

Effect of Qurse Gulnar in Heavy menstrual bleeding – a randomized single blind standard control study

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Abstract: Heavy menstrual bleeding (HMB) is defined as prolonged or heavy cyclical menstrual bleeding. Objectively, menses lasting longer than 7 days or exceeding 80 ml of blood loss are determining values. It has a worldwide prevalence of 19%, in India the prevalence is 15%. It has been shown to have a profound negative impact on many aspects of a woman's quality of life. It has been suggested that effective medical management of heavy menstrual bleeding may impact on referral and subsequent hysterectomy rates.

The goals of alternative treatment of heavy menstrual bleeding are the same as the goals of conventional treatment; control the bleeding, prevent and treat anaemia and restore an acceptable menstrual pattern.

The aim of the study is to validate scientifically the efficacy of Qurse gulnar in heavy menstrual bleeding.

Methods: The study was designed as randomized single blind standard control study, conducted in Dept. of Ilmul Qabalatwa Amraze Niswan, NIUM hospital, Bengaluru. 60 women with heavy menstrual bleeding were randomly allocated to test and control groups. The participants in test group received Qurse gulnar 2 (1gm) TDS for 4 days from the first day of menstrual cycle while in control group, tranexamic acid 1 (500mg) was given similarly. Patients were evaluated for 3 consecutive menstrual cycles; assessment for primary and secondary outcome was done by pictorial blood loss assessment chart (PBAC) and multi attribute utility scale (MAUS) scores at each follow up during and after treatment.

Results: There was a significant decrease in PBAC and MAUS score from before treatment to after treatment in both group with p value < 0.001. The intergroup comparison showed no significant difference in outcome measures after treatment with p-value > 0.05.

Conclusion: Qurse gulnar is as effective as tranexamic acid in the management of heavy menstrual bleeding.

Keywords: Heavy menstrual bleeding, Qurse gulnar, MAUS, PBAC.

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I. Introduction

Heavy menstrual bleeding HMB is defined as prolonged or heavy cyclical menstrual bleeding.¹ Objectively, menses lasting longer than 7 days or exceeding 80 ml of blood loss are determining values, while in practice, diagnosis is typically based on the subjective perception of MBL and its impact on quality of life (QOL).² It has a negative impact on a woman's physical, social, emotional and material quality of life.³ Recent work has shown that women rate the impact HMB has on their family life is higher than the impact on their physical health.⁴ The etiological FIGO classification includes nine categories of abnormal bleeding arranged according to the acronym PALMCOEIN: four have objective visual criteria detected by imaging, biopsy, or pathology PALM: **p**olyps; **a**denomyosis; **l**eiomyomata; and **m**alignancy and hyperplasia while another five are not directly related to structural abnormalities i.e., COEIN: **c**oagulopathy; **o**vulatory dysfunction; **e**ndometrial; **i**atrogenic; and **n**ot yet classified.⁵ According to the classical Unani literature heavy menstrual bleeding occurs due to disease of uterus like ulcerations, polyps, fissures which leads to weakening of uterine vessels or it may be due to alteration of temperament which causes vasodilation. Seldom the cause of excessive bleeding is the decrease in the viscosity of blood.^{1,6,7} The excessive blood loss can cause anemia, tiredness,⁸ indigestion, decreased appetite, edema and pica.⁹

Many national guidelines consider the medical alternatives as first-line treatment. Women of younger age who wish for preserving fertility seek effective medical treatment. Surgery may be indicated for women who have completed their family, when medical treatment is ineffective or not tolerated.¹⁰ Potential complications caused by surgical interventions can thus be avoided in many cases.¹¹ Medical treatment for HMB includes a wide variety, comprising of Hormonal intervention, NSAIDs, antifibrinolytics and intrauterine devices.¹² Such treatments are though effective but are not cost effective and side effects occurring from such

options cannot be neglected; unfortunately, many options can be associated with hormonal side effects, prevention of fertility and lack of efficacy, leading to discontinuation and progression to surgical interventions.¹³

The goals of alternative treatment of heavy menstrual bleeding are the same as the goals of conventional treatment; control the bleeding, prevent and treat anemia and restore an acceptable menstrual pattern.¹⁴ In Unani system of medicines various drugs have been described for Heavy menstrual bleeding,^{1,6} Hemostyptic drugs due to their properties like astringent and dessicant produce vasoconstriction or improves the coagulative property of blood, thereby helps in cessation of bleeding. Examples of this include, *pterocarpus marsupium*, *quercus infectoria*, *papaversomniferum*, *punicagranatum*, *rosa damascena*, *polijgonumbistorata*, *plantago major* potash alum, egg albumin, magnesium silicate, red earth, iron oxide, aluminium silicate, calcined pearl etc.¹⁵ In the present study, *Qurse gulnar*, Apolyherbal preparation in tablet form containing; *Punicagranatum*, gum *Acacia arabica* Armenian bole, extract of *Acacia Arabica*, *Rosa damascena*, gum *Cochlospermum gossypium*; is chosen for its hemostatic, anti-inflammatory and analgesic properties due to presence of ingredients which have astringent and hemostyptic action and possess dried and cold temperament. Unani medicine which possesses such properties tends to act as antifibrinolytics. This was a randomized single blind standard control study conducted in Dept. of Ilmul Qablatwa Amraze Niswan, NIUM hospital, Bengaluru. The aim of the study is to validate scientifically the efficacy of *Qurse gulnar* in heavy menstrual bleeding. Hypothesis was that *Qurse gulnar* is as effective as Tranexamic acid in the management of heavy menstrual bleeding.

II. Materials And Methods

2.1 Study design

Randomized single blind Standard controlled study was carried out from Nov 2016 to March 2017 in OBG Dept. National Institute of Unani Medicine Hospital, Bangalore. Ethical clearance was obtained from the institutional ethical committee and all participants gave written informed consent prior to study.

2.2 Participants

Total 122 patients were screened for the study, 46 patients denied participation and 16 patients didn't meet the inclusion criteria, hence were excluded. 60 patients were randomly allocated in two equal groups (test and control) by computer generated simple randomization table.

2.3 Selection criteria

Both Married and unmarried women in the age group of 18-40yrs with c/o heavy menstrual bleeding with regular cycles and calculated PBAC >100 were included in the study and those with irregular bleeding, Endometriosis, adenomyosis, fibroids >3 cm / & more than 3 in number, Endometrial hyperplasia, Systemic diseases, history of blood dyscrasias and malignancy, H/o taking hormonal treatment in the last 3 months were excluded from the study by performing CBC, ESR, RBS, CT, BT and pelvic ultrasound.

2.4 Study procedure

The patients fulfilling the inclusion criteria were enrolled after explaining the study in detail and receiving the informed consent. In each patient, history was evaluated and a complete physical examination including breast, abdominal examination and per vaginal examination in married women only, was performed. Personal details, history, clinical features and investigations were recorded in the CRF structured for the study.

Initial assessment and laboratory screening:

1. At enrolment a detailed menstrual history regarding amount, duration and pattern of uterine bleeding and its relation to last menstrual period were enquired.
2. The amount of bleeding judged with number of pads changed per day, history and size of clots P/V and history of episodes of flooding during menses.
3. Assessment of menstrual blood loss is done by using the pictorial bleeding assessment chart (PBAC).¹⁶
4. Assessment for improvement in quality of life was done by using multi attribute utility scale (MAUS).¹⁷
5. Treatment was subsequently started in patients fulfilling the inclusion criteria. The test or control drug as randomized was given for 4 days from the first day of menstrual cycle for two consecutive cycles. Assessment of blood loss during periods was done by PBAC score and assessment in improvement of quality of life was done by multi-attribute utility scale at baseline, each follow up during treatment and after treatment. Patients were also enquired for any side effects noted during the trial.

2.5 Intervention

Qurse gulnar (tablet gulnar)1gm contains; Punicagranatum200mg, gum Acacia Arabica 200 mg, Armenian bole 200mg, extract of Acacia Arabica 150 mg, Rosa damascena 150mg, gum Coch lospermumgossypium 100 mg, Qurse gulnar were prepared according to the standard method of preparation. Qurse gulnar (1gm) 2 TDS orally for 4 days during menses in test group and Tranexamic acid (500mg) 2 TDS for first 4 days during menses in control group for 2 consecutive cycles.

2.6 Subjective parameters:

Heavy bleeding during menses with regular cycle.

2.7 Objective parameters:

PBAC- Score (Pictorial blood loss assessment chart) to assess the amount of blood loss.

MAUS- score to assess quality of life.

2.8 Outcome measures:

Primary outcome: Change in PBAC score.

Secondary outcome: Improvement in Quality of life. (Change in Multi-attribute utility assessment scale score).

2.9 Statistical Analysis: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data.

III. Results

Table 1: Demographic data

Age in years	Test Group (n=30)	Control Group(n=30)	p value ^a
<20	6(20%)	6(20%)	0.852
20-30	16(53.3%)	15(50%)	
31-40	8(26.7%)	9(30%)	
Total	30(100%)	30(100%)	
Marital Status	Test Group	Control Group	p value ^b
Married	17(56.7%)	20(66.7%)	0.42
Single	13(43.3%)	10(33.3%)	
Socio Economic Status	Test Group	Control Group	p value ^c
Lower	0(0%)	1(3.3%)	0.187
Lower middle	11(36.7%)	12(40%)	
Upper	4(13.3%)	0(0%)	
Upper middle	15(50%)	17(56.7%)	
Diet	Test Group	Control Group	p value ^e
Mixed	30(100%)	30(100%)	1.000
Veg	0(0%)	0(0%)	
BMI (kg/m ²)	Test Group	Control Group	p value ^d
<18.5	0(0%)	3(10%)	0.385
18.5-25	21(70%)	17(56.7%)	
25-30	8(26.7%)	9(30%)	
>30	1(3.3%)	1(3.3%)	

Table 2: Amount of Flow distribution in two groups of patients studied

Amount of flow	Test Group (n=30)	Control Group (n=30)	Total (n=60)	P value
BT				1.000
• Heavy	30(100%)	30(100%)	60(100%)	
• Moderate	0(0%)	0(0%)	0(0%)	
• Mild	0(0%)	0(0%)	0(0%)	
• None	0(0%)	0(0%)	0(0%)	
T1				

• Heavy	18(60%)	21(70%)	39(65%)	0.717
• Moderate	9(30%)	7(23.3%)	16(26.7%)	
• Mild	3(10%)	2(6.7%)	5(8.3%)	
• None	0(0%)	0(0%)	0(0%)	
T2				0.832
• Heavy	15(50%)	17(56.7%)	32(53.3%)	
• Moderate	9(30%)	9(30%)	18(30%)	
• Mild	6(20%)	4(13.3%)	10(16.7%)	
• None	0(0%)	0(0%)	0(0%)	0.303
F1				
• Heavy	15(50%)	18(60%)	33(55%)	
• Moderate	10(33.3%)	11(36.7%)	21(35%)	
• Mild	5(16.7%)	1(3.3%)	6(10%)	Amount of flow Intragroup p value
• None	0(0%)	0(0%)	0(0%)	
Test Group (n=30)		Control Group (n=30)	Total (n=60)	
BT-T1	<0.001**	<0.002**	<0.001**	
BT-T2	<0.001**	<0.001**	<0.001**	
BT-F1	<0.001**	<0.001**	<0.001**	

Table 3: DOF distribution in two groups of patients studied

DOF	Test Group	Control Group	P value
BT	6.27±1.91	6.07±2.46	0.727
• T1	4.77±1.61	5.13±2.08	0.448
• T2	4.53±1.50	5.00±1.88	0.292
• F1	4.53±1.57	4.90±1.71	0.390
• P value from BT			
T1	<0.001**	0.002**	-
• T2	<0.001**	0.002**	-
• F1	<0.001**	0.001**	-
•			

Table 4: PBAC distribution in two groups of patients studied

PBAC	Test Group	Control Group	P value
BT	295.30±226.32	235.63±96.82	0.190
T1	161.60±117.70	148.30±76.81	0.606
T2	141.70±105.49	123.27±48.76	0.389
F1	138.93±97.99	138.30±73.18	0.977
P value from BT			
• T1	<0.001**	<0.001**	-
• T2	<0.001**	<0.001**	-
• F1	<0.001**	<0.001**	-

Table 5: MAUS Score distribution in two groups of patients studied

MAUS Score	Test Group	Control Group	P value
BT	27.53±22.51	27.10±19.86	0.937
T1	66.25±30.65	63.02±33.42	0.698
T2	72.99±34.84	73.47±32.62	0.957
F1	79.27±33.87	68.26±36.27	0.229
P value from BT			
• T1	<0.001**	<0.001**	-
• T2	<0.001**	<0.001**	-
• F1	<0.001**	<0.001**	-

IV. Discussion

With respect to demographic data like age, marital status, socio economic status, diet, and BMI of patients in both groups were homogenous as shown in **Table 1**.

3.1Age:

In the present study, majority of patients 31(51.7%) were in the age group of 20-30 followed by 17(28.3%) in age group of 30 – 40 years and 12(20%) in age group <20 years. (**Table 01**) An observational

study was carried out in NIUM, of 450 patients of menorrhagia maximum patients 177 (39.33%) were found in the age group of 25-34 years, which is similar to our study.¹⁸ In a study conducted by Azita Goshtasebi et al with patients having HMB; out of 76 women 32 belonged to age group 20 -30 years. This is similar to our study.¹⁹ In a study conducted by Kiranmani Gotappu¹²⁹, 71% of women with HMB were above 30 years. This is contradictory to the present study; this might be due to different study settings.²⁰

3.2 Marital status:

In the present study, heavy menstrual bleeding was observed more in married women. 37 out of 60 patients were married; 17(56.7%) patients in test group 20(66.7%) in control group. (**Table 01**) In a study carried out by Gotappu et al.²⁰ on 800 women, 77% were married; this is similar to the present study.

3.3 Socio economic status:

No patients in test group and 1(3.3%) patient in control group belong to lower, 11(36.7%) patients in test and 12(40%) patients in control group are lower middle class and 4(13.3%) in the test and no patients in control group were in upper class; 15(50%) patients in test and 17(56.7%) patients in control group are from upper middle respectively. (**Table 01**) In present study majority of participants belonged to upper middle, followed by lower middle, upper and lower class. In a study carried out by Kiranmani Gotappu et al²⁰ involved 800 patients, 77% are of low socio economic group which is contradictory to the findings of present study. This can be found due to different study settings.

3.4 Diet:

All the patients in both test and control groups were having mixed dietary habits. (**Table 01**) In a study carried out by Dr. Vijay Zutshiet al.²¹ Out of 54, 46 participants were having mixed dietary habits which is similar to the present study.

3.5 BMI:

Mean \pm SD of BMI in test group was 24.04 \pm 3.30 and 23.16 \pm 4.37 in control group with p value of 0.385 before treatment. 0(0%) patients in test and 3(10%) in control group were underweight, 21 (70%) patients in test group and 17 (56.7%) patients in control group were having normal BMI, 8 (26.7%) patients in test group and 9 (30%) patients in control group were overweight and 1(3.3 %) patients in both test and control group were found obese. (**Table 01**) In a study carried out by Michał Ząbczyk et al²² with 104 patients of HMB, the average BMI was 25.7 and 25.1 in test and control group respectively which is similar to present study, having maximum no. of participants with normal range of BMI. A study carried by Bassi R et al²³ of 196 female students, 10.7 (21%) experienced heavy flow, of them 38.1% having BMI more than normal. These findings are similar to the present study as 31.1 % of the patients were having BMI more than normal. In a study conducted by Dr. Nabila Hassan Abdellaet al²⁴, out of 124 overweight girls 8% presents with excessive amount of menstrual bleeding while 14.3% of 44 obese have similar complains. This is contradictory to present study wherein 28.35% are overweight and 3.3% were obese; this may be due to the difference in the population studied.

3.6 Outcome measure

3.6.1 Subjective parameters:

Amount of flow:

Amount of flow was assessed by the patient's perception of blood flow. It was heavy in both test group and control group with p- value 1.0 before treatment. In first cycle 3(10%) patients were having mild, 9(30%) moderate and 18(60%) heavy amount of flow in test group while 5(8.3%) patients were having mild 7(23.3%) moderate, 21(70%) complains of heavy menstrual bleeding in control group. Similarly in second cycle 6(20%), 9(30%), 15(50%) patients were having mild, moderate and heavy flow respectively in test group and 4(13.3%), 9(30%), 17(56.7%) were having mild, moderate and heavy menses respectively in control group. After treatment it was 5(16.7%) patients were having mild, 10(33.3%) moderate, 15(50%) heavy amount of flow in test group. 6(10%) complains of mild, 21(35%) moderate and 33(55%) heavy in control group with a p value of 0.303. There was a significant decrease in AOF in 1st treatment cycle and continued to second cycle and follow-up with a p value of <0.001. (**Table 02**) A systematic review on 10 studies carried by Becky Naoulou et al²⁵, shows tranexamic acid significantly decreased the blood loss by 70% in women with ($p < 0.001$). It is contradictory to our study; this may be due to perception of patient as amount of flow in present study was solely depend on patients history and it was not assessed objectively. However there is significant reduction in PBAC score and duration of flow in present study.

Duration of flow:

Mean±SD of duration of flow in test group before treatment, 1st treatment cycle, 2nd treatment cycle and first follow up after treatment were 6.27±1.91, 4.77±1.61, 4.53±1.50 and 4.53 ±1.57 respectively, There was a significant decrease in DOF in 1st treatment cycle and continued to second cycle and follow-up with a p-value of <0.001.

Similarly in control group Mean±SD of duration of flow in control group before treatment, 1st treatment cycle, 2nd treatment cycle and first follow up after treatment was 6.07±2.46, 5.13±2.08, 5.00±1.88 and 4.90 ±1.71 respectively. both heavy uterine bleeding and dysmenorrhea by decreasing production of endometrial prostaglandins¹⁹ There was a significant decrease in DOF in 1st treatment cycle and continued to second cycle and follow-up with a p value of <0.002. The intergroup comparison w.r.t. test group during first and second treatment cycle and first follow up after treatment was p >0.05. (**Table 03**) A study shows reduction in no. of days from 8.0 (1.82) to 6.65 (1.37) with a mean difference of 1.31 in group treated by *gulnar* while there is a reduction from 8.0 (1.39) days to 6.5(1.35) days in a control group with p value 0.99. This is somewhat similar to the present study.¹⁹ Tannins have an astringent property and can cause contraction of capillary endothelium that leads to decreased exudation and menorrhoea loss.¹³⁸ The phytochemical analysis of flower extract also revealed that it contains flavonoids. Flavonoids involve inhibition of both COX and LOX enzymes and a decline in prostaglandin release from cells.²⁶ Also prostaglandin synthetase inhibitors that can alleviate

3.6.2 Objective parameters:

Change in PBAC score: Significant reduction in PBAC score was observed among the participants in both the groups.

Change in MAUS score: Significant improvement in quality of life was observed among the participants of both the groups.

PBAC score:

Mean± SD of PBAC score before treatment, 1st treatment cycle, 2nd treatment cycle and first follow up after treatment in test group was 295.30±226.32, 161.60±117.70, 141.70±105.49, and 138.93±97.99 respectively with p value <0.001. Similarly Mean± SD of PBAC score in control group before treatment, 1st treatment cycle, 2nd treatment cycle and first follow up after treatment were 235.63±96.82, 148.30±76.81, 123.27±48.76 and 138.93±73.18 respectively with p value <0.001. (**Table 04**) Though there was a significant decrease in PBAC score from before treatment to after treatment in both group but did not reach normal values in either group. With respect to test group, this might be due to lower dose of test drug; as per literature it was 5 to 10 gm and given dose was 6gm. The intergroup comparison w.r.t. test group during first and second treatment cycle and first follow up after treatment was not significant with p value >0.05. The intergroup comparison showed no significant difference in outcome measures after treatment with p-value > 0.05; suggesting that *Qurse gulnar* is as effective as tranexamic acid in the management of heavy menstrual bleeding. In a study conducted by Hajar Memarzadeh et al²⁷ in which patients received 5 ml of *Gulnar* syrup; 3 times a day for seven days starting from the onset of heavy bleeding. The volume of menstrual blood loss assessed by PBAC scores also was reduced noticeably after taking the syrup. The average of the PBAC scores was decreased 36.9% in 3 months (p=0.001). The findings are similar to present study. In a study conducted by Azita Goshtasebi et al¹⁹, PBAC mean (SD) score was reduced in the tranexamic acid and *Punicagranatum* groups, respectively from 304.4 (192.7) and 304.9 (176.1) before treatment, to 143.1 (96) and 164 (100.2) in the third treatment cycle (p< 0.001), with no statistically significant difference between the groups after treatment, this is similar to present study.

MAUS score

Mean ± SD of MAUS score before treatment, 1st treatment cycle, 2nd treatment cycle and first follow up after treatment in test group was 27.53±22.51, 66.25±30.65, 72.99±34.84 and 79.27 ± 33.87, similarly mean ± SD of MAUS score in control group before treatment, 1st, 2nd treatment cycle and first follow up after treatment were 27.10±19.86, 63.02 ± 33.42, 73.47 ± 32.62 and 68.26 ± 36.27 respectively. (**Table 05**) The intergroup comparison w.r.t. test group after treatment was not significant with a p value of >0.05, suggesting that *Qurse Gulnar* is as effective as tranexamic acid in improving HMB related QoL. A longitudinal observational study, in an outpatient service of a large UK teaching hospital concluded that MAS may be a better predictor of management outcome compared to SF36v2 for HMB.²⁸

Limitation of the present study

Small sample size and loss of long term follow up for efficacy and safety, minimal dose protocol.

Further recommendations:

Large sample size of prolonged duration and a double blind study, further studies can be carried out with higher dosage for better results. Phase III clinical trials can be carried out to confirm the efficacy and potency of the research drugs.

V. Conclusion

This study confirms the efficacy of *Qurse gulnar* in heavy menstrual bleeding. Significant reduction in both primary outcome measure (PBAC score) and secondary outcome measure (MAUS score) were observed with p-value < 0.001 in both groups. The intergroup comparison showed no significant difference in outcome measures after treatment with p-value > 0.05; suggesting that *Qurse gulnar* is as effective as tranexamic acid in the management of heavy menstrual bleeding; and hence can be used as an alternate in the management of HMB.

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