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Case Report

An Integrative Approach for Improving and Managing Premenstrual Syndrome (PMS) and Premenstrual Dysphoric Disorder (PMDD): A Case Report

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Abstract

Premenstrual syndrome (PMS) describes symptoms a woman experiences in the luteal phase of menstruation, including physical, emotional, and/or behavioral changes ranging from mild to severe. Premenstrual dysphoric disorder (PMDD) shares defining emotional and behavioral attributes with PMS, though it is the most severe form classified as a depressive disorder. Women are increasingly interested in seeking natural or alternative therapies to address these conditions. The purpose of this case report is to share the experience of one woman who had improvements in premenstrual headaches, menstrual cramping and flow, and intense psychiatric symptoms associated with a diagnosis of PMDD within three months of using *Lepidium peruvianum* (maca), bio-identical progesterone therapy, and magnesium supplementation. Within four months, normalization of LH levels was achieved. Further, upon reducing or resolving symptoms, she continued to maintain this improvement for three months on *Lepidium peruvianum,* magnesium, and a B-complex. This case also provides clinical utility for personalized care utilizing a combination of natural therapies alongside bioidentical hormone therapy.

Keywords: PMS, PMDD, *Lepidium peruvianum*, Bio-identical progesterone, Magnesium, B vitamins, Case report

Abbreviations:

Bid: twice daily; cap: capsule; caps: capsules; CBC: complete blood count; CMP: comprehensive metabolic panel; DC: discontinue; FSH: follicle-stimulating hormone; GABA: gamma-aminobutyric acid; H: high; HPA: hypothalamus-pituitary-adrenal; LH: luteinizing hormone; LN: low-normal; mcg/L: micrograms per liter; mIU/mL: milli-international units per milliliter; Mg: milligrams; mg/mL: milligrams per milliliter; mm: millimeter; MRI: magnetic resonance imaging; NA: not applicable; nmol/L: nanomoles per liter; ng/mL: nanograms per milliliter; NSAIDs: nonsteroidal anti-inflammatory drugs; PHQ-9: patient health questionnaire-9; PMDD: premenstrual dysphoric disorder; pg/mL: picograms per milliliter; PMS: premenstrual syndrome; qd: once

daily; qhs: bedtime; SR: slow-release; SSRI: selective serotonin reuptake inhibitor; TSH: thyroid stimulating hormone; uIU/mL: micro: international units per milliliter; WNL: within normal limits.

Introduction

Premenstrual syndrome (PMS) describes symptoms a woman experiences in the luteal phase of menstruation, including physical, emotional, and/or behavioral changes ranging from mild to severe [1]. Symptoms include, but are not limited to, headache, fatigue, breast pain, bloating, constipation, irritability, and sadness. Research shows that over 47% of menstruating women experience PMS [2].

Premenstrual dysphoric disorder (PMDD) shares defining emotional and behavioral attributes with PMS, though it is the most severe form and is classified in the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* (DSM-5) under depressive disorders [3]. PMDD is dominated by emotional symptoms, such as depression, anxiety, anger, and irritability, that begin in the luteal phase of the menstrual cycle and, like PMS, will cease upon starting menstruation [1,4]. Often, these symptoms can impair the quality of life for women by impacting various aspects of their social, occupational, or relational functions. The criterion for diagnosing PMDD is detailed in the scientific literature [3].

It is reported that PMDD impacts 3-8 % of menstruating women, and 40-86% of those women reported suicidal ideation [5-7]. Of note, women diagnosed with bipolar disorder have a higher incidence of PMDD, with studies reporting 27-76% of these women are impacted [8].

The exact etiology of PMS and PMDD are not fully understood, though hormonal imbalances (progesterone, estrogen, allopregnanolone, and aldosterone), changes in neurotransmitters (serotonin, GABA, and glutamate), calcium and magnesium deficiencies, inflammation, past traumatic events, genetics, obesity, and smoking are all thought to contribute [3, 9-11].

The current pharmaceutical approach for the management of PMS and PMDD includes NSAIDs, over-the-counter pain relievers, hormonal contraceptives, and antidepressants [12]. While oral contraceptives are commonly prescribed, there has been little evidence of their efficacy for PMDD [3,10,13]. Further, women are increasingly interested in alternative options, including dietary or herbal supplements, nutrition, and other lifestyle changes [14].

The purpose of this case report is to share the experience of one woman who had improvements in premenstrual headaches, menstrual cramping and flow, and intense psychiatric symptoms associated with a diagnosis of PMDD within three months of using *Lepidium peruvianum* (maca), bio-identical progesterone therapy, and magnesium supplementation. Within four months, normalization of LH levels was achieved. Further, upon reducing or resolving symptoms, she continued to maintain this improvement for three months on *Lepidium peruvianum,* magnesium, and a B-complex. To our knowledge, this combination of therapies has not been reported in the scientific literature. The case report was written following the CARE guidelines [15].

Case Presentation - September 27, 2022

A 30-year-old Caucasian woman's primary reason for seeking naturopathic care was to help with ongoing emotional symptoms associated with previously diagnosed premenstrual dysphoric disorder (PMDD). Secondary reasons for the consultation included her desire to reduce premenstrual headaches, fatigue, and heavy menses accompanied by menstrual cramping.

The patient has a medical history of continued lactation three years after cessation of breastfeeding and a history of elevated prolactin levels. These factors led to additional testing and a diagnosis by her endocrinologist of a benign pituitary tumor. Additionally, she reports long-term sleep disturbances with a negative sleep study for apnea. She occasionally uses valerian or melatonin to help with sleep and takes a vitamin D supplement daily. She is currently on no pharmaceutical medications. Her family history includes her mother having a uterine ablation for menorrhagia and her maternal aunt with depressive symptoms during the menstrual cycle.

The patient recalled details of her menstrual history dating back to approximately 16 years old, describing physical symptoms, such as cramping, heavy flow, and mood difficulties the week before her menstrual cycle, namely very intense emotions. Approximately eight years ago, after the birth of her child and subsequent months of breastfeeding, her menses became heavier, and intense mood dysregulation recurred in the days before menses.

At the time of this consultation, she experienced a regular monthly menstrual cycle with menses of five to six days, including fatigue, cramps, a heavy flow during the first two days, and a headache the day before or day one of the menses. The week prior to menses, she experienced negative, ruminating thoughts, including those of suicide. She reported no plans or attempts in her history, though, upon questioning, the clinician discovered that the patient had removed all weapons from her home since the thoughts can feel intrusive at times. Screening questions, as recommended by the American Academy of Family Physicians, revealed no immediate concerns at any time during care.

She met the criteria of PMDD regarding chronicity, duration, timing, the severity of symptoms, and their impact

on her quality of life and daily activities. Symptoms reported include depression, negative, intrusive thoughts, increased irritability affecting relationships at home and work, worsened sleep, exhaustion, and lack of concentration. Additionally, she reports that she does not experience depressive or anxiety-type symptoms at other times of the month, allowing her to function without difficulty. Her medical history is absent of psychiatric diagnoses, other pre-existing medical diagnoses outside of PMDD, or medication use that would be attributed to these symptoms.

Her primary care physician previously offered therapy options to address PMDD, including hydrocodone for cramping and a selective serotonin reuptake inhibitor (SSRI) for moods. The patient declined to take both, wanting to explore natural options to address her symptoms. The previous use of oral contraceptives decreased menstrual cramping and depression but left her feeling "weird, numb, and not myself."

A normal uterine ultrasound was reported.

She reports an average stress level, a supportive social network and spiritual community, engages in moderate exercise, and demonstrates positive health habits such as being a non-smoker and avoiding alcohol and recreational drugs. In the last five years, she transitioned to a vegetarian lifestyle and reports monitoring overall protein intake and variation in food choices. A dietary assessment revealed a low intake of vegetables, frequent intake of convenient vegetarian substitute meats, and suboptimal water intake, averaging 32 ounces daily. These dietary patterns likely contributed to the report of daily but small, hard stools.

A physical exam was not conducted, as the consultation was held virtually.

Based on the initial consultation, therapeutic interventions were provided, as detailed in the Case Report Timeline and Recommendations (Table 1). The recommendations included dietary enhancements such as adequate hydration, increased fiber and cruciferous vegetable intake, and the reduction of xenoestrogens to support hormone balance, for which resources were provided. Supplement recommendations included magnesium to aid in reducing menstrual cramps and a proprietary formulation of *Lepidium peruvianum* (maca) to support hormones. Lastly, labs were ordered to be drawn in the luteal phase of the menstrual cycle.

Relevant Medical History: A 30-year-old female with a medical history of PMDD, benign pituitary tumor, and lactation for three years after cessation of breastfeeding. Normal uterine ultrasound. History of increased prolactin levels. No currently prescribed or over-the-counter medications. Supplements include occasional valerian and melatonin and daily vitamin D. The patient sought naturopathic care to address premenstrual symptoms of extreme mood fluctuation, depression, headache, fatigue, and heavy menses accompanied by menstrual cramping.

	09/27/22	10/24/22	02/06/23	03/09/23	03/23/23	05/04/23	06/01/23	08/03/23
Medications								
Prescribed by treating physician	None	Oral progesterone 100 mg cyclically	Oral progesterone 50 mg-SR nightly	Oral progesterone 50 mg-SR nightly	Oral progesterone 100 mg cyclically	DC	DC	DC
Supplement Recommendations								
FemmenessencePRO Harmony Symphony Natural Health	1 cap qd*	1 cap qd*	1 cap bid	2 caps bid	2 caps bid	2 caps bid	2 caps bid	1 cap bid
Triple Mag Vital Nutrients	500 mg qhs*	500 mg qhs*	500 mg qhs	500 mg qhs	500 mg qhs	500 mg qhs	500 mg qhs	500 mg qhs
B-Complex Vital Nutrients	NA	NA	NA	1 cap qd	1 cap qd	1 cap qd	1 cap qd	1 cap qd
Vitamin D: Continue taking as advised by another prescribing provider.								
Symptoms								

Depression/Emotions	Severe	Severe	Depression only on Day 18 of cycle	Severe after intermittent use of progesterone	Mild sadness on days 18-19 of menstrual cycle	None	Mild irritability	Mild irritability
Headache	Yes	Yes	No	No	No	No	No	No
Menstrual cramping	Yes	Yes	No	No	No	Minimal	No	No
Menstrual flow	Heavy	Heavy	Heavy Day 1 only	Heavy Day 1 only	Moderate	Moderate	Moderate	Moderate
GI Discomfort	N/A	N/A	Gas-like pain and bloating	None	None	None	None	None
Dietary Recommendations								
A whole-food vegetarian diet including: • Two servings of cruciferous vegetables daily • Increase fiber intake to 30 grams per day • Choosing fruits and vegetables according to the Environmental Working Group's "Dirty Dozen/Clean Fifteen" list • 64 ounces of water daily								
Lifestyle Recommendations								
• Reduce xenoestrogen exposure- Resource provided								
*Client began the first week of November 2022								
Abbreviations: cap: capsule; caps: capsules; qd: once daily; bid: twice daily; SR: slow-release; qhs: at bedtime; DC: discontinue; cyclically: day 14-28 of menstrual cycle								
Conclusion of Consultations 1. Normalization of prolactin levels. 2. Reduction of LH levels. 3. Resolution of physical symptoms that included headaches and menstrual cramping. 4. Resolution of extreme emotions, that included negative, ruminating, and suicidal thoughts, experiencing only mild irritability or sadness one day of the menstrual cycle. 5. Decreased menstrual flow.								

Table 1: Case Report Timeline and Recommendations.

Follow-Up Consultation #1 – October 24, 2022

The patient returned for a brief follow-up to review the completed labs (Table 2). Based on the laboratory findings of low-normal progesterone levels on day 21 of the menstrual cycle, along with the previously reported symptoms of severe premenstrual depression, treatment of cyclical bio-identical progesterone therapy was initiated by the clinician (Table 1).

At this time, the patient reported no significant interval change. However, she had increased her water intake but struggled with consuming more vegetables and had not started the maca or magnesium supplements. The clinician reiterated encouragement on dietary interventions, supplement use, and hydration (Table 1).

Interim notes

The patient messaged the clinician after initiating luteal phase progesterone. She reported a reduction in depression, which occurred for two days, compared to previously experiencing this for one week before menses. Further, she reported easier crying and general lability of emotions in the absence of depression. She had not yet purchased *Lepidium peruvianum* or magnesium; therefore, this recommendation was reinforced. The patient began to use these supplements in the first week of November 2022.

Diagnostic Tests from Other Providers				
Ultrasound	2022: Normal			
Sleep Study	2022: Normal			
MRI	2016: The report was unavailable. 2019: A 2.5 mm ventral right-focused lesion was noted. 2022: A new 4 mm left pituitary lesion with slight rightward stalk deviation. The previous right lesion is 'not definitely noted', but right heterogeneity enhancement is present.			
Biomarker	**June 2022[a]**	**October 2022[b]**	**February 2023[a]**	**March 2023[b]**
Prolactin	28 ng/ml (H)	N/A	10 ng/mL (WNL)	N/A
Progesterone	N/A	12.6 ng/mL (LN)	N/A	Lab error, missed on order
FSH	N/A	2.8 mIU/mL* (WNL)	N/A	2.5 mIU/mL (WNL)
LH	N/A	12.0 mIU/mL* (H)	N/A	4.5 mIU/mL (WNL)
CMP	N/A	N/A	N/A	All WNL
TSH	N/A	N/A	N/A	1.310 uIU/mL (WNL)
CBC	N/A	N/A	N/A	All WNL

[a] Ordered by the patient's endocrinologist or primary care physician

[b] Ordered by the treating physician

*Inverted FSH/LH ratio

Abbreviations: CBC: complete blood count; CMP: comprehensive metabolic panel; FSH: follicle-stimulating hormone; H: high; LH: luteinizing hormone; LN: low-normal; mIU/mL: milli-international units per milliliter; mm: millimeter; MRI: magnetic resonance imaging; N/A: not applicable; ng/mL: nanograms per milliliter; TSH: thyroid stimulating hormone; uIU/mL: micro-international units per milliliter; WNL: within normal limits

Table 2: Diagnostic Testing and Biomarkers.

Follow-Up Consultation #2 - February 6, 2023

After two menstrual cycles from the initiation of the combination of progesterone, magnesium, and *Lepidium peruvianum* (November 2022), the patient self-reported having depression only on day 18 of her cycle, with generalized moodiness the week before her menses. Overall, the patient reported "feeling much better" and is experiencing improved sleep on the days she takes progesterone, a common and expected outcome of this therapy.

One week before this visit, the patient messaged the clinician to report that she started experiencing random bouts of abdominal discomfort with intense gas-like pain that kept her up at night. She had an exam at her primary care physician's office, which revealed no abnormal findings. The patient believes this pain is a side effect of the progesterone, which has been reported to cause bloating in some patients. As a result, the clinician decreased progesterone to 50 mg sustained-release capsules nightly and increased *Lepidium peruvianum* to one capsule twice daily (Table 1).

Repeat labs were ordered.

Follow-Up Consultation #3 - March 9, 2023

Messaging occurred between February and March visits regarding the patient's use of progesterone. The patient revealed intermittent use due to 1) her concern about it not helping at the lower dose and 2) the potential side effects of daily use. This intermittent use appears to have caused a subsequent return of the patient's suicidal thoughts during the last menses, making this follow-up visit necessary.

The patient reported feeling more emotional, identifying with a commercial describing depression as 'the dark cloud following her.' These feelings included suicidal thoughts with no plans or ideation. Further assessment utilizing the National Institute of Health Brief Suicide Safety Assessment (BSSA) revealed that additional interventions were not needed at this time. She declined to complete the patient health questionnaire-9 (PHQ-9) during this visit, citing that she "feels fine today" since her menses began the day before this visit.

Further, her cycles continued to be regular, with a heavy flow only on day one, while cramping and headaches have resolved in the last three cycles. Additionally, based on labs drawn by her primary care provider in February, her prolactin level is within the normal range (Table 2).

She happily reported that all gastrointestinal symptoms associated with using progesterone were resolved, and she had fuller, more complete daily bowel movements. She continued to work on consuming more vegetables each day. She also reported that after years of restless sleep, she slept through the night most days of the week with or without progesterone supplementation. However, she continued to use valerian and melatonin one to two nights per week. Despite this improvement in sleep, increased stress from work and an upcoming move for her family has left her with lower energy than she would like.

After the initial slow start of the treatment plan, she reported very good compliance with progesterone, magnesium, and *Lepidium peruvianum* as prescribed.

TThe clinician concluded this visit with encouragement that many symptoms have improved despite this recent emotional flare. An additional recommendation of a methylated B-complex was provided to assist with stress and energy levels. It was reiterated that the low-dose daily progesterone was unlikely to cause side effects and, therefore, should be continued. Moreover, due to the immediacy of the need to help restore moods, the dose of *Lepidium peruvianum* was increased to two capsules twice daily (Table 1).

Follow-Up Consultation # 4 - March 23, 2023

The patient reported doing much better emotionally on the increased dose of *Lepidium peruvianum,* though she noted that she also returned to cyclical progesterone (100 mg days 14-28) on her own volition. She stated she only had mild sadness on days 18-19 of the most recent cycle. She did not have feelings of depression or suicidal thoughts and had not experienced menstrual cramping or headaches. The recommendations at this time included continuing progesterone 100 mg cyclically and continuing all other recommendations previously provided for one more menstrual cycle. At this point, a re-evaluation would occur (Table 1).

During this visit, lab results were also reviewed with the patient (Table 2). Of significance, LH reduced to normal levels, resulting in a normal FSH/LH ratio.

Follow-Up Consultations # 5 – 6: May – June 2023

In May, the patient reported stability from the previous visit and a desire to decrease the interventions since she has experienced fewer physical symptoms, including a lighter menstrual flow, minimal cramping, no headaches, less fatigue, increased energy, and no major depressive symptoms with her menses in the previous two months. The client agreed to discontinue progesterone and continue using *Lepidium peruvianum* at the higher dose of two capsules twice daily. It was discussed and agreed by the patient that she would contact the clinician if any symptoms worsened with this modification.

In June, the patient reported using the daily combination of *Lepidium peruvianum*, magnesium, and B-complex. She continued to have emotional improvements with only two days of mild irritability, no major depressive episodes, and continued resolution of physical symptoms. Therefore, she was advised to continue this protocol for two additional menstrual cycles, and if this stability remained, she could reduce *Lepidium peruvianum* to one capsule twice daily.

Results and Discussion

The patient presented in August 2023 to complete a full reassessment. This visit confirmed drastic improvements in the primary reason for seeking care, including a complete resolution of severe emotional symptoms in the menstrual cycle's luteal phase. She was experiencing a few days of irritability that no longer impacted her relationships or work. She was also relieved of premenstrual headaches and menstrual cramping and had decreased menstrual flow, with further outcomes including more complete bowel movements and improved sleep.

These results were achieved and maintained utilizing a personalized combination of therapies, including *Lepidium peruvianum*, bio-identical progesterone, magnesium, and a B-complex. At the conclusion of this visit, the goal is to maintain hormonal balance and mood stability by continuing *Lepidium peruvianum*, magnesium, and B-complex supplements for two to three more menstrual cycles. After this time, the clinician's goal is to wean the standard dose of *Lepidium peruvianum* to a maintenance dose of one capsule per day and to reassess the ongoing need for magnesium and B-complex supplements. Dietary recommendations remained the same.

Background and strength of the therapies recommended

The clinician selected evidence-informed therapies that have been used historically in naturopathic care and have been clinically useful for over 15 years with success.

Progesterone therapy was originally prescribed during this patient's luteal phase of the menstrual cycle, with a modification to nightly use before it was eventually discontinued. Evidence suggests that progesterone fluctuations are a factor in PMDD, as it influences emotion processing [16]. While still under investigation for use in PMDD, oral micronized progesterone can influence GABA receptors and induce a calming effect upon its conversion to allopregnanolone during first-pass metabolism. Despite

conflicting data as to the value of progesterone in premenstrual mood management, there is data to support the use of bio-identical, oral micronized progesterone over synthetic progestins [17-19].

Lepidium peruvianum, a proprietary formulation known as Maca-Harmony® (commonly known as maca), was also recommended. Multiple clinical trials and case reports have reported the many benefits of *Lepidium peruvianum* for women, including improvements in PMS, menstrual flow, moods, menopausal symptoms, and hormone balance, including LH [20-24]. Traditionally known as an adaptogen influencing the hypothalamus-pituitary-adrenal (HPA) axis, research on the colors of maca, along with the location and conditions where it is grown and harvested, provides a deeper understanding of the mechanism of action of this ancient food source [22,25].The varying levels of active constituents (i.e., alkaloids, glucosinolates, sterols, flavonoids, macamides, and macaenes) found in the various colors of maca may be, in part, responsible for the physiological responses that occur in the body [26-28]. Based on the available literature and years of clinical experience, the clinician believes that the unique blend of maca phenotypes used in the supplement chosen contributed to the improvements and ongoing maintenance of symptoms for this patient.

Magnesium is generally accepted as a safe mineral that can aid in muscle relaxation for premenstrual cramps, soften stools to aid in elimination, and improve sleep [2,12,29,30]. The product chosen included three forms of magnesium, oxide, malate, and glycinate, to assist in the patient's various needs. For the woman presented in this case report, magnesium was likely beneficial for reducing cramps, aiding in bowel movements, and improving sleep.

When the patient reported increased stress and fatigue, a B-complex was recommended. Vitamins B1, B6, B9 (folate), and B12 are required to regulate mood and stress [31,32]. They are needed for the methionine and folate cycles and DNA methylation while also acting on the synthesis and regulation of neurotransmitters, particularly serotonin and dopamine [32]. Further, these vitamins may also play a role in the secretion of cortisol, the stress hormone produced by the adrenal glands [31]. Methylated B vitamins bypass genetic concerns that some individuals have less ability to activate or methylate standard B vitamins to provide the cofactors for cellular energy production, mood, and stress support [33]. Multiple studies demonstrate b-vitamins' impact on mood regulation and stress, making them an ideal complement to the other therapies chosen [31-33].

Additional strengths of the case

Outside of the symptom improvements noted by the patient, the case has several additional strengths. First, the patient complied with regular follow-up consultations and communication with the provider to allow for rapid modifications in the treatment plan. Second, the patient was reasonably consistent with her diet before seeking care and made only minor changes throughout the course of care. Third, once the patient started the supplements, she was consistent and compliant in taking them daily.

Limitations

The physician acknowledges limitations of this case report. First, a case report involving one woman highlighting improvements in severe emotions associated with a diagnosis of PMDD utilizing a combination of natural therapies and bio-identical hormone therapy cannot be translated to the larger population. PMDD and depression, including suicidal ideation, require proper and immediate medical oversight and evaluation. Many treatment options may need to be considered, including prescription medication, cognitive behavior therapy, psychological therapies, and others. The authors do not suggest that the therapies used in the case report are inclusive for individuals with suicidal thoughts or PMDD. Second, there was moderate compliance by the patient with the use of bio-identical progesterone therapy, which could result in unexpected responses, such as the increased emotions the patient experienced with the intermittent use of this therapy. Third, due to the subjective nature of depression, using questionnaires at each visit could have helped clarify and identify a better measure of improvements and confounding concerns for the patient and physician. Lastly, a personalized approach that includes multiple interventions does not allow for a definitive conclusion regarding the effectiveness of any one therapy, and it is reasonable to conclude that the combined interventions contributed to the improvements noted. The authors believe that additional research should be conducted to explore how a combination of natural therapies can provide personalized patient care.

Conclusion

This case report highlights the safe and effective use of the combination of bio-identical progesterone, *Lepidium peruvianum*, and magnesium to resolve multiple symptoms within three months. This included severe emotions (depression with ruminating negative thoughts and suicidal ideation) experienced in the luteal phase of the menstrual cycle, premenstrual headaches and fatigue, menstrual cramping, and decreased menstrual flow. Further, normalization of LH and prolactin levels were achieved. At the writing of this case report, the improvements in these symptoms were also maintained for three months using only *Lepidium peruvianum*, magnesium, and a B-complex. While a cause-and-effect conclusion cannot be determined for the interventions used, this case report can provide clinicians with potential therapeutic options to consider in clinical care and researchers with combination therapies to explore in more depth.

Declarations

Informed Consent

The patient presented in this case report provided written informed consent to publish patient information in the present manuscript. The patient also received a copy of the manuscript to read and review.

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Conflict of Interest

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