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Treatment of Menstruation Disorders at Puberty: A Plant-Based Dietary Supplement Efficacy and Safety

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Abstract

Primary dysmenorrhea harms the physical and social functioning of many young women. At the Siberian State Medical University laboratory complex and Tomsk prenatal clinic No. 4 antenatal clinic, a clinical experiment was conducted to better understand the impact of diet on the treatment of menstrual problems. In the clinical experiment, sixty young women with dysmenorrhea between the ages of 14 and 18 took part. To assess the efficacy of complex treatment both objective and subjective performance criteria were used. All the participants underwent numerous examinations before the trial, and the whole process of the treatment was carefully recorded and analyzed. The supplement was prescribed to complement the conventional cyclic vitamin therapy. The tested dietary supplement demonstrated bacterial, anti-inflammatory, and immune-stimulating effects. The favorable impact of the supplement on the autonomic nervous system was registered. The participants of the experimental group experienced pain relief and demonstrated a noticeable improvement. No side effects were detected during the clinical trial.

Keywords: Dietary supplement, Dysmenorrhea, Clinical trial, Pain relief

Introduction

Dysmenorrhea is one of the most commonly encountered menstruation disorders at puberty (Siserman *et al*., 2019; Paşcalău *et al*., 2021). When appropriate relief is not provided, patients are left incapacitated by dysmenorrhea, as neurohumoral regulation of the menstruation cycle is affected (Mekereș *et al*., 2017; Gabriela *et al*., 2020). Possible causes for primary dysmenorrhea are different and include increased prostaglandin secretion, hormonal imbalance, and the psychogenic factor, which is currently one of the most frequent causes of primary dysmenorrhea. Increased excitation of the nociceptive system and underactive hypothalamus cause pain syndrome (Pokrovsky *et al*., 2002; World Report on Noncommunicable Diseases 2010 Executive Summary, 2011; Sinchikhin *et al*., 2020; Olson *et al*., 2021).

The release of prostaglandins contributes to abnormal uterine contractions, which constrict blood vessels and reduce blood flow. The failure to maintain the supply of oxygen to muscle tissue leads to hypoxia; therefore, patients experience painful menstrual cramps, although pelvic pathologies are absent (Rodionova, 2016; Tokhiriyon, 2020; Tutelyan & Nikityuk, 2020; Szabo *et al*., 2021).

The current most usual treatment for dysmenorrhea includes non-steroidal anti-inflammatory drugs (NSAIDs), which are prostaglandin synthetase inhibitors, and cyclic vitamin therapy. Alternative approaches to relieve dysmenorrhea and to improve the experience of menstruation which are supported by good evidence, but much less frequently prescribed, include using herbal remedies like calendula, cyclodinone, nettle, pink radiola, sage, Chinese lemongrass, Baikal skullcap, remens, ginseng, and aralia. However, when considering using herbal remedies, various side effects have to be taken into account. As the potential risks to the immune and neuroendocrine systems associated with using herbal remedies are not thoroughly researched, further study is required. Currently, nutrition is considered to be important for reducing the severity of primary dysmenorrhea and recent studies of plant-based dietary supplements have demonstrated significant benefits in treating dysmenorrhea (Tokhiriyon, 2019; Bernstein, 2021; Ande, 2022; Hannon & Arslanian, 2023).

Materials and Methods

A new plant-based dietary supplement to help relieve dysmenorrhea was studied. The biochemical and pharmacological studies of the composition of the supplement were conducted, with the following qualitative and quantitative composition developed: Vaccinium macrocarpon (cranberry) extract - 5%, Arctium lappa (burdock root) - 1%, underground and above-ground parts of

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Comarum palustre (marsh cinquefoil) - 2%; Esobel (natural mineral salt found in Siberian lakes) - 5%; and sorbitol - 87%.

The new plant-based dietary supplement is marketed in a granular form. The active ingredients include such compounds as prostaglandins, fulvic and humic acids, amino acids, mineral salts with potassium, sodium, magnesium, calcium, Cl, So, CO, HCO anions, 4-hydroxyproibetaine, azulene, vitamins as well as phytoncides. Sorbitol is used as a filler. The color of the granules varies from light yellow to dark brown with a sweet taste and a faint smell. The supplement has passed all the required quality assurance tests and is officially registered.

A clinical trial was carried out to assess the supplement's effectiveness in reducing dysmenorrhea symptoms. Sixty participants with dysmenorrhea aged from 14 to 18 were selected for the present study. Before the enrolment, the participants underwent a gynecological examination and a pelvic ultrasound to assess the lower abdomen and pelvis and provided information on the date of their first menarche, the length of their menstrual cycle, underlying medical conditions, etc.

On the first day of their menstrual cycle, the experimental group's participants began taking the supplement, which they were instructed to take three times a day with a spoonful of a plant-based food supplement. Before using the supplement, warm water needs to be added to dissolve it. Following the approach that is typically used, cyclic vitamin treatment was administered. Two weeks of taking one Pentovit pill three times per day, followed by two weeks of taking one Aevit capsule three times per day (both vitamin supplements are made in Russia), were recommended to the experimental group members.

Additionally, the trial group's members underwent 10 sessions of electrotherapy. In the pelvic region, electrode pads were inserted and thoroughly soaked in the 1% solution of the supplement. The treatment for the participants of the control group consisted of vitamin supplements and a placebo.

An extensive questionnaire was used to perform the initial screening. The participants replied to a list of questions about age, weight, smoking and drinking habits, underlying conditions, and their treatment. Vital signs like body temperature, blood pressure, pulse rate, and respiration rate were recorded. Then every participant underwent a physical examination together with bacteriosopic and bacteriologic tests of cervical and vaginal microflora.

The next stage involved electrocardiograms, ultrasound examinations of mammary glands, abdominal organs (pancreas, liver, and gallbladder), and the pelvis with all the data carefully recorded. To measure the heart rate variability, a VNS-Micro vegetotester was used as it provides the opportunity to perform a complex study of the autonomous nervous system. Electroencephalogram scans were performed to evaluate the electrical activity of the brain. Clinical urine tests, full blood count, blood glucose, bilirubin, total protein, creatinine, and liver function tests were carried out. The immune status was analyzed with the help of immunocytochemistry, with the subpopulation composition of lymphocytes examined. Enzyme-linked immunosorbent assay technique was used to assess both pro- and anti-inflammatory responses. A student’s test was applied to analyze the data.

The clinical experiment was conducted at Tomsk Antenatal Clinic No. 4 and the Siberian State Medical University's laboratory complex. The clinical trial was overseen by highly qualified medical professionals, including A.M. Dygai, Doctor of Medical Sciences, professor, and member of the Russian Academy of Sciences, along with L.S. Sotninikova, Professor of Obstetrics and Gynecology at Siberian State Medical University, and N.M. Usynina, Obstetrician-Gynecologist at Tomsk Antenatal Clinic No. 4. The trial conforms in every way to Good Clinical Practice and the Helsinki Declaration.

The present study aims to evaluate the efficacy and safety of a plant-based dietary supplement in treating dysmenorrhea at puberty. The following objectives were set: (a) to study the dynamics of the changes in the brain’s electrical activity and the response of the autonomic nervous system, the morphofunctional state of lymphocytes, and the cell differentiation that occurs when participants are prescribed the dietary supplement and cyclic vitamin therapy and (b) to compare two different treatments of dysmenorrhea. The first treatment is a conventional treatment of dysmenorrhea with cyclic vitamin therapy, and the second treatment is a combination of vitamin therapy and a plant-based dietary supplement.

The objective performance criteria included: (a) the data obtained upon the gynecological examination and the ultrasound examination of the pelvis; (b) the changes in the cellular and humoral mechanisms of immunity, the subpopulation composition of lymphocytes, pro- and anti-inflammatory responses; and (c) the changes in the autonomic nervous system response, the brain’s electrical activity.

The overall health of the subjects and the nature of their complaints were taken into consideration for the subjective performance criteria.

Results and Discussion

According to the clinical trial findings, the tested dietary supplement demonstrated bactericidal, anti-inflammatory, and immune-stimulating effects. In this regard, to assess the effectiveness of the dietary supplement we studied the morphofunctional state of the immune and autonomic nervous systems.

The statistical processing of the data obtained during the trial was carried out to determine the following:

- the influence that the dietary supplement can have when taken in combination with conventionally prescribed medicines;
- the dynamics of different ways of treating dysmenorrhea;
- the differences in the duration of treatment performed with and without the supplement.

The patients in the experimental group had uterine appendages that were within the range of the physiological norm one month following the food supplement prescription, according to

information from routine gynecological and ultrasound tests. The uterine appendages of the control group individuals didn't show any improvement in appearance until three months later.

At the same time, the favorable impact that the dietary supplement makes on the autonomic nervous system has been registered. The data obtained indicates that the balance between the systematic and parasympathetic nervous systems has been achieved. The results of cardiovascular tests and the spectral analysis of neurohumoral modulation demonstrated no abnormalities.

To evaluate the mental and emotional state of the participants, we used multidimensional tests. It has been registered that the active ingredients of the dietary supplement block the cascade of reactions that are triggered by the nervous system and inhibit the treatment process.

It is known that anxiety-depressive disorders and dysmenorrhea frequently co-occur with an autonomic dysfunction. The findings of the heart rate variability study demonstrated an imbalance in the functional health of the participants, with an increased activity of the sympathoadrenal system and a decreased activity of the parasympathetic system. These changes harm various aspects of participants' everyday lives. The complex study of the autonomic nervous system allowed us to evaluate the functional health of the participants and their functional reserves, monitor the treatment, make predictions about the development of dysmenorrhea, and choose the most appropriate ways of treating the condition with neurohumoral regulation taken into account. **Tables 1-3** list the data obtained during the study.

Table 1. The immune status

Indicator	Before treatment	After treatment	Normative values
Leukocytes	6.23	6.15	4.5-8.0
Stabs	1	-	2-4%
Segmented	46	53	40-60%
Lymphocytes	52	35	25-45%
Monocytes	1	7	4-8%
CD3	76	68	65-79%
CD4	31	39	34-44%
CD8	46	30	19-27%
CD16	1	8	6-18%
CD72	15	15	3-15%
CD25	4	1	
CD95	7	8	
IgM	1.04	1.73	0.8-2.5
IgG	10.13	15.64	8.0-16.0
IgA	0.55	2.22	0.7-3.0
CIC	0.12	0.120	0.040-0.100

Table 2. Bacterioscopic tests

Indicator	Cervical microflora	Vaginal microflora	Uterine microflora
Leukocytes	8-12	15-25	0-3
Epithelium	Columnar epithelium	Squamous epithelium	Columnar epithelium
Doderleïn Bacilli	negative	negative	negative
Aerobic Flora	8-16	20-24	0-1
Anaerobic Flora	20-28	36-40	0-3
Candida Albicans	negative	+0	0
Neisseria Gonorrhoeae	negative	negative	negative
Trichomonas Vaginalis	negative	negative	negative

Table 3. Cardiovascular tests

Variables	Normative values	Boundary values	Pathological condition	Before treatment with the dietary supplement	After treatment with the dietary supplement
Deep breathing ratio	>1.4	1.2-1.4	<1.2	1.0	1.04
Active orthostatic ratio	>1.35	1.2-1.35	<1.2	1.1	1.07
Valsalva maneuver ratio	>1.7	1.3-1.7	<1.3	1.2	2.89
Active orthostatic	<11	11-25	>25	-4	-4
Isometric handgrip	>15	10-15	<10	0	-1

When the patients were tested before the treatment, severe damage to the parasympathetic division of the autonomic nervous system and moderate damage to the sympathetic division of the autonomic nervous system were registered. Both the parasympathetic and sympathetic divisions had considerable damage, according to studies done following the therapy. Data on the spectrum analysis of neurohumoral regulation done before and after therapy are shown in **Tables 4 and 5**.

Table 4. The spectrum analysis of neurohumoral regulation before treatment

Variables	TP	VLF	LF	HF	LF/HF	% VLF	% LF	% HF	RR min	RR max	RRNN	SDNN
Baseline	2457	789	287	1503	0,43	32	14	62	689	1093	843	52
Deep breathing	3206	223	1351	1596	0,87	8	39	51	714	933	815	53
Valsalva maneuver	2788	254	355	2179	0,16	9	13	78	708	928	814	49
Orthostatic	1035	604	254	178	1,4	58	25	17	669	823	745	30
Isometric handgrip	9270	1629	3820	3821	1	18	41	41	263	843	736	87

Table 5. The spectrum analysis of neurohumoral regulation after treatment

Variables	TP	VLF	LF	HF	LF/HF	% VLF	% LF	% HF	RR min	RR max	RRNN	SDNN
Baseline	2181	823	295	1073	0,27	39	13	50	683	936	799	42
Deep breathing	1530	1166	249	116	2,1	76	16	8	635	812	710	38
Valsalva maneuver	13708	938	5421	7349	0,74	7	40	54	293	1622	813	119
Orthostatic	3120	627	1099	1394	0,79	20	35	45	193	1432	701	60
Isometric handgrip	1077	661	312	104	3	61	29	10	651	795	711	28

The overall strength of the neurohumoral modulation spectrum was rated as moderate. The humoral-metabolic (cerebral, ergotropic) and vagal modulations of the neurohumoral control were both moderately active, whereas sympathetic impacts were hardly perceptible. It was noted that the parasympathetic portion of the autonomous nervous system was active the most. It was judged that the functional capacity was sufficient. The findings of the orthostatic test showed that the parasympathetic division was less reactive and that the sympathetic system was adequately active. Coping capacity was found to be low.

Following treatment, the neurohumoral regulation showed a modest range of the overall strength of the neurohumoral modulation, with equal levels of vagal and humoral-metabolic impacts and a low sympathetic division influence on the activation of the heart rate. It was noted that the parasympathetic portion of the autonomous nervous system was active the most. It was judged that the functional capability was satisfactory. The findings of the orthostatic test showed decreased parasympathetic reactivity and appropriate sympathetic activity. The ability to cope was determined to be enough for the physiological system's proper operation.

Conclusion

The use of the plant-based dietary supplement as a complementary therapy in treating dysmenorrhea provides effective pain relief and noticeably improves the quality of participants' lives.

To evaluate the safety of the dietary supplement the following subjective and objective indicators were considered: (a) overall well-being and complaints, (b) ultrasounds of the abdominal organs and the pelvis, the gynecological examination, the electrocardiogram, the clinical urine and blood tests. No side effects were registered during the clinical trial. No statistically significant changes in either blood test results or clinical urine tests were recorded. Therefore, the safety of the plant-based dietary supplement is evident.

The findings of the randomized, placebo-controlled study support the following conclusions:

1. The dietary supplement provides pain relief as the active ingredients of the supplement are important for the neurohumoral regulation of the inflammatory process.
2. The use of the dietary supplement (both in oral administration and as a solution for the electrode pads) in treating dysmenorrhea is safe and effective

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Ethics statement: The study was conducted according to the guidelines of the Declaration of Helsinki.

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