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Systematic Review

Systemic review through published clinical trials of artavakshaya

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ABSTRACT

Menstrual irregularity is one of the most frequent gynaecologic disorders among women in reproductive age. In modern science, the treatment is based on mostly hormone therapy. Due to the need of an era for alternative medicine in field of gynecology, present study was tried to overview oral medicine used to treat Artavakshaya according Ayurveda classics. This systematic review was designed in order to gather information regarding oral medications for Artavakshaya in Ayurveda. This study had several steps as searching only randomised clinical trials in Ayurveda medicine literature, extracting them and finding evidences. To search Ayurveda medicine digital library was used, which includes several ancient traditional medical references. There quire data was gathered using data base such as Google scholar, PubMed, Dhara, Medknow, OMICS, Scopus, J-gate for knowledge. This paper explores different research articles related reviews and overall analysis about oral therapy which can be applied in the treatment of Artavakshaya.

Keywords: Ayurveda, Artavakshaya, Systemic review

INTRODUCTION

Over centuries the subject of menstruation has remained in the darkness of mysteries and many supersistions have prevailed through out the world. The term menstruation is derived from the Latin word "menstrus" - it means monthly. Menstruation is one of the most important changes during adolescent years. It occurs once a month as a regular rhythmic period and remains as a normal physiological phenomenon from menarche to menopause. Menstrual disorders are frequent among adolescent girls as they are closely coupled with the processes involved in the pubertal development of females.

According to Ayurveda, normal menstruation is the prime indicator of healthy and normal reproductive system, in which inter menstrual period is one month, duration of blood flow is five days (differ according to different opinion of Acharya) but not associated with pain or burning sensation.[1] The heavy menses and scanty menses are abnormal menstrual pattern, both in amount and duration. They are associated with symptom of pain in lower abdomen or back and can be counted as Vataja rajodushti.[2,3]

If the flow of manstruation is very less then can be corelated with Kshinartava and irregular, delayed with scanty menses will be taken as Artavakshaya in Ayurveda classics.[4] It may be either due to diminished quality of Rasa dhatu, Rakta Dhatu, Upadhatu (Raja/ Artava) or nutritional deficiency or hormonal deficiency. It can be corelated with oligomenorrhoea or hypomenorrhoea described in modern science. Acharya Susruta has described Artava kshaya as Lakshana, not a diseases.[5] Vata dosha is prime factor to generate all the gynecological disorders. Reproductive system is an under Apana Vata

infulence. Also, Artava is Upadhatu of Rasa and Rakta.[6] So, it is condition of Rasa and Raktakshaya due to vitiation of Vatadosha.[7] So, the treatment should be Agnivardhaka,Vatanuloama, Rasapachaka and Artavajanana.[8]

Oligomenorrhea and amenorrhea are one of the most common gynecologic complaints among women in reproductive age. The prevalence of oligomenorrhea is 13.5 percent in the general population. A polycystic ovarian disease accounts for 4 to 10 percent of oligomenorrhea in women of reproductive age (from puberty to menopause).[9]

Cycles which include long menstrual cycles and absence of menstruation, respectively.[10] Hormonal therapy based on estrogen and progesterone compounds is the mainstay of the treatment for these conditions.[11]

The present-day life style and stress may be the reason for causing all menstrual problems. Lifestyle modification or correction is the primary and utmost intervention for prevention and treatment of such menstrual diseases. However, if in three to six months of efforts at remedying risk factors prove insufficient, and then drug treatment is frequently required.

The varieties of medicinal treatment options are available to treat Artavakshaya (hypomenorrhea). Many females don't like or are not willing to take drugs. Few don't afford cost of treatment. Modern medical science gives hormonal treatment for menstrual disorders in adolescence which has many side effects if continued for long time. So, in contemporary era it is very important to provide a particular etiopathology and treatment for "Artavakshaya". Ayurveda medicine has proposed many different medicinal plants for treatment of Artavakshaya. Therefore, aim of this article is to provide an evidence base overview of the effectiveness of diffrenet ayurvedic treatment interventions to treat Artavakshaya.

METHODS

Study design

A systemic review on clinical trials of Artavakshaya was conducted between August 2021 to June 2022 and according to predefined guideline provided by PRISMA.[12]

Criteria for selection of studies

All analysis was based on previous published studies. Randomized clinical study published on Artavakshaya/ oligomenorrhea/hypomenorrhea in Ayurveda were included only.

Trials were excluded if they were observational studies, case report, case series, survey study, pilot study, reviews article, article published in souvenir and newsletter or route of drug administration were changed other than oral route.

Inclusion criteria

Studies which had concluded statistical analysis of treatment outcome on subjective parameters like interval of menstruation, duration of menstruation and amount of menstruation for 12 weeks along with their p values. Study includes those in which the target population, which consist patients undergoing Artavakshaya, the intervention was mostly 'oral medicine'.

Exclusion criteria

Studies which had not stated statistical analysis of treatment outcome on subjective parameters like interval of menstruation, duration of menstruation and amount of menstruation for 12 weeks.

Also, which have not reported p values of results were not included. Studies which had included different type of treatment modalities like Nasya, Matrabasti, Anuvasana basti, Niruha basti, Uttarabasti, and Yoga asana were excluded.

Data extraction

The literature search initially yielded 15 article relevant trials, which was compiled from search engines Google scholar (N=71), PubMed (N=8), Dhara (N=1), J-gate (N=4), Medknow (N=1), Scopus (N=0) by searched keywords through Artavakshaya, oligomenorrhea and hypomenorrhea in Ayurveda given in Figure 1.

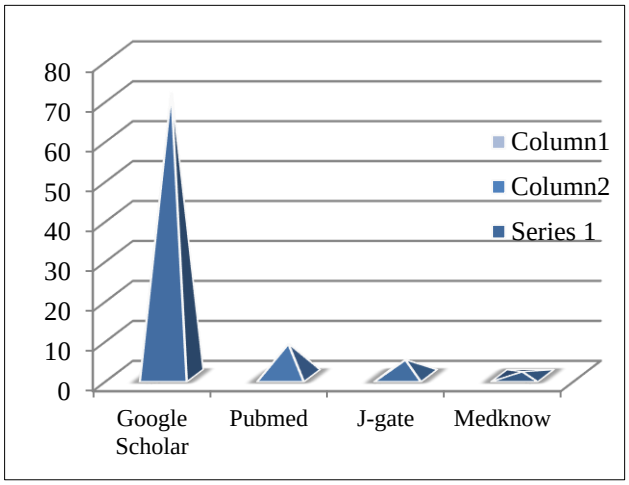

Figure 1: Data extraction from scientific database.

All the databases were searched by 1 independent investigator (M), which was last updated 21 June 2022.

Reference lists of all the selected articles were hand searched for any additional trial (Figure 2).

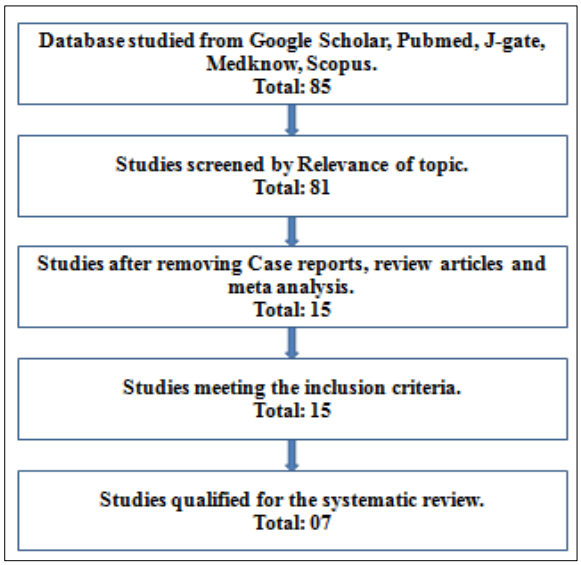

Figure 2: PRISMA flow diagram of included articles.

Most articles were the review article as well as case reports. 4 articles were excluded from this study as duplicate article. By reading the titles and abstracts of these 15, we excluded 8 articles because they did not fulfill the inclusion criteria for this study. By reading the full text of the 7 remaining articles only.

Foremost, 7 prospective ethically permitted clinical trial on Artavakshaya by Ayurveda treatment interventions. They all were open labeled and comparative RCTs trials in Ayurveda have been done or published on *Artavakshaya* till now.

RESULTS

We were tabulated and summarized focusing particulars, study design, intervention protocol, sample size, duration of follow up, outcome measurement. We were introduced the characteristics of the 7 included trails as in stated in Table 1.

Table 1: Studies included in the review, their description, statistical analysis along with p values.

Study	Study description	Statistical analysis	P value		
			Inte-rval	Dura-tion	Quant-ity
Shayan et al[13]	In this study, a clinical trial on 120 women with PCOS, who had oligomenorrhea, referring to a gynaecology OPD Fatemieh, Hamadan city, Iran, 2015. Patients meeting the requirements of the study were randomly (permuted block randomization) divided into two groups, 60 participants in each group: group A, patients taking Agnugol (each tablet OD contains 3.2-4.8 mg of chasteberry dry extract), and group B, patients taking metformin (500 mg-1 tablet TDS) for 3 months. 80% of the Agnugol- and 71.7% of the metformin-taking groups reported menstruation intervals of >45 days before the intervention. In the Agnugol- group, 65%, and in the metformin-taking group, 63.3% of women reported the length of their cycles 3-7 days prior to the intervention	Both groups showed a decreasing menstrual cycle interval from the beginning of the first to the end of the third month of drug administration. Intervals in the Agnugol group and metformin group were 28.83±1.85 and 28.66±1.31 at the end of the third month respectively showing a decrease in menstrual interval after 3 months of treatment. Also, the menstrual length increased after taking Agnugol and metformin, from an average of 5 to 6 days. The average number of pads used during menstruation increased from seven at the end of the first month and to 11 and 12 at the end of the second and thirds months in both groups. Analyzing within-subject effects of variables at time 1 (first month), time 2 (second month), and time 3 (third month) proved a significant interaction effect between the time variable and other variables in the groups ($p<0.005$)	0.571	0.885	0.210
	87% of the metformin-taking patients reported side effects such as loss of appetite, nausea, vomiting, bloating, excessive intestinal gas, diarrhea, fatigue, and stomach ache, while no such side effects were reported by the Agnugol-taking group				
Bediskar et al[14]	A randomized control clinical trial was carried out on 60 patients having complaints of irregular, scanty and painful menstruation registered from	The results were highly significant in both groups. Where the interval in between two cycle is concerned, 47.29%	<0.05	<0.05	<0.05

Continued.

Study	Study description	Statistical analysis	P value		
			Inte-rval	Dura-tion	Quant-ity
	OPD of CSMSS Ayurveda Rugnalaya and Research Centre, Aurangabad. Divided into 2 groups. They were administrated Shatapuspa and Shatavari churna (group A) and OC pill (group B) for three months in a dose of 5 g daily with cow Ghrita and Guda; OC pills (Mala N) once in a day as per standard schedule. Before treatment, mean for interval between 2 cycles is 2.36 and 1.90 in group A and group B respectively. Also, for duration of menstrual cycle, mean was 2.96 in both the groups before treatment. Before treatment, mean for quantity of menses was 1.8 and 2.50 in group A and group B respectively	reduction was seen in group A and 60.81% reduction was seen in group B. Where the amount of menstrual blood is concerned 80% relief was seen in group A while 62% relief was seen in group B. Where the duration of menstrual cycle is concerned 95.76 % increment was seen in group A and 81.05% increment was seen in group B. Shatapushpa shatavari churna is proved to be relatively better than O.C. pills in relieving the symptoms Yoni Vedana and Aratava strava pramana, whereas O.C. pills are proved to be relatively better than Shatapushpa shatavari churna in relieving symptom duration between two Artava darshana			
Devi et al[15]	For the present clinical trial, total 18 clinically diagnosed and confirmed cases of Artavakshaya were registered from OPD/IPD of P.G. Department of Prasuti Tantra-Stri Roga, National Institute of Ayurveda (N.I.A.) Hospital, Jaipur with informed consent. Out of which 15 patients completed the course of trial. Venuparvadi kwatha orally 40 ml with Guda for 60 days/2 consecutive cycles. Before treatment, mean was found 1.400, 1.800 and 2.800 in duration of bleeding, interval between 2 cycles and amount of menstruation respectively	71.42%, 85.16% and 21.42% of change was found in duration of bleeding, interval between 2 cycles and amount of menstruation after treatment. Statistically significant results ($p<0.05$) were found in Agnimandya. Statistically non-significant results ($p>0.05$) were found in Adhmana, Vibandha, Katishula, Anindra, Aruchi, Alasya, Medovriddhi and Angamard. Statistically extremely significant result ($p<0.001$) was found in erythrocyte sedimentation rate. No adverse effect or complications are produced with the use of this treatment	<0.01	<0.001	<0.01
Ghose et al[16]	A clinical trial was carried out on 30 Artavakshaya patients aged between 15- and 35-years having complaints of irregular, scanty and painful menstruations. The patients were registered from OPD and IPD of Gopabandhu Ayurveda Mahavidyalaya, Puri. They were administrated Shatapuspa churna for three months in a dose of 5 g twice daily with cow Grita. Before trail, mean of irregular of menstrual cycle, painful menses and scanty menses were 21.86, 2.73 and 9.3 respectively	It is concluded that the study discloses the effect of Shatapuspa churna on irregularity of interval of menstruation (90.47%), duration of menstruation (79.37%), amount of blood flow (90.00%) which was highly significant in clinical study. Pain in lower abdomen and back were also observed in 90% and 57% respectively, but statistically result was not satisfactory. There was an increase in Hb g% in all the cases. No untoward side effect was noticed during clinical trial	<0.01	<0.01	<0.001

Continued.

Study	Study description	Statistical analysis	P value		
			Inte-rval	Dura-tion	Quant-ity
Rathod et al[17]	This study was a randomized open labelled, three arm, comparative clinical trial among 37 subjects fulfilling criteria of diagnosis and inclusion allocated as Gp K (n=10) (Kanashatahwadi kashaya granules, 2 cap TDS Before food) and Gp P (n=10) as capsule Pconidd 2 cap. TDS BF and combined Gp C (n=10) TDS BF for a duration of 3 months with 7 drop outs. Objective was to evaluate effect of trial drugs on reduction of cyst, decrease of ovarian volume and regularization of menstrual cycle. Before treatment, 100% patients were having irregular cycles	After treatment, capsule Kanashatahwadi individually was found statistically significant in normalizing duration (45.5%), interval of menstrual cycle (63.7%), improving the quantity of menstruation (81.8%) and in reducing ovarian volume (57.3%). Capsule Pconidd individually was found statistically significant in regularizing menstrual cycle (44.8%) and improving the quantity of menstruation (55.0%), reducing ovarian volume (53.8%) and number of cysts (61.7%). Both the drugs had significant result in regularizing menstrual cycle (61.2%), reducing ovarian volume (50.1%) and number of cyst (55.4%). Thus, both the drugs either individually or in combination were highly effective in relieving Artavakshaya lakshana of PCOD	0.024	0.029	0.021
Bharathi et al[18]	This study carried out in 52 numbers of teenage girls, who are having h/o oligomenorrhoea are recruited into the study strictly according to the selection criteria and drawn from the OPD of A.L. Research Centre for Ayurveda, VHS medical campus, Chennai, after thorough clinical examination and investigation. Study carried out between 2004 and 2008. Out of 52 cases, three cases were dropped out from the study due to irregular follow-up. They were given *Kanchanara guggulu*- 1 g BD along with hot water, *Varunadi kashayam*-10 ml BD with equal water and Ashokarishtam -20 ml BD internally along with equal water for three months. Before treatment, mean and SD of efficacy of trail drug on over all parameters were 98.28 and±14.85 respectively	After treatment, mean and SD of efficacy of trail drug on over all parameters were 31.71 and ±26.84 respectively. Study carried out in 52 number of cases; of which 21 (42.86%) patients have shown good response, 10 (20.41%) cases have shown fair response, 03 (06.12%) cases have shown poor response, 15 (32.61%) did not show any response and 03 cases were dropped out from the study. On statistical analysis, efficacy of the trial drugs is found highly significant in all parameters	<0.001	<0.001	<0.001
Khandale et al[19]	The clinical trial was carried out at Government Ayurveda College, Nanded (M.S.) on 80 patients of Artavakshaya in two groups. In experimental group 100 mg of Krishnabola powder was given orally with lukewarm water before meal twice a day to 40 patients and in control group placebo (Indian arrow root powder) was administered for three	After intervention, Krishnabola increased the amount of menstrual blood (72%), period of menstruation and decreased inter menstrual period (69%) as well as incidences of dysmenorrhoea (66%). Krishnabola improved the functions of Apana vayu. Being	<0.01	<0.01	<0.01

Continued.

Study	Study description	Statistical analysis	P value		
			Inte-rval	Dura-tion	Quant-ity
	consecutive menstrual cycles. Then the effect on functions of Apana vayu and duration of menstrual period, inter menstrual cycle period, amount of menstrual blood was observed	emmenagogue, Krishnabola increased amount of menstrual blood, duration of menstruation and decreased inter menstrual period significantly. Statistical Z test showed significant results			

DISCUSSION

Artavakshaya is condition where less volume of menstruation and prolonged interval between two menstrual cycles associated with pain during menstruation. It is condition where Vata and Kapha dosha anubandha. The Samprapti of Artavakshaya involves two mechanisms. These are Dhatukshayajanya and Margaavarodhajanya, which are seen in mostly lean and obese patients respectively. Also, as per Srotodushti types, Sanga or Vimargagamana process can be compared in this condition. So, as per patients, we should treat her with Vatanulomana, Agnidiapana, Rasapachaka, Artavajanana and Artavapravartaka oral medicines.

In above gathered literature review, various types of oral medicines like Shatapushpa choorna, Shatavari-Shatapushpa choorna, Venuparvadi Kashaya, Kanasatahadi kashaya, Pconidd capsule, Kanchanara Guggulu, Varunadi kashaya, Ashokarishta, Krishnabola powder have been taken for study to evaluate their effect over Artavakshaya.[14-17,19] As per Rasapanchaka of drug and Nidanapanchaka of patient, prognosis can be drawn. It is not necessary that all medicine must affect this condition well. The literature review of existing RCT, control trial, single arm study, comparative studies reveal that different types of oral treatment modalities result in improvement of clinical outcome measures of interval of menstruation, duration of menstruation and pain throughout menstruation period, ovarian volume, ovarian cyst, Hb%, and hormonal essay.

Limitations

Our systemic review has some limitations. Due to the limited number of included trials, it might some clinical trials left. We included different type of treatment modalities like Nasya, Matrabasti, Anuvasana basti, Niruha basti, Uttarabasti, Yoga asana, oral Tailapana, and NSAID. Not any particular type of treatment modality we taken or control trial.

Our review was the first to attempts to include all available ayurvedic treatment modalities in prospective evidence comparing to each other's.

CONCLUSION

In nutshell, it can be concluded that there is certain Ayurveda oral medicine is truly useful for the treatment of Artavakshaya effectively. It is clear that the various drugs need to be explore more in the areas of research and studies to develop its more therapeutic and pharmacological properties to promote its more medicinal value in the field of Ayurveda and medical sciences.

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