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REVIEW ARTICLE

Vitex agnus castus for premenstrual syndrome and premenstrual dysphoric disorder: a systematic review

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Abstract The objective of this study was to evaluate whether *Vitex agnus castus* is a safe and effective treatment for PMS and premenstrual dysphoric disorder (PMDD) and to discuss the implications of these findings for clinical practice. A systematic review of literature was conducted using PubMed and Scielo databases. The inclusion criteria were randomized controlled trials (RCT) using *V. agnus castus* in individuals with PMS or PMDD that compared this intervention with placebo or an active comparator and included a description of blinding and dropouts/withdrawals. The search was conducted by two independent investigators who reached consensus on the included trials. A total of eight RCTs were included in this study. Most studies focused on PMS, and the diagnostic criteria of PMS and PMDD changed over the years. Three different preparations of *V. agnus castus* (VAC) were tested, and there was significant variability in the measurement of treatment outcomes between the studies. Nevertheless, all eight studies were positive for VAC in the treatment of PMS or PMDD and VAC was overall well tolerated. Main limitations were differences in definition of diagnostic criteria, the instruments used as main outcome measures, and different preparations of VAC extracts limit the comparison of results between studies. In conclusion, the RCTs using VAC for treatment of PMS/PMDD suggested that the VAC extract is a safe and efficacious alternative to be considered for the treatment of PMS/PMDD symptoms.

Keywords *Vitex agnus castus* · Chasteberry · Premenstrual syndrome · Premenstrual dysphoric disorder · Treatment

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Introduction

The premenstrual period is associated with increased sensitivity to physical symptoms, as well as emotional and behavioral changes (Vigod et al. 2010). Classically, clinical manifestations are cyclic and recurrent, occurring in the late luteal phase of the menstrual cycle and ceasing shortly after the beginning of the menstrual flow (Ryu and Kim 2015). It is estimated that during menacme, approximately 70–85% of women report at least one premenstrual symptom, whereas 20–30% have a history of premenstrual syndrome (PMS) (Vigod et al. 2010; Dueñas et al. 2011). PMS, previously called premenstrual tension syndrome (PMTS), includes physical and psychological manifestations occurring in the late luteal phase of the menstrual cycle, where in most cases, these symptoms do not cause significant impact on women's ability to function (Valadares et al. 2006; Demarque et al. 2013). However, about 2–8% of all women present a severe or more extreme form of PMS, currently known as premenstrual dysphoric disorder (PMDD) (Yonkers et al. 2008). While the PMS and PMDD symptoms are essentially the same, the diagnosis of PMDD is based on marked emotional distress and/or a significant negative impact on the women's function (Vigod et al. 2010; Delara et al. 2012). It is also important to rule out general medical conditions as well as the possibility that the symptoms represent an exacerbation of other psychiatric conditions in premenstrual period. But most importantly, DSM-5 classification requires that the presence and severity of the symptoms are

prospectively confirmed using daily ratings for at least two consecutive menstrual cycles. A "provisional" diagnosis may be made during this period.

Several treatment options are available for the clinical management of PMS and PMDD. Guidelines point out the importance of prioritizing non-pharmacological interventions, such as physical exercise, stress reduction techniques, and/or a healthy diet with low levels of caffeine and alcohol intake. In cases of moderate to severe PMS and PMDD, pharmacotherapy based on the use of antidepressants or ovarian suppression may be indicated (Steiner 2000; Steiner et al. 2006; Panay 2011). In spite of the well-established efficacy of antidepressants (Marjoribanks et al. 2013) and oral contraceptives (Lopez et al. 2009), there is still a need to evaluate treatment options for women who do not benefit from or cannot tolerate these agents (Fisher et al. 2016).

Alternative and complementary medicine have been suggested as potential options in the treatment of PMS and PMDD, including the use of *Vitex agnus castus* (VAC) (Wong et al. 1998; Sarris 2007; Sarris et al. 2011; Melzer et al. 2013). VAC (chasteberry) is a branched shrub whose fruits have several active compounds, including flavonoids, essential oils, diterpenes, and glycosides, with some of these compounds having an effect on hormones, neurotransmitters, the opioid system, and in pain and inflammatory pathways (Jarry et al. 1994; Webster et al. 2006; Choudhary et al. 2009; Webster et al. 2011). Although there is a high demand in the search of nutraceutics or alternative/complimentary medicine for treatment of PMS and PMDD, a critical assessment of the scientific evidence supporting the use VAC is lacking. Therefore, the aim of this study was to conduct a systematic review of randomized controlled trials (RCTs) that tested the effectiveness of *V. agnus castus* in the treatment of PMS and PMDD.

Methods

A systematic review of literature was conducted using PubMed and Scielo databases on Jun 18, 2016. The strategy search was to use the keywords "premenstrual syndrome" OR "premenstrual dysphoric disorder" OR "PMS" OR "PMDD" AND "*Vitex agnus castus*" OR "Vitex" OR "Agnus castus." Results were limited to English, French, Italian, Spanish, and Portuguese languages. Potentially relevant articles from references list of selected studies were also assessed.

The inclusion criteria were RCTs in individuals with PMS or PMDD that compared VAC to either placebo or an active treatment and included a description of blinding and dropouts/withdrawals. We excluded clinical trials that used VAC adjunctive to another treatment intervention, as well as studies that investigated the efficacy of VAC treatment as a secondary outcome.

The search was conducted by two independent investigators (ROC, EL) who reached consensus on the included trials.

Results

The PubMed and ScieLo search strategy identified 29 references. There were no duplicates. The screening of the titles and abstracts identified 11 potentially relevant studies, for which full-text articles were obtained for further evaluation using the established eligibility criteria (See flowchart of the references selection process—Fig. 1). A total of 8 RCTs published between 1997 and 2012 were included in this review (Lauritzen et al. 1997; Schellenberg 2001; Atmaca et al. 2003; He et al. 2009; Ma et al. 2010a, b; Ciotta et al. 2011; Schellenberg et al. 2012; Zamani et al. 2012). Table 1 summarizes the main characteristics of the included studies.

Differences in diagnostic criteria between studies

Six studies investigated patients with PMS (Lauritzen et al. 1997; Schellenberg 2001; He et al. 2009; Ma et al. 2010a, b; Schellenberg et al. 2012; Zamani et al. 2012). Lauritzen et al. (1997) included women who presented with recurrent PMTS symptoms during luteal that were severe enough to affect quality of life. Schellenberg (2001) diagnosed individuals with PMS based on DSM-III-R criteria, as did Schellenberg et al. (2012), with the latter study also requiring that women had a minimal of 30% of worsening in PMS symptoms during the 6 days prior to menstruation compared to days 5–10 of the menstrual cycle. Zamani et al. (2012) based the diagnosis on the DSM-IV criteria, confirmed by a prospective evaluation with an instrument that includes a daily self-assessment of 17 common PMDD symptoms, the Penn Daily Symptom Reports (DSR), for two menstrual cycles prior to the beginning of the study. An increase of ≥ 30% in total premenstrual DSR score compared with postmenstrual was considered. On the other hand, He et al. (2009) and Ma et al. (2010a, b) utilized another self-assessment symptom rating scale, the premenstrual syndrome diary (PMSD), and its sum score of potential patients to diagnose women with moderate to severe PMS. The diagnosis was confirmed by a prospective evaluation before treatment phase. The PMSD scores of the luteal phase had to present an increase of at least 16 points as compared to the follicular phase of the previous 2 cycles prior the start of the study. Both clinical trials using a diagnostic of PMDD had their patients diagnosed according to the DSM-IV criteria (Atmaca et al. 2003; Ciotta et al. 2011); however, it is unclear whether the diagnosis of PMDD was confirmed with prospective daily symptom charting in the study of Ciotta et al. (2011).

VAC preparations and administration

Different preparations were used in these studies. Three different dry extract tablets were utilized in five studies (VAC extract BNO 1095, Ze 440 and Agnolyt©) (Lauritzen et al.

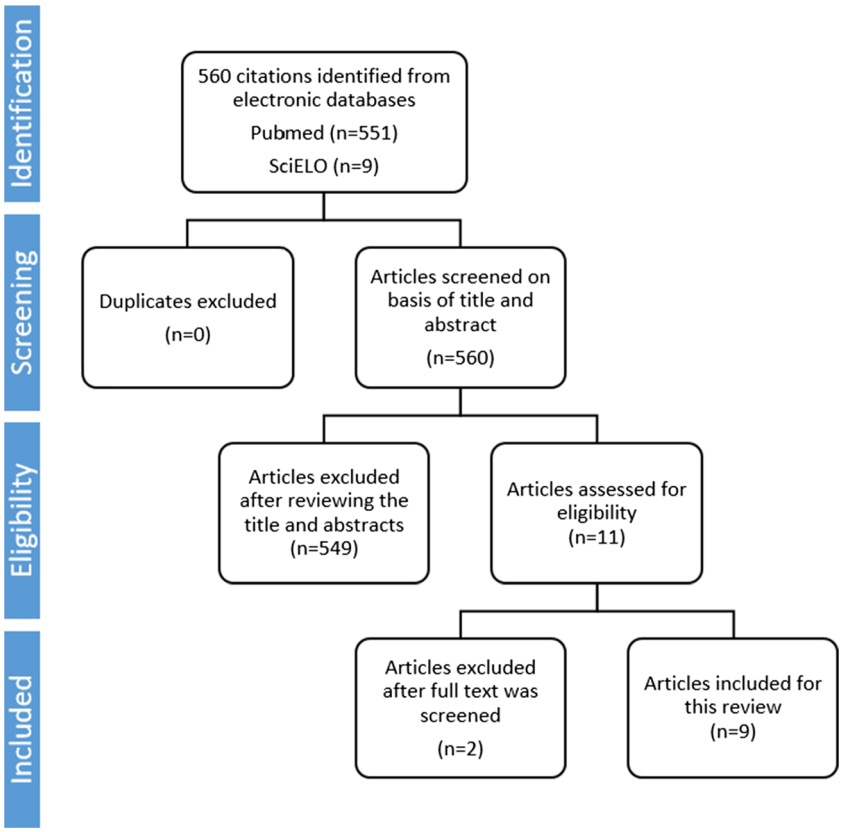

Fig. 1 Systematic review flowchart

1997; Schellenberg 2001; He et al. 2009; Ma et al. 2010a, b; Schellenberg et al. 2012) and one study utilized drops of VAC extract (Zamani et al. 2012), all of them taken orally. Two studies specified doses, but not the preparations nor the route of administration (Atmaca et al. 2003; Ciotta et al. 2011). He et al. (2009) and Ma et al. (2010a, b) administered tablets which contained VAC extract BNO 1095. Each tablet contained 4.0 mg of dried ethanolic (70%) extract of VAC, corresponding to 40 mg of herbal drug, and was taken once daily, orally. Schellenberg (2001) and Schellenberg et al. (2012) used tablets which contained fruit extract Ze 440, a preparation with extract ratio 6–12:1, standardized for casticin. In the first one, the dosage was 20 mg; the following study used three different dosages: 8, 20, and 30 mg. Lauritzen et al. (1997) utilized capsules of Agnolyt©: each one contains 3.5–4.2 mg dried extract of VAC fruit with extract ratio 9.58–11.5:1. Zamani et al. (2012) stated the treatment phase as 40 drops (~ 4.5 mg) of VAC in a glass of fruit juice daily before breakfast. Atmaca et al. (2003) and Ciotta et al. (2011) did not specify the dosages; they only provided the dosages of 40 mg daily and 20–40 mg daily, respectively.

Methods of assessment of efficacy of VAC

Schellenberg (2001) enrolled 178 women with PMS in a prospective, randomized, placebo controlled study for three menstrual cycles, in which 170 women had at least one postbaseline visit in an intention-to-treat analysis. The main outcome measure was change from baseline to endpoint of the sum scores of self-assessed symptoms (irritability, mood alteration, anger, headache, other menstrual symptoms including bloating and breast fullness) rated on a visual analogue scale (VAS). Differences in the mean values of VAS in the VAC and placebo groups were respectively − 128.5 and − 78.1, with a significant superiority of VAC over placebo ($p < 0.001$). Treatment emergent adverse events were reported by four patients in VAC group (acne, multiple abscesses, intermenstrual bleeding, and urticaria) and by three in placebo group (acne, early menstrual period, and gastric upset).

Ma et al. (2010a, b) conducted two studies using a prospective, randomized, double-blind, placebo-controlled design for 3 menstrual cycles with 67 women diagnosed with moderate to severe PMS. The main outcome measure was the percentage of PMSD total score and four symptom factor scores during the luteal phase at the third treatment cycle. In this study, PMS total score in VAC group was significantly lower than that of placebo group ($p = 0.015$) and differences were found especially on negative affect ($p = 0.047$) and water retention ($p = 0.036$). While the percentage of improvement varied from 80.1 to 92.4% in the VAC group, in the placebo group, improvement varied from 48.9 to 73.7%. Only one adverse event (prolonged menstrual period) was reported in the VAC group.

Table 1 Overview on eight RCTs on VAC in PMS and PMDD

tbcolw80ptAuthor, year, and country	tbcolw100ptStudy design	tbcolw50ptCondition	tbcolw30ptNumber	tbcolw95ptIntervention	tbcolw110ptEfficacy results	tbcolw140ptSafety results
VAC vs. placebo						
Schellenberg 2001, Germany	Prospective, randomized, placebo controlled study for three menstrual cycles	PMS	170	VAC extract Ze 440–20 mg 1 tablet daily	VAC group had significant improvement in combined symptoms over placebo group.	Seven women reported mild adverse events (four active; three placebo), none of which caused discontinuation of treatment.
He et al. 2009, China	Prospective, randomized, double-blind for 3 menstrual cycles	Moderate to severe PMS	227	VAC extract BNO 1095–4 mg 1 tablet daily	VAC group had a bigger decrease in severity compared to placebo group	Nineteen adverse events were reported (treatment group 9, 8.5%; and placebo group 10, 9.4%). The most frequently reported adverse effect was headache (treatment group 2 and placebo 2), which may be related to PMS itself. A statistically significant difference was not found in the rate of adverse effect between the two groups. No serious adverse event occurred.
Ma et al. 2010a, b, China	Prospective, randomized, double-blind for 3 menstrual cycles	Moderate to severe PMS	67	VAC extract BNO 1095–4 mg 1 tablet daily	VAC group had a significantly better improvement in PMSD scores than placebo group.	There were no detailed data about side effect rates in the two groups.
Zamani et al. 2012, Iran	Prospective, randomized, double-blind, crossover trial for 6 menstrual cycles	PMS	128	40 drops of VAC in one glass of fruit juice daily Only in the 6 days before menses	The PMS VAS scores decrease was more pronounced in the VAC group than that in placebo group.	There were no detailed data about side effect rates in the two groups.
Schellenberg et al. 2012, Germany	Prospective, randomized, double-blind, placebo-controlled, multicenter for 3 menstrual cycles	PMS	162	VAC extract Ze 440–8, 20, or 30 mg 1 tablet daily	20 mg was considered the optimum dose.	No serious adverse events occurred in the study. In the placebo group, 3 adverse events occurred in 3 patients (no toleration of the study drug in the morning, malaise after the intake, and severe headache). In the 8 mg group, there were 2 adverse events documented in 2 patients (mild headache in the beginning and mild interim spotting). One adverse event (mild hypertension) occurred in a patient of the 20 mg. In the 30 mg group, there occurred 4 adverse events in 4 patients (headache, vaginal fungal infection with severe itching, abdominal bloating, and impure skin).
VAC vs. active comparator						
Lauritzen et al. 1997, Germany	Prospective, randomized, controlled, double-blind, multicenter for 3 menstrual cycles	PMTS	175	VAC extract Agnolyt©—dose 3.5–4.2 mg 1 capsule daily and 1 placebo capsule Pyridoxine HCL-100 mg 2 capsules daily on days 16 to 35 of menstrual cycle and 1 placebo	The mean score reduction in the PMTS scale scores in VAC group was higher than that in pyridoxine group.	Adverse events (gastrointestinal and lower abdominal complaints, skin manifestations, and transitory headache) occurred in 5 patients under B6 and in 12 patients under VAC. Serious adverse events were not observed.

Table 1 (continued)

tbcolw80ptAuthor, year, and country	tbcolw100ptStudy design	tbcolw50ptCondition	tbcolw30ptNumber	tbcolw95ptIntervention	tbcolw110ptEfficacy results	tbcolw140ptSafety results
				capsule between days 1 and 15		
Atmaca et al. 2003, Turkey	Prospective, randomized, single-blind, rater-blinded trial for 8 weeks	PMDD	42	VAC: 20–40 mg/day. Preparation not informed Fluoxetine: 20–40 mg/day	Both groups presented improvement of symptoms. Fluoxetine was more effective for psychological symptoms and VAC extract for physical symptoms.	Adverse events were reported by 17 patients (9 patients from the fluoxetine group and 8 from the VAC group). There was withdrawal from the study in 2 (9.5%) of the fluoxetine group and in 1 (5.0%) of the VAC group. Most frequently experienced side effects in the fluoxetine group were nausea, headache, and insomnia whereas in the VAC group, they were nausea and headache. In the fluoxetine group, two patients experienced sexual dysfunction.
Ciotta et al. 2011, Italy	Prospective, randomized, double-blind for 2 months	PMDD	57	VAC 40 mg/day Fluoxetine: 20 mg/day	Improvement of symptoms was observed in both groups. Fluoxetine had a significant superiority over VAC group.	Rates of side effects in both groups were not described.

Zamani et al. (2012) conducted a randomized, placebo-controlled, double-blind, cross-over trial for six menstrual cycles. This study included 128 patients with PMS. To measure treatment efficacy, they used mean ranks of VAC and placebo groups obtained from changes in variables before and after the study. The PMS VAS scores decreased in both groups, but the improvement was greater in the VAC group ($p < 0.0001$). None of the participants reported adverse effects.

He et al. (2009) conducted a prospective, double-blind, placebo controlled, parallel group, multicenter trial during 3 menstrual cycles with 227 women suffering from moderate to severe PMS. Data from 208 individuals were included in the full analysis set (FAS), and 202 finished treatment phase and their data were analyzed in the per-protocol set (PPS).

The main outcome measure was change in the mean total PMSD scores from baseline to end point. In FAS, the improvements from baseline to the end of the third cycle were 29.23 to 6.41 in the VAC and 28.14 to 12.64 in the placebo group, with superiority of VAC treatment compared to placebo. Results of PPS were similar to FAS. Nineteen adverse events were reported, 9 in treatment group and 10 in placebo group. The most frequently reported adverse effect was headache and occurred in both VAC ($n = 2$) and placebo groups ($n = 2$).

Schellenberg et al. (2012) conducted a prospective, double-blind, placebo-controlled, randomized, multicenter trial for three menstrual cycles. A total of 162 women with PMS were randomized to placebo ($n = 40$), 8 mg Ze 440 ($n = 42$), 20 mg Ze 440 ($n = 41$), and 30 mg Ze 440 ($n = 39$). Of these, 142 completed an intention-to-treat (ITT) analysis. The main outcome measure was change from baseline to endpoint in the total symptom score (TSS) based in a self-reported VAS of 6 symptoms (irritability, mood alteration, anger, headache, bloating, and breast fullness). Both 20 and 30 mg were more efficacious than placebo and 8 mg, with no significant differences between 20 and 30 mg. No serious adverse events were reported, and a total of 10 adverse events occurred in the following groups: placebo group ($n = 3$, including no toleration of the study drug in the morning, malaise, and severe headache), 8 mg group ($n = 2$, mild headache and mild spotting), 20 mg group ($n = 1$, mild hypertension), and 30 mg group ($n = 4$, headache, vaginal fungal infection, abdominal bloating, and impure skin).

Efficacy of VAC versus active comparators

Three studies compared the efficacy of VAC with active comparators: two of them against fluoxetine and one against pyridoxine. Atmaca et al. (2003) conducted an 8-week, randomized, single-blind, rater-blinded, prospective, and parallel-group trial of VAC versus fluoxetine 20–40 mg daily in 42 women with PMDD. Treatment efficacy was evaluated with three main outcome measures: premenstrual scores from the DSR, Hamilton Depression Rating Scale (HAM-D), and

Clinical Global Impression—Severity scale (CGI-S). At endpoint, there was no significant difference from baseline to endpoint between VAC and fluoxetine 20–40 mg on DSR, CGI-S or HAM-D (all $p > 0.05$). Adverse events were reported by 17 patients, 8 from VAC group, and 9 from fluoxetine group. In the fluoxetine group, the most frequent side effects were nausea ($n = 6$), headache ($n = 4$), and insomnia ($n = 3$) whereas in the VAC group, nausea ($n = 5$) and headache ($n = 4$). Sexual dysfunction ($n = 2$) were experienced only in the fluoxetine group. A major limitation of this study was that the treating physicians were aware of the prescription, which could have influenced the outcomes.

Ciotta et al. (2011) conducted a 2-month, randomized, double-blind trial with 57 women with PMDD: 26 received fluoxetine 20–40 mg daily and 31 received VAC 40 mg daily. Four of 21 symptoms assessed by HAM-D considered typical manifestations of PMDD were evaluated to compare the efficacy of VAC against fluoxetine: depressed mood, psychic anxiety, loss of interest, and impairments in work general physical symptoms. There was a significant superiority of fluoxetine compared to VAC group over dysphoric symptomatology ($p < 0.02$), loss of interests and impairment in activities ($p < 0.05$), psychic anxiety ($p < 0.003$), and general physical symptoms ($p < 0.05$). None of the patients reported adverse events.

Lauritzen et al. (1997) conducted a multicenter, randomized, double-blind controlled trial with 175 women with PMTS: 85 were given VAC and 90 were given pyridoxine 200 mg on days 16 to 35 of menstrual cycle plus a placebo capsule from days 1 to 15. The efficacy was assessed by PMTS scale modified by Steiner et al. (1980). Primary outcome measure was change of sum scores in PMTS scale after treatment phase during three menstrual cycles. Intent-to-treat analysis showed a significant difference between the treatments favoring VAC ($p = 0.0377$). The patients (36.1%) in the VAC group were free from adverse events against 21.1% in the pyridoxine group. While skin reactions ($n = 2$) and transient headache ($n = 1$) were reported in VAC group, gastrointestinal disturbances were similar in frequency in both study groups. Therefore, this study supported a higher efficacy of VAC compared to pyridoxine.

Discussion

This systematic review of RCTs investigating the effectiveness of VAC in the treatment of PMS/PMDD supports the clinical use of VAC for treatment of PMS/PMDD. To our knowledge, this is the first review focusing on the use of VAC to treat PMS or PMDD.

Most studies used prospective symptom charting in the diagnosis of PMS/PMSS, in line with DSM criteria. The study by Lauritzen et al. (1997) was the only one focused on PMTS, an old terminology of premenstrual disorders, and their methods for screening, diagnosis, and inclusion of study participants were unclear whether it was conducted with retrospective or prospective evaluation, as well as which symptoms were taken into account. In all placebo-controlled trials, VAC extract was superior than placebo. In addition, VAC extract was more efficacious than pyridoxine in the alleviation of PMS symptoms, whereas fluoxetine was superior than VAC in the alleviation of the psychological symptoms of PMS. VAC was generally very well tolerated, with most side effects being mild and transient. Dosage and timing of administration of VAC were better described in more recent trials: Schellenberg et al. (2012) found that 20 mg was the optimum dosage, and Zamani et al. (2012) showed that the use of VAC extract only during the 6 days prior to menses was efficacious and superior to placebo. These two trials provided critical data to inform the rational of dose selection and the possibility of cyclical VAC extract administration. Trials comparing fluoxetine with VAC suggested that fluoxetine was more effective for psychological symptoms (Atmaca et al. 2003; Ciotta et al. 2011). These results are in line with extensive literature showing efficacy of selective serotonin reuptake inhibitors in the treatment of PMS/PMDD (Marjoribanks et al. 2013). These results also open a possibility for future research of adjunctive psychotherapy along VAC extract in the treatment of PMS/PMDD.

The findings summarized in this systematic review need to be interpreted in view of the study limitations. The RCTs have several differences in terms of diagnostic criteria, instruments used as main outcomes, and different preparations of VAC. For instance, some studies followed the DSM criteria, while others defined the groups solely based on daily symptom questionnaires, and in some diagnosis, the diagnosis of PMS/PMDD was "clinical." Here it is worth mentioning that to date, there is not a standardization of instruments used to monitor the premenstrual symptoms longitudinally. These approaches can lead to inclusion of patients with similar symptom clusters, but not necessarily individuals with the same underlying pathophysiological process and/or response to treatment. Also, the various types of VAC extracts and overall lack of information used in different studies limit the comparison of studies, since even small differences in strength and pharmacokinetic profile of these drugs can substantially affect treatment response. Future clinical trials should strictly follow the DSM-5 criteria for study eligibility, clearly describe the type and dosage/strength of VAC extract, and use prospective premenstrual symptom charting for a minimal of three menstrual cycles. Finally, considering that the length of treatment in the majority of studies were two to three menstrual cycles, future studies should also evaluate the longer term efficacy of VAC in women who respond to short-term VAC treatment.

In conclusion, despite the abovementioned limitations, available RCTs support the short-term use of VAC extracts in the treatment of PMS/PMDD. The studies suggest that the

use of VAC extract is a safe and valid alternative to be considered for the treatment of PMS/PMDD symptoms, particularly in the alleviation of somatic PMS symptoms. Longer studies (more than just a few cycles) are important to evaluate the safety and efficacy of VAC in the long term.

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Compliance with ethical standards This study did not involved research with human beings and did not require ethical approval and informed consent.

Conflict of interest The authors declare that they have no conflict of interest.

References

Atmaca M1, Kumru S, Tezcan E (2003) Fluoxetine versus Vitex agnus castus extract in the treatment of premenstrual dysphoric disorder. Hum Psychopharmacol 18(3):191–195

Choudhary MI, Azizuddin JS et al (2009) Antiinflammatory and lipoxygenase inhibitory compounds from Vitex agnus-castus. Phyther Res 23:1336–1339

Ciotta L1, Pagano I, Stracquadanio M, Di Leo S, Andò A, Formuso C (2011) Psychic aspects of the premenstrual dysphoric disorders. New therapeutic strategies: our experience with Vitex agnus castus. Minerva Ginecol 63:237–245

Delara M, Ghofranipour F, Azadfallah P et al (2012) Health related quality of life among adolescents with premenstrual disorders: a cross sectional study. Health Qual Life Outcomes 10:1

Demarque R, Rennó J Jr, Ribeiro HL et al (2013) Premenstrual dysphoric disorder: brief review. Rev Debates em Psiquiatr 5:6–11

Dueñas JL, Lete I, Bermejo R et al (2011) Prevalence of premenstrual syndrome and premenstrual dysphoric disorder in a representative cohort of Spanish women of fertile age. Eur J Obstet Gynecol Reprod Biol 156:72–77

Fisher C, Adams J, Hickman L, Sibbritt D (2016) The use of complementary and alternative medicine by 7427 Australian women with cyclic perimenstrual pain and discomfort: a cross-sectional study. BMC Complement Altern Med 16:129

He Z, Chen R, Zhou Y, Geng L, Zhang Z, Chen S, Yao Y, Lu J, Lin S (2009) Treatment for premenstrual syndrome with Vitex agnus castus: a prospective, randomized, multi-center placebo controlled study in China. Maturitas 63(1):99–103

Jarry H, Leonhardt S, Gorkow CH, Wuttke W (1994) In vitro prolactin but not LH and FSH release is inhibited by compounds in extracts of Agnus castus: direct evidence for a dopaminergic principle by the dopamine receptor assay. Exp Clin Endocrinol Diabetes 102:448–454

Lauritzen C, Reuter HD, Repges R, Böhnert KJ, Schmidt U (1997) Treatment of premenstrual tension syndrome with Vitex agnus castus controlled, double-blind study versus pyridoxine. Phytomedicine 4(3):183–9

Lopez LM, A a K, Helmerhorst FM (2009) Oral contraceptives containing drospirenone for premenstrual syndrome. Cochrane Database of Systematic Reviews: 13 reviews. Cochrane Database Syst Rev 2009(2)

Ma L, Lin S, Chen R, Wang X (2010a) Treatment of moderate to severe premenstrual syndrome with Vitex agnus castus (BNO 1095) in Chinese women. Gynecol Endocrinol 26(8):612–616

Ma L, Lin S, Chen R, Zhang Y, Chen F, Wang X (2010b) Evaluating therapeutic effect in symptoms of moderateto-severe premenstrual syndrome with Vitexagnus castus (BNO 1095) in Chinese women. Aust N Z J Obstet Gynaecol 50(2):189–193

Marjoribanks J, Brown J, O'Brien PMS, Wyatt K (2013) Selective serotonin reuptake inhibitors for premenstrual syndrome. Cochrane Database Syst Rev 6:CD001396

Melzer J, Deter H-C, Uehleke B (2013) CAM in psychiatry

Panay N (2011) Management of premenstrual syndrome: evidence-based guidelines. Obstet Gynaecol Reprod Med 21:221–228

Ryu A, Kim T-H (2015) Premenstrual syndrome: a mini review. Maturitas 82:436–440

Sarris J (2007) Herbal medicines in the treatment of psychiatric disorders: a systematic review. Phytother Res 21:703–716

Sarris J, Panossian A, Schweitzer I et al (2011) Herbal medicine for depression, anxiety and insomnia: a review of psychopharmacology and clinical evidence. Eur Neuropsychopharmacol 21:841–860

Schellenberg R (2001) Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebo controlled study. BMJ 322:134–137

Schellenberg R, Zimmermann C, Drewe J, Hoexter G, Zahner C (2012) Dose-dependent efficacy of the Vitex agnus castus extract Ze 440 in patients suffering from premenstrual syndrome. Phytomedicine 19(14):1325–1331

Steiner M (2000) Premenstrual syndrome and premenstrual dysphoric disorder: guidelines for management. J Psychiatry Neurosci 25: 459–468

Steiner M, Pearlstein T, Cohen LS et al (2006) Expert guidelines for the treatment of severe PMS, PMDD, and comorbidities: the role of SSRIs. J Women's Health (Larchmt) 15:57–69

Valadares GC, Ferreira LV, Filho HC, Romano-Silva MA (2006) Premenstrual dysphoric disorder review—concept, history, epidemiology and etiology. Rev Psiquiatr Clin 33:117–123

Vigod SN, Frey BN, Soares CN, Steiner M (2010) Approach to premenstrual dysphoria for the mental health practitioner. Psychiatr Clin N Am 33:257–272

Webster DE, Lu J, Chen SN et al (2006) Activation of the μ-opiate receptor by Vitex agnus-castus methanol extracts: implication for its use in PMS. J Ethnopharmacol 106:216–221

Webster DE, He Y, Chen SN et al (2011) Opioidergic mechanisms underlying the actions of Vitex agnus-castus L. Biochem Pharmacol 81:170–177

Wong AH, Smith M, Boon HS (1998) Herbal remedies in psychiatric practice. Arch Gen Psychiatry 55:1033–1044

Yonkers KA, O'Brien PMS, Eriksson E (2008) Premenstrual syndrome. Lancet 371:1200–1210

Zamani M1, Neghab N, Torabian S (2012) Therapeutic effect of Vitex agnus castus in patients with premenstrual syndrome. Acta Med Iran 50(2):101–6