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RESEARCH ARTICLE

ORMELOXIFENE IN DUB

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ABSTRACT

Dysfunctional uterine bleedind is a common gynecological disorder which Usually ends up in hysterectomy and causes both psychological & physiological stress. Medical management with hormones and NSAIDs has their inherent side effects Hence an attempt is made to medically manage them using ORMELOXIFENE, a Selective estrogen receptor modulator.

INTRODUCTION

Ormeloxifene is a selective estrogen receptor modulators, or SERMs, (Tandon Annu *et al.,* 2009) a class of medication which acts on the estrogen receptor. It is best known as a *non-hormonal*, *non-steroidal* oral contraceptive which is taken once per week. In India, ormeloxifene is available for birth control since 1990s Currently marketed under the trade name Saheli. Ormeloxifene is also licensed under trade names CENTRON and SEVISTA.Ormeloxifene has also been licensed under the trade names, Novex-DS, Centron and Sevista. Ormeloxifene is primarily used as a contraceptive, but it may also be effective for dysfunctional uterine bleeding and advanced breast cancer. Ormeloxifene may be used as a weekly oral contraceptive (Lal, 2010). The weekly schedule is an advantage for women who prefer an oral contraceptive, but they find it difficult or impractical to adhere to a daily schedule which is required by other oral contraceptives. For the first twelve weeks of use, it is advised to take the ormeloxifene pill twice per week (Lal *et al*., 2001). From the thirteenth week on, it is taken once per week (Lal *et al*., 2001). The standard dose is 30mg weekly, but the 60mg loading doses can reduce the pregnancy rates by 38% (Singh, 2001). It has a failure rate of about 1-2% with an ideal use, which is slightly less effective than that which is found for the combined oral contraceptive pills (Singh, 2001). Ormeloxifene has also been tested in experimental settings as a treatment for menorrhagia (Kriplani *et al*., 2009). Its use in the treatment of mastalgia and fibroadenoma has also been described.

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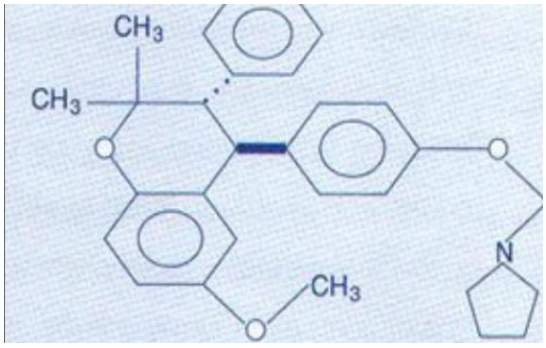
Mechanism of action of Ormeloxifene

Chemical name—Trans-7-methyl-2-2-dimethyl-3 phenyl-4(4-(2-pyroldinoethoxy)phenyl (chroman hydrochloride), related to centchroman.



The individual elements of the modulator structure gives a tissue selectivity- different DNA transcription in different tissues:

Basic Amine Side chain causes Uterine Anti estrogenic action
Pyrolidine side chain causes antagonistic action.
Benzopyron group causes agonistic action.

It has very strong affinity for Estrogen receptors, Slow nuclear binding & prolonged release of ER
Hence long half life & prolonged action.

Ormeloxifene acts as an oestrogen receptor modulator -- SERM. It has weak estrogenic and potent anti oestrogenic actions. As a contraceptive it prevents proliferation and decidualisation of the endometrium, Enhances blastocyst formation and embryo transport through oviducts. Normalizes bleeding from uterine cavity by regularizing expression of estrogen receptorson the endometrium. It is Well absorbed from the GI tract. Peak levels are attained in 4 hours, terminal half-life is approximately 170 hours. It is widely distributed in tissues. It has little affinity to plasma proteins.

Indications of Use

It is Currently indicated for DUB in all ages, but not suitable for women desiring pregnancy. It has got special benefit for peri menopausal women by causing relief of PMS symptoms. It is already approved for National Family Welfare programme.

Contraindications

1. Recent Liver disease or Jaundice
2. PCOD
3. Cx dysplasia or Ch cervicitis
4. Hypersensitivity to drug.
5. Chronic illness.
6. Nursing mothers.
7. Allergic conditions.

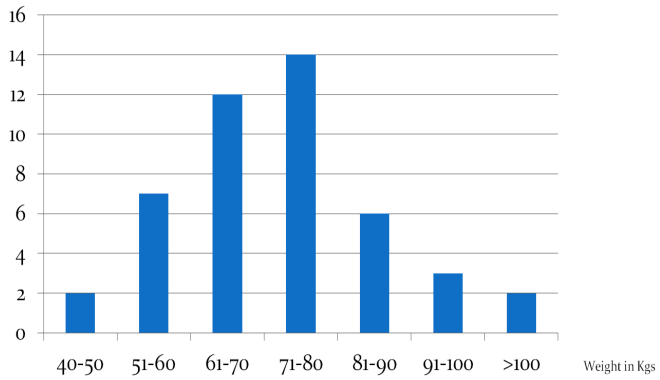
MATERIALS AND METHODS

A Prospective study was undertaken on diagnosed 48 cases of DUB for a duration of 2 years. Presenting complaints were bleeding PV, pain in the abdomen, white discharge and irregular menstrual cycles An inclusion criteria was taken as all cases of DUB, after excluding other causes for AUB. And exclusion criteria was defined as a group of women who had chronic cervicitis, Patients desiring pregnancy, Nursing mothers and patients not willing for follow up. All patients were counseled about medical management, follow up and informed consent was taken. History of the patient was taken. A local speculum examination was done & PAP smear was taken, basic investigations (Hb%, RBS, HIV, HbsAg, LFT, CT&BT, CBP), Ultrasound pelvic scan for endometrial thickness was done. D&C was done. D&C done in 44 pts out of 48 (4pts unmarried) 34 pts had proliferative phase, 8 had secretory phase, 2 had scanty endometrial scrapings.

Treatment with ormiloxifene was started. The treatment with ormeloxifene was evaluated by measuring the Hb g/dl and the endometrial thickness before and after 3 months of treatment. ormeloxifene was given in the dosage of a 60 mg tablet twice a week for 3 months, followed by once a week for another 3 months. The endometrial thickness was measured in the premenstrual phase and it was measured by a transabdominal ultrasound scan which was done by a radiologist.

Table 1. Age Distribution

30-35 yrs	35-40 yrs	40-45 yrs	45-50 yrs
5	14	18	11



Graph 1. Weight distribution

RESULTS

Most of the pts-40-45 yrs. The Common c/o was menorrhagia 80% responded to Ormeloxifene. Most of the patients ended up in amenorrhea lasting for 12-18 months. 6 pts needed Medroxy progesterone for initial 3weeks. 14 pts received initial tranexamic acid for Menorrhagia. 2 patients had relapse of symptoms after 18 months and were started on 2nd course of Ormeloxifene and responded. 3 pts had no response even after 3 monthsand hence opted for LAVH. No major complications were noticed.

The details of endometrial thickness and relief of symptoms are given in (Table 2).

Table 2. Endometrial thickness and relief of symptoms

c/o	4wks	8wks	12wks	6mo	12mo	18mo
Menorrhagea	28	11	9			
Poly menorrhea			11			
dysmenorrhea	10	20	8			
amenorrhea		34	38	22	4	
Delayed periods		22				
No response		4		3		
Endometrial thickness	8mm-(34)	6mm-(44)				

Table 3. Ormeloxifene Benefits

Tissue	IDEAL SERM	Ormeloxifene	Relaxofene	Tamoxafene
Endometrium	AE	AE	AE	AE
Breast	AE	AE	AE	AE
Vagina	E	E	AE	AE
Bone	E	E	E	E
Liver & CVS	E	E	E+	E
CNS	E	E	E?	AE
E---	*ESTROGENIC*		*AE--*	*ANTI ESTROGENIC*

DISCUSSION

The traditional treatment for menorrhagia is Hysterectomy. While hysterectomy offers an effective cure, it is suitable only for those, who have no further wish to conceive. The procedure involves major surgery with significant postoperative morbid it. Endometrial ablation techniques offer

an alternative surgical treatment option with significantly reduced postoperative morbidity. But again may be unsuitable for women wishing to retain their menstrual and reproductive function, moreover this requires technical expertise, which is not routinely available. Ormeloxifene is a benzopyran SERM, which blocks the cytosol receptors by its competitive binding over estradiol. It has mils estrogenic activity on vagina, bone mineral density, CNS and lipids. The drug is primarily a potent estrogen antagonist but also has a weak agonist activity in selected tissues. The drug demonstrates a suppressive or a stimulatory effect on gonadotropin release. Such anti estrogens are expected to exert contraceptive effects. It normalizes the bleeding from uterine cavity by regularizing the expression of estrogen receptors on endometrium and hence the drug was tried in patients with DUB. It is a also a potent antiproliferative agent in Breast tissue. Additional bene it of this drug is that it decreases total cholesterol, LDL cholesterol by about 20 to 30%.

Conclusion

The ease of administration of the drug Ormeloxifene facilitates patients compliance and acceptability and marked relief of symptoms results in higher patient satisfaction. Therefore Ormeloxifene should be the drug of choice in patients with DUB.

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