

Efficacy of black seed (*Nigella sativa* L.) and honey on stone excretion and metabolic disorders in patients with kidney stones: A non-randomized clinical trial

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Efficacy of black seed (*Nigella sativa* L.) and honey on stone excretion and metabolic disorders in patients with kidney stones: A non-randomized clinical trial

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Abstract

Kidney stones can negatively affect various aspect of patient's daily life. This study aims to investigate the therapeutic effects of black seed capsules on kidney stones. 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. The results revealed a significant decrease in the number and size of kidney stones. The average levels of creatinine, blood urea nitrogen, uric acid, and citrate increased, while the average levels of calcium and oxalate decreased significantly. 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.

Keywords: black seed, honey, kidney stones, *Nigella sativa* L.

INTRODUCTION

Kidney stones are a prevalent urinary tract disorder conditions (Hadjzadeh et al. 2007). Globally, around 1 to 15 percent of people experience kidney stones at some point in their lives.

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 (Pearle et al. 2014). 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 (Moe 2006).

Nigella sativa L., commonly known as black seed, belongs to the Ranunculaceae family. The combination of black seed and honey has been used in traditional medicine as a simple yet effective remedy for various ailments (Hadjzadeh et al. 2007). Essential oil derived from black seed has identified key compounds including thymoquinone, p-cymene, carvacrol, longifolene, nigellisine, nigellidine, nigellimine, nigellone, dithymoquinone, and thymohydroquinone. Previous studies have explored the anticancer, antioxidant, anti- urolithiasis and hepatoprotective effects of the black seed and honey combination (Hadjzadeh et al. 2007) (EL-Kholy et al. 2009; Al Ameen et al. 2011; Hassan et al. 2012). This study aims to investigate the therapeutic effects of black seed capsules on kidney stones in patients attending the Imam Ali Clinic in Shahrekord.

METHODS

Trial design

This study was designed as a non-controlled clinical trial conducted at the Imam Ali Clinic in Shahrekord. The aim was to evaluate the effects of *Nigella sativa* L. and honey on kidney stones larger than 5 millimeters.

Participants and eligibility criteria

The current study was designed as a non-controlled clinical trial. A total of 60 patients at Imam Ali Clinic in Shahrekord who were diagnosed with kidney stones larger than 5 millimeters through ultrasound, were recruited for the study.

Patients with a medical history of diabetes, hypertension, concurrent use of TCA 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.

Interventions

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 was administered as syrup. To make honey syrup, a tablespoon of honey was diluted in 150 ml of lukewarm water. The intervention lasted for 30 days, during which participants adhered to the prescribed regimen of black seed and honey.

Outcomes

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.

Sample Size

The sample size of 60 participants was determined based on available patient population and study feasibility (Figure 1).

Randomization

This study was non-randomized and did not include a control group, so no randomization procedures were employed.

Blinding

Blinding was not implemented in this study, as it was a non-controlled trial, and all participants received the same intervention.

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Statistical analysis

Data were analyzed using SPSS software. Descriptive statistics were used to summarize the data, and statistical tests, including the T-test and Chi-square test, were employed to compare pre- and post-intervention results. A p-value < 0.05 was considered statistically significant.

Ethical considerations

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.

RESULTS

The patients had a mean age of 49.9 ± 77.36 years. The youngest patient was 20 years old, while the oldest was 50 years old. Of 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**
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*P<0.05 **P<0.001

Table 2 shows biochemical factors before and after the intervention. The average levels of creatinine, blood urea nitrogen, uric acid, and citrate increased, while the average 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)	0.96±0.10	1.08±0.13	<0.001**
Urea nitrogen (mg/dl)	11.52 ± 2.32	14.32±2.75	<0.001**
Calcium (mg/dl)	278.5 ± 64.67	194.47±60.44	<0.001**
Uric acid (mg/dl)	372.73 ± 115.86	459.00±138.29	<0.001**
Oxalate (mg/dl)	59.95±17.22	39.03 ± 12.53	<0.001**
Citrate (mmol/lit)	2.06±0.61	2.76±0.61	<0.001**

**P<0.001

DISCUSSION

This study is the first to demonstrate 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 shown protective effects of black seeds against kidney stones. The study by Khoei et al found that treatment with black seed hydroalcoholic extract resulted in a reduction in the size and number of calcium oxalate crystal deposits in the kidneys of rats (Hadjzadeh et al. 2007). This is consistent with the findings of the present study.

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. Therefore, the reduction in stone accumulation and number can be attributed to these changes (Dollah et al. 2013; Khazaei and Mirazi 2016) .

However, it should be noted that the increase in levels of creatinine, blood urea nitrogen, and uric acid observed after one month of black seed treatment contradicts previous studies conducted on rats, which showed a decrease in these markers in rats with kidney damage following black seed consumption. It is possible that the increase in these markers in the present study is due to the side effects of black seeds. Additionally, the use of a combination of black seeds and honey or dietary changes in patients may have contributed to the increase in blood creatinine levels. Future studies should evaluate blood creatinine levels at multiple time intervals during the treatment period to provide more definitive conclusions.

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 (Holoch and Tracy 2011). 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 (Fazly Bazzaz et al. 1997). The flavonoid compounds found in black seed include flavonoid glycosides such as kaempferol, quercetin, and isorhamnetin. Studies have demonstrated the antioxidant effects of black seed against oxidative stress induced by carbon tetrachloride in rats (Fazly Bazzaz et al. 1997), oxidative stress and cell damage in beta-cells caused by streptozotocin in diabetic rats (Kanter et al. 2004), and oxidative stress caused by potassium bromate (Khan 2013). Furthermore, black seed has been found to have anti-inflammatory effects. These anti-inflammatory effects suggest that black seed may prevent crystal accumulation by reducing kidney inflammation. Recent studies also propose that kidney stones, including struvite stones, may have an infectious origin. Given that black seed compounds have antimicrobial effects, it is possible that part of the therapeutic effects of black seed in treating kidney stones is related to its ability to inhibit infectious agents, potentially including nanobacteria (Hanafy and Hatem 1991). Lipid disorders contribute to the development of kidney stones (Schmiedl et al. 2000). It is possible that the lipid-lowering effects of black seed play a role in reducing the number and size of kidney stones.

CONCLUSION

In the present study, 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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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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