

## **EveCare Syrup in Dysfunctional Uterine Bleeding**

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### **ABSTRACT**

*Thirty six women suffering from symptoms of dysfunctional uterine bleeding were selected for trial with EveCare Syrup, a polyherbomineral formulation. EveCare Syrup was administered at a dose of 2 teaspoonsful, twice daily for 3 months.*

*56.6% of the women were completely cured and 33.3% had partial relief. No side effects were observed during the study. Thus, EveCare Syrup is effective in controlling dysfunctional uterine bleeding and regularizing the menstrual cycle.*

### **INTRODUCTION**

Every healthy woman menstruates regularly and rhythmically every month during her reproductive era. The menstrual cycle is significant in the fertility of a woman. Any abnormality may put the woman in distress. The regularity of menstruation depends upon hypothalamo-pituitary-ovarian function, whereas, the amount of blood loss depends upon the uterine condition.

About 28% of women consider their menstrual loss excessive and plan their activities around their menstrual cycle and nearly 10% of employed women take time off from work due to excessive loss<sup>1</sup>. Six percent of women between 25-44 consult their family physician for excessive loss every year<sup>2</sup>. Among 35% of these are referred to hospitals<sup>3</sup> and 60% will go in for a hysterectomy in the next 5 years<sup>4</sup>. Over 7500 hysterectomies are carried out every year with 30% of them for menstrual disturbances<sup>5</sup>. The exact pathophysiology is difficult to understand and hence the disorder is broadly referred as dysfunctional uterine bleeding.

According to Kistner, in cases of dysfunctional uterine bleeding, 57.5% had a normal endometrium, in 30.8% of cases hyperplasia of the endometrium was observed, the incidence of irregular ripening and irregular shedding was present in 7.8% and atrophy was seen in 3.9% of the cases<sup>6</sup>.

Various treatments prescribed in modern medicine like hormone therapy, anti-prostaglandins and antifibrinolytic agents have not proved their definite efficacy. In Ayurveda, a number of herbal drugs have been mentioned which are very effective in menstrual disorders.

EveCare Syrup, a uterine tonic was formulated containing extracts of different herbs by The Himalaya Drug Company, Bangalore. An open clinical trial was conducted to evaluate its efficacy in dysfunctional uterine bleeding.

## **MATERIAL AND METHODS**

Patients attending the out patient department of Prasuti Tantra, S.S Hospital, Varanasi were selected at random with complaints of abnormal and excessive vaginal bleeding for more than 3 consecutive cycles. Thirty six women were enrolled in the trial.

### ***Inclusion criteria***

- Patients who complained of excessive irregular/prolonged bleeding *per* vaginum.
- Patients who did not use oral contraceptive pills, hormonal treatment or IUCDs.
- Patients who had no systemic illness like hypertension, renal disease, tuberculosis, hepatic disease, diabetes, coagulation disorder, etc.
- Patients who had no organic lesion of the reproductive tract especially any benign or malignant growth, extensive cervical erosion, cervical polyps, endometriosis, tubercular endometritis and acute infective disorder.
- Patients having Hb  $\geq$  8 gm% (to avoid severe anaemia leading to blood loss).
- Patients whose history excluded recent delivery or abortion.

All the women had complete physical and gynecological examinations along with screening for haemogram bleeding, clotting time and platelet count.

### ***Drug Dose Schedule and Subjective Assessment***

Patients were given EveCare Syrup, at a dose of 2 teaspoonsful twice daily for 3 months. All the patients were reviewed at regular intervals of one month for three months for subjective assessment.

### ***Method of Scoring***

To facilitate the data recording of proforma, the scoring of various symptoms were done as follows:

### ***Amount of Blood Loss***

This was assessed on the basis of statements given by patients. Each case was asked the day when maximum bleeding took place as it varies from person to person. Hence the number of sanitary pads used on the day of maximum bleeding was recorded. Women were advised to use standard size sanitary pads i.e. 6" x 3" x 1.5" of average weight made of cotton.

<b>Amount</b>	<b>No. of sanitary pads used/day</b>	<b>Score</b>
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Normal	3-4	1
Excessive	5-6	2
Very excessive	7 and above	3

### ***Duration of Menstrual Cycle***

Cases were asked for the duration of bleeding in the number of days in a month.

<b>Duration</b>	<b>No. of days</b>	<b>Score</b>
Normal	2-3	1
Prolonged	4-6	2
Very prolonged	7 and above	3

### ***Intermenstrual Interval***

<b>Interval</b>	<b>No. of days</b>	<b>Score</b>
Normal interval	26-30	1
Early periods	21-25	2
Frequent	15-20	3

### ***Cure Score***

At the end of 3 follow ups, patients were assessed again on the basis of the change towards normalcy in amount, duration, and intermenstrual interval and improvement in associated symptoms.

### ***Complete Relief***

- Normal amount of blood loss
- Normal duration of blood loss
- Normal interval between the cycles
- Normal consistency of menstrual blood
- Relief in associated symptoms

### ***Partial Relief***

Cases having any 2 of the above criteria with relief in associated symptoms

### ***Unchanged***

No improvement in any of the above criteria

### ***Statistical analysis***

The student's paired t-test was applied to evaluate the significant difference within a group. The Z-test was also used to evaluate the significant difference between the initial and follow up periods after treatment.

## RESULTS

The factors responsible for dysfunctional uterine bleeding are:

1. Tension, anxiety or emotional factors<sup>7,8</sup>.
2. Infections of the uterus and adenaxae<sup>9</sup>.
3. Inflammation of the uterus and adenaxae<sup>10</sup>.
4. Hormonal imbalance<sup>11</sup>.
5. Fibrinolytic activity<sup>12</sup>.
6. Delayed endometrial regeneration<sup>13</sup>.

Menorrhagia may be associated with nausea, loss of appetite, backache, anxiety, oedema, bodyache, general weakness and anaemia.

In the trial, all the patients enrolled were in their reproductive years. The youngest patient in the study was of 18 years and the eldest was 42 years with a mean of  $27.4 \pm 7.4$  years.

Frequency distribution of age at menarche is given in Table 1.

The frequency distribution of gravida, parity and abortion is given in Tables 2, 3 and 4, respectively.

Percentage of dysmenorrhoea, duration of bleeding and quantity of bleeding are described in Tables 5, 6 and 7, respectively.

Age	Frequency	Percentage
12	1	3.3
13	7	23.3
14	7	23.3
15	2	6.7
16	4	13.3
18	2	6.7
20	2	6.7
Missing	5	16.7
Total	30	100.0

Gravida	Frequency	Percentage
0.00	5	16.7
1.00	2	6.7
2.00	4	13.3
3.00	4	13.3
4.00	4	13.3
5.00	3	10.0
9.00	1	3.3
Missing	7	23.3
Total	30	100.0

<b>Table 3: Parity</b>		
The parity of the women ranged from 0 to 9 with a M(SD) of 2.6 (2.1). The frequency distribution of parity is presented below:		
Para	Frequency	Percentage
0.00	4	13.3
1.00	2	6.7
2.00	6	20.0
3.00	5	16.7
4.00	3	10.0
5.00	2	6.7
9.00	1	3.3
Missing	7	23.3
Total	30	100.0

<b>Table 4: Abortions</b>		
The abortions of the women ranged from 0 to 2 with a M(SD) of 0.8 (1.0). The frequency distribution of parity is presented below:		
Abortion	Frequency	Percentage
0.00	2	6.7
1.00	1	3.3
2.00	1	3.3
Missing	26	86.7
Total	30	100.0

<b>Table 5: Dysmenorrhoea</b>		
The incidence of dysmenorrhoea at baseline and at each monthly assessment is presented below:		
Time point	No.	Percentage
Baseline	27	90
Month 1	23	76.7
Month 2	14	46.7
Month 3	10	33.3
Thus, it is clear that there was a >50% drop in the number of women who complained of dysmenorrhoea; most women who responded did so between one and two months of treatment.		

<b>Table 6: Duration of bleeding</b>					
The duration of bleeding (in days) during the periods is presented below.					
Time point	Mean	Std Dev.	Minimum	Maximum	N
Baseline	5.63	2.75	0	12	30
Month 1	5.00	1.44	3	8	30
Month 2	4.87	1.50	3	8	30
Month 3	4.84	1.57	2	8	25
(Data from 5 women were missing from the last time point). Although the duration of bleeding decreased progressively from baseline to month 3, the decrease was not statistically significant (Pillai's trace=0.21, F=2.01, df=3,22, p=0.14). It is possible that the results may have been significant had the sample been larger.					

The duration of cycle, reduced cycle, regular cycles and intermenstrual bleeding are shown in Tables 8, 9, 10 and 11, respectively.

<b>Table 7: Quantity of bleeding</b>					
The quantity of bleeding during each menstrual period presented in terms of pads changed per day, is shown below:					
Time point	Mean	Std Dev.	Minimum	Maximum	N
Baseline	4.35	2.39	2	9	20
Month 1	4.61	1.90	2	9	23
Month 2	4.61	1.95	2	9	23
Month 3	4.68	2.03	2	9	19

Complete data for all time points was available for only 13 women. There was no significant change across time in the number of pads changed daily during the menstrual period (Pillai's trace=0.44, F=2.62, df=3,10, p=0.11).

<b>Table 8: Duration of cycle</b>					
The duration of the menstrual cycle (in days) at each time point of assessment is presented below:					
Time point	Mean	Std Dev	Minimum	Maximum	N
Baseline	27.24	6.28	12	40	21
Month 1	27.79	3.92	20	38	28
Month 2	27.86	2.20	22	32	29
Month 3	27.83	1.93	22	30	29

There was no significant change across time (Pillai's trace=0.02, F=0.10, df=3,18, p=0.96).

<b>Table 9: Reduced cycles</b>		
The incidence of reduced cycles at each time point of assessment is presented below:		
Time point	No.	Percentage
Base line	15	50.0
Month 1	7	23.3
Month 2	4	13.3
Month 3	1	3.3

Most of the women who improved, showed improvement within the first month of treatment.

<b>Table 10: Irregular cyclical bleeding</b>		
The incidence of irregular cyclical bleeding at each time point of assessment is presented below:		
Time point	No.	Percentage
Baseline	8	26.7
Month 1	3	10.0
Month 2	3	10.0
Month 3	3	10.0

As previously noted, most of the women who improved, showed improvement within the first month of treatment.

<b>Table 11: Intermenstrual bleeding</b>		
The incidence of intermenstrual bleeding at each time point of assessment is presented below:		
Time point	No.	Percentage
Baseline	1	3.3
Month 1	1	3.3
Month 2	0	0.0
Month 3	0	0.0

As with other features, most women who improved showed improvement within the first month of treatment.

There was a significant decrease in the overall severity of menstrual symptoms (Table 12).

Age was unrelated to response at any time, which suggests that women of all ages responded to EveCare Syrup treatment (Table 13).

Overall, the amount of excessive blood loss was reduced significantly. There was no intermenstrual bleeding and menstrual cycles were regularized during the next 3 months (Table 14).

**Table 12: Overall improvement in symptoms**

In order to ascertain the overall improvement in the clinical picture, composite (total) scores were computed at each time point by summing the ratings for dysmenorrhoea, reduced cycles, irregular cyclical bleeding and intermenstrual bleeding at each time point. For this purpose, each symptom was rated as 0 if absent and 1 if present.

The total scores are presented below:

Time point	Mean	Std Dev	Minimum	Maximum	N
Baseline	1.70	0.75	1.00	4.00	30
Month 1	1.14	0.58	0.00	2.00	29
Month 2	0.69	0.81	0.00	2.00	29
Month 3	0.55	0.74	0.00	2.00	29

There was a statistically significant decrease in overall severity of menstrual symptoms across time (Pillai's trace=0.62, F=13.87, df=3,25,  $p<0.001$ ).

**Table 13: Age and response**

In order to ascertain the relationship between age and response, Pearson's correlation coefficients were derived between age and the total score at each assessment point. These coefficients are presented below:

Correlations	Age	TOT0	TOT1	TOT2	TOT3
Age	1.0000	-0.1378	-0.1457	-0.0253	-0.0472

From the correlation coefficients, it is clear that age was unrelated to response at any time point; in other words, women of all ages can be expected to respond to EveCare Syrup.

**Table 14: Showing change in duration, amount of blood loss and intermenstrual period before starting the treatment and in subsequent follow-ups with statistical analysis.**

Blood loss	Initial	1 <sup>st</sup> FU	2 <sup>nd</sup> FU	3 <sup>rd</sup> FU	'Z' value
Normal	8 (26.66%)	19 (63.3%)	20 (66.6%)	21 (70%)	3.8***
Excessive	1 (36.66%)	8 (26.665%)	6 (20%)	6 (20%)	1.45*
Very excessive	11 (36.66%)	3 (10.0%)	4 (13.33%)	3 (10%)	2.58**
<b>Duration of menstrual cycle</b>					
Normal	5 (16.6%)	13 (43.3%)	16 (53.33%)	19 (63.33%)	4.23***
Prolonged	12 (40%)	12 (40%)	10 (33.33%)	7 (23.33%)	1.44*
Very prolonged	13 (43.3%)	5 (16.6%)	4 (13.33%)	4 (13.33%)	2.74**
<b>Intermenstrual interval</b>					
Normal	14 (46.66%)	20 (66.6%)	24 (80%)	24 (80%)	2.84**
Early	7 (23.33%)	7 (23.33%)	6 (20%)	6 (20%)	0.28*
Frequent	9 (30%)	3 (10%)	0 (0%)	0 (0%)	3.61***

\* No Significant, \*\* $p<0.01$ , \*\*\* $p<0.001$

## DISCUSSION

An open clinical trial of EveCare Syrup, a polyherbal formulation produced significant symptomatic relief in women with dysfunctional uterine bleeding. The various constituents of EveCare Syrup are known in Ayurveda for their benefits in various menstrual disorders including dysfunctional uterine bleeding.

*Saraca indica*<sup>14</sup> has been well proven for its effectiveness in menorrhagia and dysmenorrhoea. It also has a stimulatory effect on the ovarian tissue which may produce an oestrogen-like activity that enhances the repair of the endometrium and stops bleeding. *Symplocos racemosa*<sup>15</sup> has been reported to be useful in the treatment of menorrhagia and other uterine disorders. The ethanolic extract of *Boerhaavia diffusa*<sup>16</sup> was found to stop intra-uterine-contraceptive-device-induced bleeding in monkeys. This herb is also known for its anti-inflammatory and analgesic property which is comparable to that of ibuprofen. The drug has also proved useful as a haematinic. *Symplocos racemosa*<sup>17</sup> exhibit relaxant and antispasmodic effects on several spasmogens on uterine smooth muscles, attributing favorable actions to the drug in dysmenorrhoea and as a uterine sedative. *Cyperus rotundus*<sup>18</sup> has been utilized in the treatment of anaemia and general weakness. *Aloe vera*<sup>19</sup> also possesses oxytocic property.

Taking into consideration the results of the trial and the proven reports of the herbs used in the formulation, it can be concluded that EveCare Syrup can effectively control dysmenorrhoea, the manifestation of dysfunctional uterine bleeding.

In the first follow up, 43.3% cases showed normal duration, 63.3% reached the normal amount and 46.66% had a normal intermenstrual period. In the third follow up, 70% of the cases had normal blood loss, 63.33% cases had normal duration and 80% had normal intermenstrual period.

On the basis of the 'cure score' mentioned earlier, in the present study 56.6% (17 cases) were completely cured, 33.3% (10 cases) had partial relief and 10% (3 cases) remained unchanged.

No side effects were observed. Along with normalizing bleeding *per vaginum*, which is excessively significant, relief in associated symptoms also contributed to the efficacy of this trial drug.

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