by 12 patients. according to this collected data Mala N drug was mostly used by patents compare to other hormonal therapy drugs.

Table 8 shows distribution based on type of Therpy

Therapies	No of patients(n=100)	Percentage%
Mono therapy	59	59%
Two drug therapy	41	41%

Among 100 selected patients, Mono therapy was given for 59 female patients, and Two drug combination therapy was given for 41female patients.This collected data shows who under went for mono therapy treatment patients were more.

Table 9 shows drug interactions found with hormonal therapy drugs

S.NO	Type of interactions	Serious	Significant	Minor	No.ofpatients affected
1.	**Rifampin+estradiol**	Rifampin will decrease the level of effect of estradiol by affecting hepatic/intestinal enzyme CYP3A4 metabolism			**1**
2.	**Rifampin+ethynyl estradiol**	Rifampin will decrease the level or effect of ethynyl estradiol by affecting hepatic/intestinal enzyme CYPA4 metabolism.avoid or use alternat drug.the efficacy of hormonal contraceptives may be reduced.use of non hormonal contraceptive is recommended.			**1**
3.	**Ethynyl estradiol+ Theophylline**		Ethynyl estradiol will increase the level or effect of theophylline by affecting hepatic enzyme CYP1A2 metabolism.		**9**
4.	**Rifampin+Levonorgestrol**		Rifampin decrease levels of levonorgestrol by affecting hepatic/intestinalCYPA4 metabolism.		**1**
6.	**Isoniazid+estradiol**			Isoniazid will increase the level of effect of amlodipine by affecting hepatic intestinal enzyme CYP3A4 metabolism.	**1**

The above table shows these are the drug interactions found during the study i,e, Rifampin+Estradiol, Rifampin+Ethynyl Estradiol, Ethynyl Estradiol+ Theophylline Rifampin+ Levonorgestrel, Isoniazid+ Estradiol.

Table 10 shows distribution based on Adverse drug effects reported

Common adrs	No.of patients(n=34)	Percentage(%)
Weight gain	8	23.5%
Vaginal dryness	11	32.35%
Mood changes	7	20.5%
Nausea,vomiting	8	23.5%

Table 11 shows comparision of hormonal therapy in various gynecological problems

Hormonal therapy used in gynecology	Mean and S.D	P value(0.05)
Progesterone	46.16±3.12	<0.05*
Estradiol	29.36±2.19	>0.05
Mala N	52.32±4.14	<0.05*
Mala D	33.16±1.19	>0.05
Levonorgestrol	31.16±1.16	>0.05
Oxytocin	42.27±2.16	<0.05*

Level of significance is <0.05*

According to the collected data out of 100 patients, 34 patients had adverse effects. among them 11 patients had vaginal dryness, than 8 patients had Weight gain, 7 patients had Mood changes, and 8 patients had Nausea and Vomiting.

According to the data Mala N shows significant difference,followed by Oxytocin and Progesterone . while Estradiol, Mala D and Levonorgestrel does not show any difference.

This study shows Mala N was commonly used and effective drug in Dysfunctional uterine bleeding patients than other hormonal therapy drugs. similarly Progesterone and Oxytocin were also used.

CONCLUSION:

Hormone therapy (HT) is a treatment that is used to supplement the body with either Estrogen alone or Progesterone in combination. The combination of these hormonal supplements plays a major role in the gynecological problems such as dysfunctional uterine bleeding ,menorrhagia,and other conditions.

Hormonal therapy is mostly used for the purpose of to maintain hormonal imbalance, it helps in reducing bleeding and keeps bones healthy.

Our study shows that usage of mala N drug is most common and effective in dysfunctional uterine bleeding(DUB)patients, compare to other hormonal supplements like progesterone, malaD, estrdiol, oxytocin, and levonorgestrol. This can be used for maintainence of inventory.

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