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EFFECTS OF *NIGELLA SATIVA* SEEDS ON THE SEVERITY AND SYSTEMIC SYMPTOMS OF DYSMENORRHEA

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ABSTRACT

Objective: To determine the effects of *Nigella sativa* seeds on primary dysmenorrhea. **Methods:** This was a prospective study. Participants were 70 students with primary dysmenorrhea from University of Brothers Mentouri, Constantine who were divided into five groups. The control group and the ibuprofen group received 400 mg ibuprofen capsules. The third, fourth and fifth groups was administered orally respectively by *Nigella sativa* at 1g, 2g and 3g a day. The intervention continued for two consecutive menstrual cycles. During the first three days of menstruation. Data were collected from the students using a self-reported questionnaire and a visual analogue scale. **Results:** The results indicate that, after treatment, there were an improvement of systemic symptoms associated with dysmenorrhea compared to the control group in ibuprofen group and *Nigella sativa* groups respectively. Differences were significant in improvement of nausea ($p< 0.05$), breast pain ($p< 0.001$) and irritability ($p< 0.01$). In the control group, pain severity decreased from 4,94 at baseline to 3,66 in the second cycle, whereas that in the Ibuprofen group decreased from 7,90 to 1,80. That in *Nigella sativa* seeds groups also decreased from 6,57 to 3,85 , from 5,21 to 2,42 and from 6,42 to 2,07 about different doses 1g, 2g and 3g respectively. Differences were significant. **Conclusion:** *Nigella sativa* was as effective as ibuprofen in relieving pain and systemic signs in students with primary dysmenorrhea.

KEYWORDS: *Nigella Sativa*, Primary dysmenorrhea, Menstrual pain, Symptoms.

INTRODUCTION

In primary dysmenorrhea, pain is spasmodic in character and felt mainly in the lower abdomen, but it may radiate to the back and along the thighs. There may be associated systemic symptoms like nausea, vomiting, diarrhea, headache, fatigue, and dizziness, and in severe cases, syncope.[1,2] Increased concentrations of prostaglandins, vasopressin, leukotrienes, and emotional factors may also result in dysmenorrhea.[3] Dysmenorrhea causes considerable personal and family disruption. Furthermore, dysmenorrhic girls have lower school marks and more school adjustment problems than do non dysmenorrhic ones counterpart.[4] The prevalence of primary dysmenorrhea in general population is from 47 to 80%, depending on the studied age group.[5,6]

Recent evidences suggest a definite physiologic basis for dysmenorrhea and links to increased levels of prostaglandins, which results in uterine contraction and ischemia.[7,8] Falling progesterone level during the luteal phase brings about these elevations, specifically of PGF2α and PGE2. The role of prostaglandin synthesis inhibitors is in reducing painful symptoms accompanying menstrual discharge.[9]

Various non-invasive nutritional and psychological interventions have been suggested as treatments. These include psychotherapy, yoga, hypnotherapy, massage, transcutaneous electrical nerve stimulation, vitamins and nutritional supplements. Prescribed medications include inhibitors of prostaglandin synthesis and non-steroidal anti-inflammatory drugs (NSAIDs) for the relief of pain as well as oral contraceptives. Non-pharmaceutical treatments include acupuncture and surgery. Several of these treatments may have adverse effects or may be contraindicated in certain groups of women.[10,11]

Traditional medicines like brewed herbs have been used to treat dysmenorrhea across the world.[12] Many women believe that dysmenorrhea is a normal cycle of menstruation and does not need pharmacological treatment.[13] Naturally occurring agents used to treat dysmenorrhea include herbal brews (*eg.*, mint, chamomile, and oregano) the roots of plants (*eg.*, carrots and turnips) and the petals of plants (marigold, hyacinth, and fenugreek).[11,14] Phytoestrogens are herbal compounds with estrogenic activity; fenugreek contains phytoestrogen compounds.[15]

Hence, the present study was under taken to evaluate the effects of oral administration of *Nigella sativa* seeds on primary dysmenorrhea.

Nigella Sativa Linn belongs to family Ranulaceae. The herb is widely known in different parts of the world and its seeds are used as condiment. In subcontinent it is known as '*kalonji*' and its Arabic name is '*Haba Sauda*'. In the west it is known as "Black Cumin".[16] The seed of this plant is referred to by the prophet Mohammed as having healing powers.[17]

MATERIAL AND METHODS

This was a prospective study. It involved unmarried students, 18 years old and over, from University of Brothers Mentouri, Constantine. They were informed about the purpose and methods of the study and provided with written consent forms for participation.

A sample of 70 volunteers participants were divided into five groups. The first was served as control. The second group received 400 mg ibuprofen capsules three times a day. *Nigella sativa* seeds powder was administered orally to the third, fourth and fifth groups respectively at 1g, 2g two times and 3g three times a day. The intervention continued for two consecutive menstrual cycles. During the first three days of menstruation.

The severity of dysmenorrhea, demographic data, and menstrual characteristics were assessed by a self-administered questionnaire. We employed a 10 *cm* visual analogue scale (VAS)[18] to assess the severity of dysmenorrhea experienced by the responder. Mean pain scores were calculated for each treatment.

Statistical Analysis

SPSS ver20 (SPSS, Chicago, IL, USA) was used for the statistical analyses. Descriptive data are presented as frequencies, mean values and standard deviations. t-test, analysis of variance and Friedman test were used to identify the difference between the groups in improvement of systemic signs and severity of pain. A *p* value of 0.05 was considered significant.

RESULTS

Among 70 unmarried female students, 100 % reported primary dysmenorrhea. Mean age of the students in the study group was 22,85 ± 2,31 years. After the first and the second treatment, the results show that the ibuprofen group indicated the highest frequency of improvement of systemic symptoms associated with dysmenorrhea compared to the control group, followed by the groups treated with all doses of *Nigella sativa* seeds, in the first place the group treated with 3 g for the majority of signs. There were significant differences between the groups before or after treatment, depending on the type of treatment, in improvement of nausea ($p< 0.05$), breast pain ($p< 0.001$) and irritability ($p< 0.01$) (Table. 1, Table. 2).

Table 1: Improvement of systemic signs associated with dysmenorrhea after the first cycle.

Signs	Control		Ibuprofen		1g N.S		2g N.S		3g N.S		p
	n	%	n	%	n	%	n	%	n	%	
Nausea	3	16,66	5	50	5	7,14	5	35,71	2	14,28	0***
Diarrhea	6	33,66	4	40	8	28,57	5	35,71	6	42,85	0,236
Breast pain	4	22,22	7	70	4	14,28	7	50	10	71,42	0,03*
Vomiting	4	22,22	6	60	5	7,14	2	14,28	2	14,28	0,411
Abdominal loating	4	22,22	6	60	8	28,57	7	50	10	71,42	0,449
Headache	4	22,22	4	40	9	21,42	6	42,85	6	42,85	0,242
Syncope	1	5,55	2	20	3	14,28	1	7,14	1	7,14	0,417
Depressed mood	2	11,11	3	30	5	14,28	7	50	4	28,75	0,086
Nervousness	4	22,22	8	80	12	28,57	12	85,71	13	92,85	0,079
Insomnia	4	22,22	4	40	7	14,28	3	21,42	4	28,57	0,202
Irritability	4	22,22	3	30	8	21,42	5	50	4	28,57	0,004**

* p< 0,05 , ** p<0,01, *** p<0,001 vs control.

Table 2: Improvement of systemic signs associated with dysmenorrhea after the second cycle.

Signs	Control		Ibuprofen		1g N.S		2g N.S		3g N.S		p
	N	%	n	%	n	%	n	%	n	%	
Nausea	3	16,66	6	60	5	35,71	5	35,71	2	14,28	0***
Diarrhea	6	33,33	4	40	8	57,14	5	35,71	6	21,42	0,236
Breast pain	4	22,22	7	70	7	50	7	50	10	42,85	0,04*
vomiting	5	27,77	6	60	5	35,71	2	14,28	2	14,28	0,375
Abdominal loating	5	27,77	6	60	8	57,14	7	50	10	71,42	0,189
Headache	4	22,22	4	40	9	64,28	6	42,85	6	42,85	0,242
Syncop	1	5,55	2	20	3	21,42	1	7,14	1	7,14	0,417
Depressed mood	2	11,11	3	30	5	35,71	7	50	4	28,57	0,086
Nervousness	4	22,22	8	80	12	85,71	12	85,71	13	92,85	0,159
Insomnia	5	27,77	4	40	7	50	3	21,42	4	28,57	0,398
Irritability	3	16,66	3	30	8	57,14	5	35,71	4	28,57	0,009**

Pain severity at baseline does differ significantly between the groups. In the control group, pain severity decreased from 4,94 at baseline to 3,66 in the second cycle, whereas that in the Ibuprofen group decreased from 7,90 to 1,80. That in *Nigella sativa* seeds groups also decreased from 6,57 to 3,85, from 5,21 to 2,42 and from 6,42 to 2,07 about different doses 1g, 2g and 3g respectively. Our results showed that the severity of pain decreased with increasing of the dose of *Nigella sativa* seeds. Pain severity in each intervention cycle differed significantly between the groups, with pain reduction in each cycle being significantly larger in the Ibuprofen group and 3g of *Nigella sativa* seeds group respectively (Table. 3).

Table 3: Pain severity measured on a 10 *cm* visual analog scale[a].

	Control	Ibuprofen	1g NS	2g NS	3g NS	p-Value[b]
Baseline	4,94 ± 2,46	7,90 ± 2,13	6,57 ±1,82	5,21± 2,25	6,42 ± 1,86	0,007**
1st Cycle	3,72 ± 2,24	1,80 ± 1,39	3,85 ±2,47	2,57 ± 1,98	2,07 ± 1,63	0,028*
2nd Cycle	3,66 ± 2,24	1,80 ± 1,39	3,85 ±2,47	2,42 ± 1,91	2,07 ± 1,63	0,027*
p-value[c]	0,000***	0,000***	0,001**	0,000***	0,000***	--

[a] Values are given as mean ± SD unless otherwise indicated [b] ANOVA test [c] Friedman test

DISCUSSION

Mefenamic acid and ibuprofen are the drugs of choice for treating primary dysmenorrhea,[19] with up to 80% efficiency[20] The effects of many herbs such as fennel,[21,22] cumin, ginger 23 and chamomile on dysmenorrhea have been studied.[24] However, in a search of the literature, we found no study that assessed the effects of *Nigella sativa* on dysmenorrhea; that's why in this study; we examined the effect of *Nigella sativa* seeds on dysmenorrhea. Our findings showed that *Nigella sativa* was as effective as ibuprofen in relieving menstrual pain.

The seeds of *Nigella sativa* L. have been used in traditional medicine by many Asian, Middle Eastern and Far Eastern Countries to treat headache, coughs, abdominal pain, asthma, rheumatism and other diseases.[25]

The ethanol extract and volatile oil of *N. sativa* seeds inhibited spontaneous movements of the rabbit jejunum.[26] Further, the volatile oil inhibited contractions of the rabbit jejunum which were induced by high potassium (K+) solution or acetylcholine. This inhibition was dose-dependent, reversible and not affected by the addition of calcium to the organ bath. The data suggested that *N. sativa* seed had an antispasmodic effect, possibly due to a calcium antagonistic activity. Aqel[27] also reported that *N. sativa* volatile seed oil inhibited contractions of rabbit aortic rings induced by norepinephrine stimulation in Ca 2+ -containing solution. This inhibition was dose- dependent and reversible. The data suggested that the volatile oil of *N. sativa* seeds possessed a direct vascular smooth muscle relaxant effect, possibly by interfering with the influx of extra cellular Ca2+. The crude extract of *Nigella sativa* seeds exhibited spasmolytic and bronchodilator activities in isolated rabbit jejunum and guinea-pig tracheal preparations mediated possibly through calcium channel blockade.[28] The antispasmodic effect of *Nigella sativa* seeds on gastrointestinal system has been recognized and this may justify its effectiveness in dysmenorrhea.

Different theories exist regarding dysmenorrhea-inducing mechanisms, one of which is increased production of PGs in the endometrium. PGs originate from arachidonic acid in cyclooxygenase and lipooxygenase pathways. Studies have shown that the menstrual blood of women with dysmenorrhea has greater amount of two PGs-PGE2 and PGF2_. In women with primary dysmenorrhea, pain results from myometrial contractions induced by PGs (mainly PGF2_) originating in secretory endometrium.[29] Anti-prostaglandins such as NSAIDs can relieve

dysmenorrheal pain. Mefenamic acid from fenamate groups and ibuprofen from propionic acids act as inhibitors of PGs synthesis.[30]

The crude fixed *N. sativa* seed oil and pure thymoquinone both inhibited the cyclooxygenase and 5-lipoxygenase pathways of arachidonate metabolism in rat peritoneal leukocytes stimulated with calcium ionophore A23187.[31] These pharmacological properties supported the traditional use of *N. sativa* and its derived products as a treatment for rheumatism and related inflammatory diseases. Oberg et al.[32]

Considering the results of the present study, and the data of literature, it seems that *Nigella sativa* seeds had antiprostaglandin effects similar to this of ibuprofen. Measuring PGs in plasma or menstrual blood throughout the treatment may help to clarify the mechanism of action of this seeds on primary dysmenorrhea.

In dysmenorrhea the cramps are frequently accompanied by backache, nausea, vomiting, and diarrhea in a high percentage of cases. NSAIDs have numerous adverse effects, including nausea, vomiting, dizziness, purpura, petechiae, hyperkalemia, peripheral edema, peptic ulcers and gastric bleeding.[33] In the present study the effectiveness of *Nigella sativa* in symptoms of dysmenorrhea and its harmlessness have been observed. Therefore, our results show that *Nigella sativa* seeds may reduce dysmenorrhea-associated systemic symptoms (nausea, vomiting, lack of energy, headache, diarrhea, mood swings, syncope, and fatigue). This effect can be explained by the antihistaminic effect of this seeds.[34]

Further studies will be necessary to isolate, fractionate, purify and characterize the active principles which are responsible for improvement of symptoms and pain associated with dysmenorrhea and to understand exacts its mechanisms of actions.

CONCLUSION

The present study showed that *Nigella sativa* reduced the severity of primary dysmenorrhea. *Nigella sativa* is as effective as ibuprofen in relieving pain in women with primary dysmenorrhea. Furthermore, the effects of this seeds on symptoms associated with dysmenorrhea were lower than witch of ibuprofen. Further studies regarding the effects of *Nigella sativa* on other symptoms associated with dysmenorrhea, the efficacy and safety of various doses and treatment durations, and the exact mechanism of action are warranted.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest related to this article.

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