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ORIGINAL ARTICLE

Effectiveness of Black Seed (*Nigella sativa* L.) and Honey on Kidney Stone Expulsion and Metabolic Disorders in Patients with Kidney Stones: A Non-Randomized Clinical Trial

Arezu Mohammadi[1], Faramarz Beigi[*2], Zahra Lori Gooini[3], Fatemeh Drees[4]

[1]*Student Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran*

[2]*Department of Urology, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran*

[3]*Medical Plants Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Science, Shahrekord, Iran*

[4]*Department of Epidemiology and Biostatistics, School of Health Modeling in Health Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran*

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KEYWORDS

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ABSTRACT: Kidney stones can negatively affect various aspect of patient's daily life. This study aims to assess the therapeutic effects of black seed capsules on kidney stones expulsion. A total of 60 patients were diagnosed with kidney stones larger than 5 millimeters through ultrasound, were recruited for the study. The patients were instructed to consume capsules containing 500 milligrams of black seed four times a day. Honey was administered as syrup. To make honey syrup, a tablespoon of honey was diluted in 150 ml of lukewarm water. The patients underwent sonography and a 24-hour urine test to assess the levels of calcium, uric acid, oxalate, cystine, and citrate. Data were analyzed using SPSS version 22 software. The results revealed a significant decrease in the number and size of kidney stones ($p<0.05$). The mean levels of creatinine, blood urea nitrogen, uric acid, and citrate increased, while the mean levels of calcium and oxalate decreased significantly ($p<0.05$). Treatment of patients with kidney stones using black seed capsules and honey for one month led to decrease in the number and size of kidney stones in both the right and left kidneys. Furthermore, this treatment resulted in decreased levels of oxalate and calcium in the blood and increased levels of citrate.

INTRODUCTION

Kidney stones are a prevalent urinary tract disorder conditions around the world that can affect patients, their family, and health system [1]. Changes in lifestyle, such as a sedentary lifestyle, obesity, and nutritional habits, may contribute to the increasing occurrence of kidney stones in recent years [1-3]. Kidney stones can impair patient's health-related quality of life (HRQOL) an interfere with their daily life [4]. Surgical treatment or fragmentation procedures can be costly and carry potential side effects such as urinary tract infections and, in some cases, systemic infections due to extensive kidney tissue damage [5-6]. Therefore, finding effective, efficient and safe treatment methods seems a necessity. Today, the use of natural medicines and their derivatives, especially silymarin, in the treatment of various diseases, including liver and blood diseases, has shown

*Corresponding author: farazbeigi@yahoo.com (F. Beigi)
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satisfactory results [7-8]. As a result, there is a growing interest in the use of herbal remedies, considering the high costs and potential risks associated with surgical interventions.

Nigella sativa L., also called black seed, is a member of the *Ranunculaceae* family. That revealed immunomodulator, anti-inflammatory, antioxidant, gastroprotective, analgesic, spasmolytic, antimicrobial, and bronchodilator activity [9]. Essential oil derived from black seed has identified key compounds including thymoquinone, p-cymene, carvacrol, longifolene, nigellisine, nigellidine, nigellimine, nigellone, dithymoquinone, and thymohydroquinone [10]. The combination of black seed and honey has been used in traditional medicine as a simple yet effective remedy for various disorders [11-12]. Previous studies indicated that *Nigella sativa* combined with honey or alone can expulsion of kidney stones and improve biochemical markers [11, 13]. Considering the high prevalence of Kidney stones and considering the many complications of this disease and the need for safe and non-invasive treatments, this study was conducted to assess the therapeutic effects of black seed with honey capsules on kidney stones in patients.

MATERIALS AND METHODS

This study was designed as a non-controlled clinical trial conducted at the Imam Ali Clinic in Shahrekord. In this study 60 participants (kidney stones larger than 5 millimeters through ultrasound) were determined based on available patient population and study feasibility.

Patients with a medical history of diabetes, hypertension, concurrent use of tricyclic antidepressants (TCAs) medications, or pregnancy were excluded from participation. Furthermore, individuals with kidney stones smaller than 5 millimeters, those who withdrew from the study, and those who reported allergy to black seed were also not included. Prior to their involvement, all participants were provided with comprehensive information regarding the properties and potential side effects of black seed, as well as details about the methodology and duration of the experiment.

Participants were instructed to consume capsules containing 500 milligrams of black seed four times daily. In accordance with traditional medicine recommendations, they were also advised to consume a spoonful of honey alongside the medication. Honey syrup was made by diluting a tablespoon of honey in 150 ml lukewarm water. Honey was given in the form of syrup. The intervention lasted for 30 days, during which participants adhered to the prescribed regimen of black seed and honey.

The primary outcome measures included changes in the size and number of kidney stones as determined by follow-up sonography. Secondary outcome measures involved changes in biochemical parameters, including levels of calcium, uric acid, oxalate, cystine, and citrate in 24-hour urine tests, as well as creatinine and blood urea nitrogen in blood samples.

Baseline sonography and 24-hour urine tests were conducted to assess initial levels of relevant biochemical parameters. Blood samples were also collected at baseline to measure creatinine and blood urea nitrogen levels. After the 30-day intervention, follow-up assessments were conducted using the same sonographic and biochemical tests to evaluate the effects of the intervention.

This study was non-randomized and did not include a control group, so no randomization procedures were employed. Blinding was not implemented in this study, as it was a non-controlled trial, and all participants received the same intervention.

The data was analyzed using SPSS version 22 software. Summary statistics were used to describe the data, and statistical analyses, such as the T-test and Chi-square test, were conducted to compare the results before and after the intervention. A p-value less than 0.05 was deemed to be statistically significant.

RESULTS

The patients had a mean age of 49.9 ± 77.36 years. The youngest individual treated was 20, and the oldest was 50. Among the patients, 35 (58.3%) were male, and 25 (41.7%) were female.

The results (Table 1) show the effects of black seeds and honey on the size and number of kidney stones. The paired t-test results revealed a significant decrease in the number and size of kidney stones.

Table 1. The effects of black seeds and honey on the size and number of kidney stones

Variables	Before (Mean±SD)	After (Mean±SD)	p-value
The number of stones in the right kidney	1.52±0.97	1.40±0.94	0.007*
The number of stones in the left kidney	1.62±0.94	1.52±0.89	0.013*
The total number of stones in the right and left kidneys	3.13 ± 1.17	2.92±1.11	0.001**
Stone size in the right kidney (mm)	14.27±5.53	11.86±5.63	<0.001**
Stone size in the left kidney (mm)	13.35±6.54	11.12±6.35	<0.001**
Total stone size in right and left kidneys	22.87±8.91	18.92±8.39	<0.001**

*P<0.05; **P<0.001

Table 2 shows biochemical factors before and after the intervention. The mean levels of creatinine, blood urea nitrogen, uric acid, and citrate increased, while the mean levels of calcium and oxalate decreased significantly (p<0.001).

Table 2. The results before and after the intervention of biochemical factors.

Variables	Before (Mean±SD)	After (Mean±SD)	p-value
Creatinine (mg dl^{-1})	0.96 ± 0.10	1.08±0.13	<0.001**
Urea nitrogen (mg dl^{-1})	11.52 ± 2.32	14.32±2.75	<0.001**
Calcium (mg dl^{-1})	278.5 ± 64.67	194.47±60.44	<0.001**
Uric acid (mg dl^{-1})	372.73 ± 115.86	459.00±138.29	<0.001**
Oxalate (mg dl^{-1})	59.95 ± 17.22	39.03 ± 12.53	<0.001**
Citrate (mmol lit^{-1})	2.06 ± 0.61	2.76±0.61	<0.001**

**P<0.001

DISCUSSION

This study demonstrates the beneficial effects of black seeds and honey in reducing the number and size of kidney stones in patients with kidney stones. Previous animal studies have also indicated protective effects of black seeds against kidney stones. A study on 60 patients with kidney stones participated in a randomized-controlled trial. Intervention group received either black seed capsules (500 mg). In this group, 44.4% completely excreted their stones, while 51.8% saw a reduction in stone size. In the group that received the placebo, 15.3% wholly excreted stones, and 11.5% experienced size reduction and indicating that *Nigella sativa* L. had a positive effect on reducing kidney stones [11]. A clinical trial evaluated the effects of *Nigella sativa* L. on patients with kidney stones smaller than 6 mm who did not have hydronephrosis and did not require medication. The treatment group was given 8 grams of *Nigella sativa* combined with honey in a glass of warm water daily for one month, while the control group received no treatment. Both groups consumed 6-8 glasses of water daily. The results showed that the treatment group had a significantly higher rate of stone expulsion compared to the control group [13]. These results were consistent with the results of our study, which can be caused by various causes such as the capacity to regulate kidney biochemical activities, antioxidant and anti-inflammatory properties of honey and *Nigella sativa* L [14-17]. The study by Hadjzadeh et al. indicated that the administering ethanolic extract of *Nigella sativa* L. to rats reduced the number of calcium oxalate deposits and lowered the urine concentration of calcium oxalate [18]. Citrate is a crucial substance that inhibits stone formation in urine. It binds to calcium in the urine, preventing it from reaching saturation and precipitating. Individuals with low levels of urinary citrate are at a higher risk of developing calcium stones. In the present study, most of the patients had high levels of oxalate and calcium and low levels of citrate in their urine. Furthermore, treatment with black seeds and honey led to a significant decrease in urinary oxalate and calcium levels and a significant increase in citrate and improve kidney biochemical tests [19-20]. Another study demonstrated that Nigella sativa can

safeguard the kidneys from ischemic shock by employing various mechanisms, including its antioxidant, anti-inflammatory, and anti-apoptotic properties. These protective effects involve regulation of the antioxidant defense system, nuclear factor-kappa B (NF-κB) signaling, caspase pathways, and transforming growth factor-beta (TGF-β) signaling. Clinical trials have shown that black seed oil helps normalize blood and urine parameters and improves outcomes in patients with advanced chronic kidney disease [17]. Furthermore, it has been observed that the levels of antioxidants such as alpha-carotene, beta-carotene, and beta-cryptoxanthin significantly decrease in the serum of patients with kidney stones [21]. Individuals with higher levels of these antioxidants tend to have a lower risk of developing kidney stones. This suggests that antioxidant compounds play a vital role in preventing the formation and growth of kidney stones. Black seed contains compounds like tannins, flavonoids, and alkaloids [22].

CONCLUSIONS

The treatment of patients with kidney stones using black seed capsules and honey for one month led to a significant reduction in the number and size of kidney stones in both the right and left kidneys. This treatment also resulted in decreased levels of oxalate and calcium in the blood and increased levels of citrate. Apart from its ability to lower oxalate and calcium levels, the effectiveness of black seed may be attributed to its anti-inflammatory, antioxidant effects, and lipid-lowering properties. Surprisingly, the treatment with black seed capsules and honey was found to increase the levels of blood urea nitrogen, creatinine, and urea nitrogen, which contradict the initial expectations. To gain a better understanding, it is recommended that future studies evaluate these parameters at shorter intervals throughout the treatment period.

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ETHICAL CONSIDERATION

The studies involving human participants were reviewed and approved by Shahrekord University of Medical Sciences (IR.SKUMS.REC.1395.298). The patients/participants provided their written informed consent to participate in this study.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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