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THE ROLE OF ORMELOXIFENE IN THE MANAGEMENT OF ABNORMAL UTERINE BLEEDING

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ABSTRACT

Objective: The complaints of menorrhagia (excessive menstrual bleeding) have a substantial impact over the gynaecological services in our country. In most cases, no organic pathology is ever identified. NSAIDS (Nonsteroidal anti-inflammatory drugs) as well as tranexamic acid offer a simple therapy which is taken during menstruation, which results in reductions of 25-35% and upto 50% in the Menstrual Blood Loss (MBL) respectively. Danazol and the GNRH (gonadatrophin-releasing hormone) analogues are also highly effective. Their side-effects make them suitable for a short-term use only. In the present study, the role of ormeloxifene was studied in the patients of AUB. **Materials & Methods:** The subjects were diagnosed cases of AUB. After ruling out various possible causes of the abnormal uterine bleeding, the diagnosis of AUB was made and then treatment with ormiloxifene was started. The number of cases were 40. The treatment was evaluated by measuring the Hb in g/dl as well as the endometrial thickness before and after 3 months of treatment with ormeloxifene. It was given in the dosage of 60 mg tablet twice a week for 3 months then tapered by once a week for another 3 months. **Observation & Results:** There was a significant increase in the Hb g/dl ($p < 0.001$) and a significant decrease in the endometrial thickness ($p < 0.001$) after the treatment with ormeloxifene. **Conclusion:** Ormeloxifene can be used as an effective drug in the treatment of abnormal uterine bleeding.

KEYWORDS :

INTRODUCTION

Ormeloxifene (which is also known as centchroman) is one of the known selective oestrogen receptor modulators (SERMs) [1]. This is a class of medications which acts over the oestrogen receptors. It is best known as a non-steroidal, non-hormonal oral contraceptive which is taken only once per week. In our country, ormeloxifene has been available widely as a birth control pill since the early 1990s. It is currently marketed in India under the trade name of Saheli [1]. Ormeloxifene is also been licensed under the trade names of Cen- tron, Novex-DS, and Ormiloxifene. Ormeloxifene is primarily used as an oral contraceptive, but it may also be effective for abnormal uterine bleeding and also for advanced breast cancer. It may be used as weekly oral contraceptive pill. [2]. The weekly schedule is an advantage for women who prefer oral contraceptive, but have poor compliance with daily oral dose. For the first 12 weeks of use, it is actually advised to take the ormeloxifene pill twice per week [3]. Then from the thirteenth week on it is taken once per week [3]. The overall consensus is that the backup protection in the first month is a cautious but a sensible choice. The 60mg loading doses can effectively reduce the pregnancy rates by 38%. The standard dose is 30mg weekly. It has a failure rate of 1-2%, which is only slightly less effective than that of which is found for the combined OCPs [4]. As a treatment for menorrhagia Ormeloxifene has also been tested in the experimental settings [5]. Its use in the treatment of fibroadenoma and mastalgia. There are also concerns that ormeloxifene may lead to uterine prolapse or urinary incontinence.

METHOD OF ACTION

It is a SERM (selective estrogen receptor modulator. Its action is oestrogenic (i.e., in the bones). Again in other parts of the body, its action is antioestrogenic (in the uterus and the breasts) [6,7]. Although its exact mode of action is not been well defined it causes asynchrony in the menstrual cycle in between the ovulation and the development of the uterine lining. In various clinical trials in some women, it caused the ovulation to occur later than it normally would. [4] It did not affect the ovulation in a majority of the women, while it causes the lining of the uterus to build more slowly. It also speeds the transport of any fertilized egg through the fallopian tubes much more quickly, than is normal [4]. This combination of effects leads to such an environment that even if fertilization occurs, an implantation may not be be possible [4].

The hypothesis of this present study is that ormiloxifene is effective in management of abnormal uterine bleeding. Role of ormeloxifene was studied in the patients of AUB by estimating haemoglobin as well as by measuring the endometrial thickness before and after the treatment.

MATERIALS AND METHODS

All the patients were diagnosed cases of AUB. The number of cases were 40 cases. The main presenting complaints were pain in the abdomen, bleeding PV, irregular menstrual cycles and a white discharge. The mean age of our study group was 45 ± 5 years. A well written and informed consent was obtained from the patients selected for the study.The patients were selected randomly. A history of parity was obtained. All the subjects were multiparous. Causes for the abnormal uterine bleeding were ruled out by taking the history, performing a detailed clinical examination. Investigations like the complete blood count, thyroid profile, coagulation profile, ultrasonogram of the the pelvis and abdomen and history of any dilation and curettage. After we ruled out the various possible causes of abnormal uterine bleeding, diagnosis of AUB was made and the treatment with ormiloxifene was started. The treatment with ormiloxifene was evaluated by measuring the Hb in g/dl and also the endometrial thickness before and after 3 months of successful treatment with ormiloxifene. Ormiloxifene was given in the dosage of 60 mg tablet twice a week continuously for 3 months then followed by once a week for another 3 months. The endometrial thickness was measured in the premenstrual phase with help of transabdominal ultrasound scan.

RESULTS

The details of Hb in g/dl is given in (table 1) and that of endometrial thickness is given in (Table2). The P values which were obtained by using the paired Student t test , were then presented in Mean ± SD.

There was a statistically significant increase in the Hb g/dl ($p < 0.001$) and also a statistically significant decrease in the endometrial thickness ($p < 0.001$) after continuous treatment with ormiloxifene as described earlier.

[Table1]: Evaluation of treatment based on Hb in g/dl

Hb g/dl	Pre-treatment	Post-treatment	P value
Min-Max	6.52-9.82	9.63-11.51	P<0.001
Mean ± SD	8.28±0.90	10.60±0.48	
95%CI	7.94-8.57	10.42-10.76	

[Table2]: Evaluation of treatment based on uterine endometrial thickness

Endometrial thickness	Pre-treatment	Post-treatment	P value
Min-Max	4.24-14.43	2.02-9.05	P<0.001
Mean ± SD	8.37±2.37	4.90±1.61	

DISCUSSION

In present study, results suggested that there occurred a significant increase in the Hb g/dl and a significant decrease in the endometrial thickness. Our findings with respect to Hb in g/ dl, were well in accordance with findings which were obtained in the study by Kripalini A et al., In their study which was done by Kripalini A et al., the menstrual blood loss (MBL) was measured objectively by the Pictorial Blood Assessment Chart score and also subjectively by using a Visual Analog Scale. In our study, we measured Hb in g/dl whereas Kripalini A et al., measured PBAC. In both the studies the blood loss was decreased significantly after administering ormeloxifene.

Abnormal uterine bleeding is the diagnosis in the majority of the cases of menorrhagia. The symptoms of menorrhagia accounts for significant proportion of referrals to gynaecologists in our country. There is no hormonal defect in abnormal uterine bleeding however, disturbances in the endometrial mediators were noted. A majority of the cases were associated with ovulatory cycles when the cycle control is not an issue, and they can thus be treated with non-hormonal methods.

Those patients who have anovulatory cycles may further benefit from an exogenous control of the pattern of bleeding by the use of various hormonal preparations. When patient also requires effective contraception, the use of either a combined OCP or the levonorgestrel releasing Intrauterine System are suitable choices. The medical management of abnormal bleeding should ideally based among the community. Referral to a hospital should be reserved for those cases only where the menorrhagia is thought to de due to certain underlying pathology or when the initial treatment given appears to fail [8].

Aetiology investigations, surgical and medical management have been described. In about 50% of the cases of menorrhagia, no pathology is actually found at hysterectomy. Abnormal levels of fibrinolytic system or the prostaglandins in the endometrium are implicated. The effective treatments which are suitable for long-term use include antifibrinolytic agents (tranexamic acid) and nonsteroidal antiinflammatory agents (mefenamic acid) and intrauterine progestogens. There has been an increasing use of endometrial destructive techniques over the past few decades as an alternative to hysterectomy. Advent of fibroid embolization and their further refinement has increased the options which are available for women [9].

For chronic menorrhagia medical management is the first line of therapy. The agents that have been used to treat menorrhagia include cyclooxygenase inhibitors, iron, desmopressin, antifibrin- olytics, gonadotropin-releasing hormone agonists, combined oral contraceptives, androgens and progestins. Progestins can also be administered systemically or locally and they may be given continuously or cyclically. The increased use of now a days effective medical therapy has the potential for reduction of the number of surgical procedures like such as endometrial ablation and hysterectomy [10].

The complaints of menorrhagia (excessive menstrual bleeding) have a substantial impact over the gynaecological services and in most of cases, no organic pathology is ever identified. About 50% of the women who present with complaint suggesting menorrhagia have blood loss within the normal range. A medical therapy is an indication for the patients who do not want to undergo surgery or for whom a surgery is not feasible. Nonsteroidal anti-inflammatory drugs (NSAIDS) and tranexamic acid offer a very simple therapy which can be taken during menstruation, with effective reductions of 25-35% and upto 50% respectively in the MBL. Danazol and the gonadatro- phin-releasing hormone analogues are highly effective, but their side-effects make them suitable only for a short-term use. The combined oral contraceptive pill and the levonorgestrel intrauter- ine system give reductions of 50% and 80% in MBL, with an ad- ditional contraceptive cover. The cyclical progestogens are the commonly prescribed therapy in United Kingdom but they are highly ineffective for management of the ovulatory menorrhagia unless they are being taken at higher doses (10-15mg daily) for atleast 3 weeks [4,11].

Kripalani et al., also studied the safety and the efficacy of ormeloxifene in the management of menorrhagia: it was found that Ormeloxifene was effective as well as safe therapeutic option for the management of menorrhagia [5].

Limitations of our Study: The number of study group was less. A larger study group is indeed needed. Hysteroscopy of the patients was not done. A long term follow up of the study group should be done.

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