THE THERAPEUTIC ACTIVITY OF MICRONIZED FLAVONOID FRACTION (DAFLON 500 MG) IN IUCD INDUCED BLEEDING

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SUMMARY

Daflon 500 mg. contains 450 mgs. of micronized Diosmin and 50 mg. flavonoids expressed as Hesperidin per tablet. The combination has a demonstrated pharmacological action in reducing capillary fragility (Tsouderos Y. 1988). This was therefore expected to play a role in controlling bleeding associated with IUCD use. The IUCD is known to cause mechanical irritation of the uterine mucosa which leads to bleeding as a side-effect.

An open study to evaluate the efficacy of Daflon 500 in controlling IUCD induced bleeding was undertaken on 30 subjects for 3 months. It was observed that 83% of the subjects improved on usage of the drug. The acceptability of the drug was excellent and the side-effects minimal.

INTRODUCTION

Intra uterine contraceptive device (IUCD) is a commonly used method of contraception. It has an advantage of good cost efficacy ratio and low failure rare compared to most other modes of contraception. The IUCD causes mechanical irritation of the uterine mucosa, resulting in increased capillary fragility[1,2]. Biopsies of the endometrial mucosa from women using IUCD's show local micro-injuries in the mucosa leading to haemorrhagic damage. It has been reported that the use of an IUCD very often increases menstrual bleeding[3]. Almost 50% of women fitted with an IUCD suffer from menorrhagia characterized by heavier menstrual bleeding and/or prolonged duration of the menstruation. As a general rule there is no tendency towards spontaneous normalization[4]. This increases the risk of anemia following IUCD related bleeding. Daflon 500 mg. containing micronized 450 mg Diosmin and 50 mg flavonoids expressed as Hesperidin per tablet, has a demonstrated pharmacological action[5] in reducing the capillary fragility.

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This could play an effective role in controlling the bleeding associated with an IUCD. The aim of this study was to evaluate the clinical efficacy and acceptability of Daflon 500 mg in IUCD related bleeding over a period of 3 consecutive cycles.

MATERIAL AND METHODS

Outpatients with IUCD related bleeding were included in the trial. Patients with uterine bleeding unrelated to the IUCD insertion and those on anti-inflammatory, anti-coagulant and hormonal therapy were excluded. Patients who were on phlebotonic therapy should have stopped the treatment 15 days prior to entering the trial. Daflon 500 mg was administered at a dose of 2 tablets per day (one at each of the two main meals) for a period of 3 consecutive cycles.

Patients included in the trial were questioned in details about the menstrual, gynaecological and obstetric history. The mean periodicity and duration of the menses and presence of dysmenorrhoea was noted. The history of menorrhagia and metrorrhagia was found out. The number of pregnancies were noted. The mean difference between IUCD insertion and the onset of treatment was detailed. The patients were evaluated on entering the trial (T_0) and then for three consecutive cycles (T_1, T_2, T_3). A general examination of cardiovascular, neurological and gastrointestinal system was carried out. The general data regarding blood pressure, heart rate and weight of the patient was evaluated (T_0, T_1, T_2 and T_3). The symptoms and signs were related on a four point scale ranging from 0 (absent) to 3 (severe). The analysis of the efficacy was based on the duration of the menses along with the amount of flow as compared to T_0. The subjective symptom of dysmenorrhoea was also analysed.

The overall efficacy of Daflon 500 mg was assessed by the clinician and rated as excellent, good, fair or no improvement at the end of the 3 cycles. Clinical acceptability was assessed at the end of each cycle.

The statistical analysis[6] was quantitatively expressed as a mean ± SEM (standard error of the mean). The type-1 error was set at 0.05 for all analysis. The changes over time of haemodynamic variables was assessed by using a two-way analysis of variance (time x patient) and if the time effect was significant a Newman-Keuls test was performed.

RESULTS

Population studied

Thirty women were enrolled in the trial. The main clinical characteristics are summarized in table I.

Table I

Description of Population (n = 31)

	Variables	Mean (sem)	Min	Max
General Data	Age	24.97 (0.74)	20	40
	Number of pregnancies	2.1 (0.2)	1	1
Menses	Duration (days)	8.7 (0.5)	5	20
	Periodicity (days)	28.6 (0.9)	15	45
Time between IUCD insertion and Daflon 500	(days)	276.2 (50.9)	39	1638

The amount of flow during menstruation after IUCD insertion was important in 27 patients (90%) and dysmenorrhoea was noted in 18 patients (41.9%). There was history of menorrhagia in 22 patients (91.7%) and metrorrhagia in 6 patients (19.3%). Two patients withdrew from the trial due to change of residence. This was observed when interruption of the treatment was noted at T_2 and T_3.

Therapeutic Efficacy

The efficacy of Daflon 500 mg was studied in 20 patients who completed the trial. An analysis of the duration of menses showed that in comparison to the duration at T_0 (10.4 ± 1.1), a significant reduction was noted at T_1 (6.4 ± 0.5 $P < 0.01$), with further improvement at T_2 and T_3 (5.5 ± 0.5 $P < 0.01$).

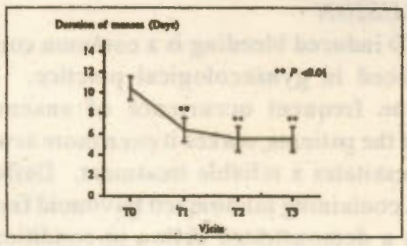

Fig. 1 : Change over time of duration of menses.

The amount of flow during menses in these 28 patients showed the following results in comparison with the mean score at T_0 (2.1) : a significant reduction was noted at T_1 (1.6 ± 01 $P < 0.05$), $\%_2$ (1.4 ± 0.1 $P < 0.01$), and T_3 (1.2 ± 0.1 $P < 0.01$).

23 patients - 82.1% of the population studied improved at T_3 as compared to T_0 i.e. more than 8 out of 10 patients had amelioration of the bleeding with Daflon 500 mg. There was no aggravation of the condition in any patient.

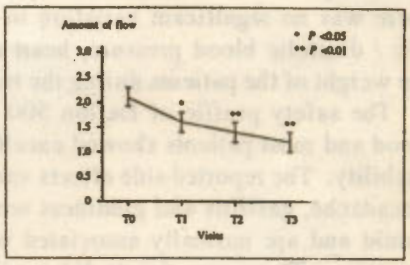

Fig. 2 : Change over time of amount of flow during menses.

The patient suffering from dysmenorrhoea showed a significant decrease in the mean score during the period of the trial. In comparison to the severity of the symptom at T_0 (1.03 ± 0.1), a marked improvement was noted at T_1 (0.7 ± 0.1 $P < 0.05$), T_2 and T_3 (0.5 ± 0.1 $P < 0.01$).

There was amelioration of the symptoms of dysmenorrhoea in 13 patients - 72% of the population studied and in the remaining 5 patients the condition was unchanged.

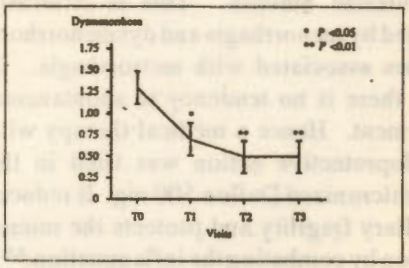

Fig. 3 : Change over time of dysmenorrhoea.

Metrorrhagia could not be statistically analysed because the sample size was too small. Nevertheless there was a trend towards the amelioration and stability of bleeding in the patients at T_3 when compared to T_0.

Acceptability

There was no significant variation in the systolic / diastolic blood pressure, heart rate and the weight of the patients during the treatment. The safety profile of Daflon 500 mg was good and most patients showed excellent acceptability. The reported side effects varied from headache, gastritis and giddiness which were mild and are normally associated with menstruation. These complaints did not lead to interruption of the treatment with Daflon 500 mg.

The global assessment by the clinician in terms of both efficacy and acceptability was as follows : excellent in 4 patients, good in 10 patients, and fair in 10 patients at the end of the trial. Thus Daflon 500 mg was clinically effective in 24 patients - 85.7% of the population studied. The overall assessment showed that more than 8 our of 10 patients improved with Daflon 500 mg.

DISCUSSION

Bleeding related with an IUCD is an iatrogenic phenomenon seen in almost 50% of women[7] fitted with the device. It is associated with increased capillary fragility due to mechanical trauma and inflammation caused by the IUCD on the uterine mucosa. This is clinically manifested by menorrhagia and dysmenorrhoea sometimes associated with metrorrhagia. In general, there is no tendency to spontaneous improvement. Hence a medical therapy with a vasculoprotective action was tried in the form of micronized Daflon 500 mg. It reduces the capillary fragility and protects the microcirculation by combating the inflammation.[8,9,10]

The patients included in our trial complained commonly of prolonged duration of the menses with increased amount of flow. The efficacy of Daflon 500 mg is demonstrated by a statistically significant decrease in the duration of the menses (in days) at the end of the trial (T_3) as compared to T_0. The amount of flow during the menses which was rated (0 to 3) according to the severity, was also significantly reduced. There was a decrease in amount of flow in 23 of the 28 patients at the end of the trial. Dysmenorrhoea, as a symptom, improved in 13 out of the 18 patients who complained of dysmenorrhoea on inclusion into the trial. The patients who suffered from metrorrhagia showed a trend towards improvement with Daflon 500 mg. The results demonstrated an excellent safety profile as the side effects were unrelated to Daflon 500 mg. The compliance with the treatment was good, only two patients withdrew from the trial and no patient was excluded for not observing the protocol.

CONCLUSION

IUCD induced bleeding is a common complaint faced in gynaecological practice. In India, the frequent occurrence of anaemia amongst the patients, makes it even more acute and necessitates a reliable treatment. Daflon 500 mg. containing micronized flavonoid fraction has a demonstrated action in conditions associated with increased capillary fragility like haemorrhoids[11,12]. In this open trial the efficacy of Daflon 500 mg. in IUCD induced bleeding was studied and found to be very satisfactory 85.7% of the population was excellent with minimal side effects. Based on this experience, we consider the use of Daflon 500 mg. as a valuable tool in the treatment of IUCD induced bleeding

REFERENCES

1. *Tsouderos Y. : Act Med. Int. Angiol. : 5, 9, 1988.*