THE EFFECT OF DANAZOL IN DYSFUNCTIONAL UTERINE BLEEDING

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SUMMARY

Effect of Danazol was studied in women with Dysfunctional uterine bleeding. Danazol 200 mg/day for three months improved the excessive bleeding and this effect was carried on even after cessation of therapy. There was no significant improvement in placebo group. In this dose schedule there was no effect on liver functions and mild increase in weight was welcomed by patients. Patients had improvement in haemoglobin. Hence Danazol in doses of 200 mg/day is a good medical treatment for Dysfunctional Uterine Bleeding.

INTRODUCTION

Management of DUB is still a challenging job for a gynaecologist. There are different modalities in the management ranging from hormonal manipulation to hysterectomy. Currettage or ergot type drugs have been widely used but the clinical effect has been doubtful. Hysterectomy may be a satisfactory procedure in some women in the forties or fifties but is inappropriate in younger women who wish to retain fertility and womanhood. So in clinical practice there is a need for adequate treatment of D. U. B. to prevent anaemia and diminish the individual discomfort caused by a heavy blood loss. The ideal medical therapy for D. U. B. is yet to be discovered. The commonest treatment has been cyclical hormone therapy either progesterone alone or the combined oestrogen progesterone pills which may cause serious side effects, or may be contraindicated in some-women, who have an increased risk of thrombosis or heart disease. Danazol is an orally active pituitary gonadotrophin inhibitory agent devoid of oestrogenic and progestational activity and causes antiproliferative effect endometrial atrophy and hence reduces the menstrual blood loss. (Dmowski (1979) & Barbiery & Rayan 1981).

PATIENTS AND METHODS

This study has been conducted on patients with heavy menstrual period at Sardar Patel Medical College and associated groups of

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Thorough general physical examination detailed history, age of menarche, previous menstrual cycle, present menstrual cycle, last menstrual period, obstetrical history, and associated medical disorder, bimanual examination and curettage of the uterine cavity was done to ensure that none of the women in the study had clinically detectable pelvic pathology.

Ultrasonography was done for the women taken into study group to confirm the clinical findings and to rule out any pelvic pathology especially enlargement of ovaries.

Women taking any hormonal treatment or using any intra uterine contraceptive devices were not included in the study. Patients with hepatic, renal or heart disease were excluded from study.

Women of child bearing age were included in this study. However majority of women subjected to the study had completed their families but had not undergone family planning operation of any kind.

This study comprised of studying hundred patients of functional uterine bleeding. The patients were divided into two groups, each group comprising of fifty patients.

One group of patients was given Danazol 200 mg daily to a period of three months.

The other group was taken as control group and given placebo treatment in form of haematinic.

In none of these patients was it impressed that a study was being conducted upon them. Instead they were made aware that an active form of treatment was being conferred upon them.

Each patient was asked the number of sanitary pads or napkins during the two periods to the start of therapy, during the therapy and after the completion of therapy for these months. She was asked to use sanitary napkins of the same quality and same brands every time as far as possible.

All patients were called for examination as soon as their menses occurred and were enquired about the length of the cycle, the number of days of menstruation and the side effects of therapy.

On every visit bimanual examination was done to exclude the ovarian enlargement.

General and physical examination was also done on each visit. Body weight recording and presence or absence of oedema was noted. Blood pressure was recorded on each visit. Patients were asked about any discomfort like subjective weight gain, headache, nausea, acne.

All of these patients, except six who were residing in rural areas were of urban localities.

OBSERVATIONS

Hundred women chiefly complaining of heavy periods were taken in study from January 1991 to December 1991. Fifty women were given 200 mg Danazol daily orally for a period of three months and fifty women were taken as control and given placebo in the form of haematinics. Among the fifty patients of control group three patients could not be followed after one month and one discontinued placebo therapy after 45 days and switched over to homeopathic medicine. Of the fifty women on Danazol therapy, two patients discontinued the therapy after one month due to cost factor and another one because of hirsuitism. One patient could not be followed after 35 days. Two of the patients in this group had ovarian enlargement after one month so. These had to be excluded from study.

Age of the patients varied from 30 years to 47 years with a mean of 38.5 years and maximum number of patients were in the age group of 36 to 45 years.

Duration of complaints are shown in table I.

Haemoglobin was 6 to 8 gm% in 4.35% cases in control group, 8-10 gm% in 78.26% in control and 88.64% in study group respectively. About 17.39% in control and 11.36%

in study group had Hb more than 10 gm%. Number of days menstrual bleeding in both groups were as shown in table II and number of sanitary pads were shown in table III.

After 3 months of Danazol treatment 80.8% of patients had light/scanty period, 4.55% had amenorrhoea and irregular bleeding while 9.09% women had no change in menses but none of the women had heavy menses.

Relationship of relief of symptoms is shown in table V.

Parity of patients varied from primagravida to 6th gravida. About 75% of cases were in the group third gravida or more. Weight of patients varied from 44 kg to 60 kg. One patient weighed more than 60 kg. Fifty percent of patients were in the weight group 51-55 kg. All the patients with symptoms for 1-2 years had complete relief, while between 2-4 years about 83.33% had relief and more than 4 years 66.66% had relief of symptoms. There was no significant difference in relief of symptoms by parity and weight of patient. After three months of treatment weight gain in the patients varied from ½ to 5 kg with a mean of 2.26 kg. Various side effects in patients with Danazol therapy has been shown in table VI.

Haemoglobin of patients increased from .5 gm to 2 gm%. About 81-82% patients had between .4 to 1 gm%. None of the patients had deranged liver functions tests after 3 months of therapy.

Table I

Distribution by duration of complaints in Patients of FUB

Duration	Control group	Percentage	Study group	Percentage
1 years	4	8.69	7	15.90
2 years	19	41.31	15	34.09
3 years	11	23.92	13	29.54
4 years	6	13.04	6	13.65
More than 4 years	6	13.04	3	6.82
Total	46	100.00	44	100.00

Table II

Showing menstrual blood loss in days

Number of days	Number of patients with percentage Control group	Percentage	Study group	Percentage
5 - 6	1	2.18	3	6.82%
6 - 8	37	80.43%	30	68.18%
More than 8	8	17.39	11	25.00%

Table III

Showing menstrual blood loss in Pads

Number of pads per cycle	Number of Patients			
	Control		Study	
	Before therapy	After therapy	Before therapy	After therapy
5 - 10	nil	nil	nil	nil
10 - 15	2	—	—	—
16 - 20	33	—	27	—
More than 20	11	1	17	—

Table IV

Relief of Symptoms

Effect	Number of Patients	
	Control	Study
No relief	42	4
Parital relief	2	—
Complete relief	2	40
Aggravation of symptoms	—	—

Table V

Showing relief with danazol therapy

Number of days	Number of Patients	
	At two months	At three months
Less than 6 days	12	4
5 days	21	1
4 days	1	26
3 days	1	10
2 days	—	1
Amenorrhoea	—	2

Table VI

Distribution of Patients according to the side effects of danazol therapy

Side effects	Number of Patients	%
Muscle Cramps	2	4.26
Acne	1	2.12
Oedema	1	2.12
Weight gain	5	10.65
Depression	1	2.12
Deepening of voice		
Hot flushes		
Nervousness		
Hirsuitism	1	2.12
Decrease in breast size	—	
Ovarian enlargement	2	4.26
No side effect	34	72.35
Total	47	100.00

In followup visit patients were observed from 9 months to 1½ yeas. Patients had their menstral period heavier than Danazol therapy, but simulating their normal menstrual period.

DISCUSSION

Dysfunctional uterine Bleeding is considered to have emotional origin in some patient, in such patients placebo therapy and reassurance is effective and others do not have effect of placebo therapy. Menorrhagia was observed maximum in patient with three or more parity in the age group 36 to 45 years weighing between 35 to 55 kg. There was no relation in relief of patients to age, weight and parity of patients. Dose of Danazol 200 mg/day for 3 months was most suitable to 100 mg/day which was less effective and doses more than 200 mg has more side effects (Chimbira et al 1980). Patients had less effect when duration of symptoms exceeded 4 years. In present study blood loss was measured by using size and type of sanitary pads. Average number of pads used per cycle before therapy were between 16-25 and after therapy, came down to 10-12/cycle as per table III. About 90% patients relief of symptoms both in reduction in number of days bleeding and total loss of blood per cycle after 3 months of treatment while in control same number of patients continued with the same symptoms after placebo therapy. None of patients in both groups had aggravation of symptoms. But two patients each had irregular bleeding and amenorrhea in Danazol group.

Mean increase in weight of patient by 2.26 kg was welcomed by patient and was comparable of 2.3 kg in 200 mg dose group of Chimbara at al. And there was increase in haemoglobin between ½ gm% to 2 gm%. Majority of patients had no major side effect but 27.65% had minor side effect and one had withdrawn therapy which is contrary to Chimbara et al (1980) where none of patient had to withdraw therapy due to side effects.

Patients were followed up from 9 months to 1½ years. The effect was carried on upto the period of 1½ years. None of the patient liked the idea of amenorrhea during Danazol therapy for fear of pregnancy.

Danazol in the doses of 200 mg did not impair liver functions.

Through it is more expensive than other medical treatments, in the long run it is more economical as it causes the most effective reduction in menstrual blood loss along with carryover effect after stopping therapy.

Hormonal pills are contraindicated in heart disease and thromboembolism, but Danazol can be given in such patients. Hysterectomy should be considered only as the last resort in D. U. B. persisting even after adequate medical treatment.

Finally it is concluded that Danazol in doses of 200 mg/day for 3 months is an effective form of medical treatment for D. U. B. The effect is maintained even after cessation of treatment without side effect and improvement in both Hb% and weight.

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