

THE ROLE OF DYDROGESTERONE IN THE MEDICAL MANAGEMENT OF 100 CASES OF DYSFUNCTIONAL UTERINE BLEEDING (DUB) ABOVE 35 YEARS OF AGE

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ABSTRACT

Objective: Dysfunctional uterine bleeding or DUB are a large number of patients presenting in our OPDs and the problem is a major contributor to anaemia and disease in our society, mostly necessitating hysterectomy.

Material and Methods: This was a hospital based prospective study of 100 patients with DUB who were randomly selected, in our out patients (OPDs) between 1st August 2001-31st July 2002. Common presentation was either menorrhagia or poly menorrhagia with ages varying between 35-50 years. 68 (68%) patients were between 35-44 years age group and 32 (32%) patients were 44-50 years old. In addition to Hb gm%, detailed haematological investigations were carried out. Transvaginal ultrasounds were done to specifically look for endometrial thickness or pathology and ovarian screening to exclude any organic cause.

Results: 64 out of 100 patients showed increased endometrial thickness or irregularity and 32 out of these who were above 40 years of age had an endometrial biopsy to exclude any premalignant or malignant condition of the endometrium. All patients were put on dydrogesterone 10 mg daily starting from day 14th to day 28th of the cycle for 3-6 months. Remarkably good cycle control and reduction in the amount of bleeding and days of menstruations, and improvement of Hb gm% levels were seen in 41 patients. 3 were lost to the follow up and 6 patients eventually needed hysterectomy.

Conclusion: The study proved that dydrogesterone is an effective agent for medical treatment of Dysfunctional uterine bleeding. Its use saved

patients from hysterectomy thus decreasing exposure to the risk of general anesthesia and surgery, also decreasing workload and economic burden on hospital, staff and the state.

Key words: Dydrogesterone, Dysfunctional uterine studies, Menorrhagia.

INTRODUCTION

The menstrual disorders continue to pose, significant physical and financial burdens on patients and increase work load on gynaecologists.

Dysfunctional uterine bleeding one of the most frequently encountered conditions in our practice, forms 10% of admissions¹ and 20% of OPD patients² Medical management is preferred for DUB treatment³ progestones having been used to induce regular uterine shedding.

The objective definition of menorrhagia is taken as a monthly menstrual blood loss of 80 ml or greater, and it is these women who are at increased risk of developing anaemia. Menorrhagia is cyclical heavy bleeding whilst polymenorrhagia is irregular heavy bleeding in which there is no approximate cycle length and bleeding can start any day and the problem tends to be protracted.

Menorrhagia may be due to underlying pathology, such as fibroids, malignancy, infection or bleeding disorders, but in the majority of cases there is no organic disease and the bleeding is termed dysfunctional. In 10-20% of women, particularly at the extremes of reproductive life DUB is associated with anovulation. In most women, the problem is thought to originate in the endometrium itself. Systemic factors affecting endometrium are hormones, oestrogens and progesterones and principal local factors implicated in the pathogenesis have been prostaglandins and the components of endometrial fibrinolytic system.

Irregular bleeding or menorrhagia can be dealt with medically or surgically For medical treatment of DUB, NSAIDS (Mefenemic acid, inhibitors of fibrinolysis), hormonal treatments, synthetic progestogens (LNG-IUS), combined pills, Danazol, antisteroids, (gestrinone), GnRH agonists have all been implicated. Conservative surgical techniques are not available in our country. Hysterectomy is the choice in most cases which being an invasive procedure, has its own risks. A successful therapeutic agent is more than welcome if its use avoids need for Hysterectomy and associated risks.

Dydrogesterone is a retroprogesterone with a molecular structure differing only slightly from natural progesterones.⁴ This structural difference accounts for its oral activity.⁵ It has a potent progestational and antioestrogenic effects on the endometium.⁶ Unlike other synthetic progestins it does not affect lipid parameters and carbohydrate metabolism.⁷ In addition there are no androgenic or estrogenic metabolites and thus no masculinizing or estrogenic effects. When administered in dysfunctional uterine bleeding or irregular cycles, it restores normal menses without inhibiting ovulation or interfering with maturation of HPO axis and with absence of thermogenic effect.⁸

MATERIAL AND METHODS

This trial was designed to study the effect of dydrogesterone on patients with DUB. 100 patients, above 35 years of age, presenting to our OPD with DUB were

randomly selected between August 2001–July 2002. They belonged to the reproductive and the perimenopausal age groups initially a detailed history was taken and clinical examination and investigations were done. All patients taking any hormonal therapies or having any organic lesions were excluded from the study.

In addition to Hematological studies, transvaginal ultrasound was done to specifically look for endometrial pathology and ovarian screening. 64 out of 100 patients showed increased endometrial thickness or pathology and had an endometrial biopsy.

Symptoms reported included Menorrhagia, polymenorrhoea and poly menorrhagia. 66 out of 100 ladies had an Hb less than 10 gm%(Table-1).Parameters assessed were; amount and duration of bleeding, presence of clots in menstrual blood, amount and duration of bleeding and length of cycle. They were given dydrogesterone from day 14th to day 28th of the cycle. Therapy was continued for 3-5 consecutive cycles. All patients were asked for follow up every month between day 5th – 7th of the cycle and any new symptoms noted.

Efficacy was assessed as regards patient compliance, good cycle control, decrease in the number of days of bleeding and reduction in amount of bleeding, moderate flow and absence of clots in menstrual blood, and improvement of Hb gm% in anaemic ladies.

DISTRIBUTION OF ANAEMIA IN LADIES WITH DUB.

n = 50

Hb gm%	N	Percentage
< 9gm%	N=28	28
Between 9-10gm%	N=38	38
Between 10-11 gm%	N=34	34

TABLE - 1

RESULTS

Out of a total of 100 patients, 82 (82%) showed remarkably good results in the form of good cycle control, and improvement of symptoms, reduction in the amount of bleeding and number of days of menstrual phase of the cycle, and increase in Hb gm%. 6(6%) patients were lost to the follow up and 12 patients (12%) eventually needed Hysterectomy because of continuing symptoms.

The age distribution has been shown in Table-2. Patients were categorized according to their symptoms into two main groups, (Table-3) with menorrhagia only and with irregular cycles.

Of the 32 patients with menorrhagia but no cycle disturbance 26 (81.25%) patients were significantly relieved but 6 (18.75%) did not report such improvement and had to undergo hysterectomy.

In patients with irregular cycles 16 patients had polymenorrhoea and all 16(100%) showed excellent cycle control with mean cycle duration of 29.5 days. 10 patients had metrorrhagia and 8 (80%) out of them showed improvement with regular cyclical bleeding and 2 patient had to undergo hysterectomy. 12 patients had menometrorrhagia, 8 (66.6%) responded well, two were lost to follow up and 2 had hysterectomy.

The polymenorrhoea and menorrhagia group was the largest with 38 patients. 34 (89.47%) out of them were cured of the

AGE DISTRIBUTION OF PATIENTS (BETWEEN 35-50 YEARS OF AGE)

n = 50

Age in years	N	%
Between 35-44 years	N=68	68%
Between 44-50 years	N = 32	32%

TABLE - 2

PERCENTAGE OF PATIENTS REPORTING RELIEF AFTER DYDROGESTERONE THERAPY

Groups	Symptoms	Reporting symptoms (No.)	Those relieved of symptoms	
			No.	%
1. Menorrhagia	1. Menorrhagia	32	26	81.25%
	2. Dysmenorrhea			
2. Irregular cycles	1. Poly menorrhoea	16	16	100%
	2. Metrorrhagia	10	8	80%
	3. Menometrorrhagia	12	8	66.6%
	4. Polymenorrhoea + menorrhagia	38	34	89.4%

TABLE - 3

symptoms, showed good cycle control with mean duration of 29 days, decrease in the amount of blood lost, improvement in Dysmenorrhoea, no passage of clots during menses and improvement in Hb_{gm}% of the patients who had anaemia on initial presentation. 2 patients out of this group were lost to follow up and 2 had hysterectomy.

No side effects were reported by the patients through out the study and the drug was well tolerated.

DISCUSSION

The results of our study showed that dydrogesterone restored normal menses both in terms of regularity and quality in more than 82% of the patients. It also decreased the amount of bleeding as well as reduced the duration of bleeding in days to an average of 4.5 days. The associated pain was also relieved by the treatment. The cycles were regularized as well. More over the drug was well tolerated by all patients and no adverse effects were reported. Tabaste et al 1984⁷ also studied the effect of dydrogesterone in menstrual disturbances and reported an efficacy of 92%.

Disturbances in the pattern of menstruation are a common clinical presentation for abnormalities of hypophyseal pituitary ovarian axis-DUB is defined as heavy and/or

irregular menses in the absence of recognizable pelvic pathology, pregnancy or general bleeding disorder.

Its presence in our set up exaggerates the already existent suffering of Pakistani women who are under privileged, anaemic, have lesser access to good treatment and due to poverty and ignorance will usually get treatment and surgery done in smaller hospitals with less trained staff thus exposing themselves to high morbidity and mortality.^{9,10} The need therefore exists to a proper conservative approach to the problem of DUB or menorrhagia and surgery should only be resorted to in absolutely necessary cases.

The abnormalities of ovarian activity after 35 years of age may be anovulatory DUB e.g. in polycystic ovarian disease or premenopausally "Ovulatory" e.g. inadequate luteal phase. Hormonal treatments for menorrhagia have been available for at least 25 years. The most widely prescribed are the synthetic progestogens. There is histological evidence that in women with metropathia haemorrhagica, progestogen administration will cause secretory change in the endometrium accompanied by subjective decrease in blood loss.^{11,12}

Progesterones may be given orally, as depot, or intra uterine device (LNG-IUS). Overall the progesterones are very safe and

oral progestones should be considered for all those with an irregular menstrual cycle.

In the developed world, where conservative surgical methods like endometrial ablation and transcervical resection of endometrium are being promoted, we are short of these facilities and techniques and laparoscopic surgery is not widespread in Pakistan. Therefore to limit the morbidity, expense and complications associated with hysterectomy, due consideration should be given to an effective conservative treatment of DUB/menorrhagia.

CONCLUSION

Dydrogesterone is a highly effective drug for the management of dysfunctional uterine bleeding, especially in a third world country like ours with high morbidity and mortality rates, in already anaemic ladies, with increased blood loss exaggerating the existing state of pathology.¹³ It is well tolerated by patients and helps avoid major surgery and its risks.¹⁴ The absence of undesirable effects coupled with its effectiveness makes dydrogesterone a viable therapeutic tool in normalizing cycles, both in terms of regulatory and quality.

REFERENCES

1. Nesse RE. Managing abnormal vaginal bleeding. *Post grad Med* 1991; 89(1): 205.
2. Chuong CJ, Brenner PE. Management of abnormal uterine bleeding. *Am J Obstet Gynecol* 1996; 175(3): 787.
3. Progestins: Present and Future, editorial, *J. Steroid Bio Chem Molec Biol.* 1996; 59(516): 357.

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4. Martin AJ, Progestins, *Mod Med* 1986; 31(12): 1.
5. Lane G, Siddle NC, Ryder TA, Pryse-Davies J, King RJB, White head MI. Effects of dydrogesterone on the estrogenized postmenopausal endometrium. *BJ Obstet Gynaecol* 1986; 93: 55.
6. Van der Mooren MJ, Demaker NB, Thomas CMG, Borm GF, Rolland RA. 2 year study on the beneficial effects of 17 beta estradiol-dydrogesterone therapy on serum Lipoproteins and Lp (a) in women: no additional unfavourable effects of dydrogesterone *Eur J. Obstet Gynaecol. Reprod Biol* 1993; 52: 117.
7. Tabaste JL, Servand M, Steiner E, Dabir P, Bene B, Pouzet M. Action of dydrogesterone in post pubertal menstrual disturbances. *Rev Fr Gynecol Obstet* 1984; 79(1): 19.
8. Gath D, Osborne M, Bungay G. Psychiatric disorders and gynecological symptoms in middle aged women: a community survey *BMJ* 1987; 294: 213.
9. Anon. National Confidential enquiry into perioperative deaths 1996-97. London, HMSO, 1998.
10. Fraser IS. Treatment of ovulatory and anovulatory dysfunctional uterine bleeding with oral progestogens. *Aust NZJ Obstet Gynaecol* 1990; 30: 353.
11. Fraser I. Treatment of ovulatory and anovulatory dysfunctional uterine bleeding with oral progestogens. *Australian and New Zealand journal of Obstetrics and Gynecology* 1990; 30: 353.
12. Cohen BJB, Gibor Y. Anaemia and menstrual blood loss. *Obstetrical and Gynaecological survey* 1980; 35: 597.
13. Dicker RC, Green Span JR, Strauss LT, et al. Complications of abdominal and vaginal hysterectomy among women of reproductive age in the United States. *American Journal of Obstetrics and Gynecology.* 1982; 144: 841.
14. Menonk, Devi PK, Rao KB. *Post graduate Obstetrics and Gynaecology Madras: Orient Longman* 1989; 320.