Comparison efficacy of oral *Nigella sativa* seeds and tamsulosin on pain relief and passage of 4 to 10 mm stones of kidney and ureter; a randomized clinical trial

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**Abstract**

**Introduction**: Urinary stones are the third most common urinary tract disease after urinary tract infections and prostate diseases. The prevalence varies from 1% to 15% in different communities (average prevalence of 5%), causing serious complications including severe pain, urinary tract infection and renal failure (2, 3). *Nigella sativa* is an annual plant from the Ranunculaceae family, a plant with white, pale blue flowers and milky-white seeds that turn black in contact with the air (4-6).

**Patients and Methods**: In this randomized clinical trial study conducted from March 2018-2019, 80 patients over 18 years old with kidney and ureteral stones sized between 4 to 10 mm were assigned to two groups by the simple random sampling method. In group one, after performing ultrasonography and confirming the presence of 4 to 10 mm stones, one 0.4 mg capsule of tamsulosin was prescribed each night for two weeks. In group 2, one gram of *Nigella* prescribed every 12 hours after each meal with a glass of water for two weeks. After 2 weeks, patients were visited while a urinary tract sonography was conducted and the modification in size of stones and the existence of residual stones were measured and noted. The pain severity was measured through the visual analog scale (VAS). Data was gathered and analyzed throughout treatment and at the end of the study by the SPSS version 21 software, chi-square and independent t tests.

**Results**: Mean sizes of stones before treatment with *Nigella* versus tamsulosin groups were 10.3 ± 1.81 and 9.41 ± 1.68 mm respectively (P=0.06). Mean size of stones after treatment with *Nigella* versus tamsulosin groups were 4.97 ± 4.33 and 5.21 ± 3.63 mm respectively (P=0.39). There was no significant difference between two groups regarding average of the pain score after treatment (P=0.05), but after intervention this score significantly declined in both groups, indicating more substantial in *Nigella sativa* group (P=0.001). Efficacy of treatment in *Nigella* and tamsulosin groups was 78.5 and 61.6, respectively (P=0.005).

**Conclusion**: The present study indicated that both *Nigella sativa* seed and tamsulosin reduce urinary stone size and numbers without significant difference, however stone passage and pain control was more in the group of *Nigella sativa*.

**Trial Registration**: The trial protocol was approved by the Iranian Registry of Clinical Trial (identifier: IRCT20081011001323N23; https://irct.ir/user/trial/35993/, ethical code: IR.YUMS.REC.1397.155).

**Implication for health policy/practice/research/medical education**: In a randomized clinical trial, we found *Nigella sativa* seed and tamsulosin reduce urinary stone size and numbers without significant difference; however, stone passage and pain control were more in the *N. sativa* group.

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is also used as a diuretic to induce menstruation and to increase milk production (6-11). Black seed compounds; four types of alkaloids, namely A (1), A (2), B (1), B (2), that have been extracted from the seeds of _Nigella sativa_ (12, 13). The main active constituents in aqueous extracts of plant seeds are thymoquinone, dithymoquinone, thymohydroquinone, and thymol (14-17).

**Objectives**
The aim of this study was to compare the efficacy of _Nigella sativa_ seeds and tamsulosin on expulsion and pain relief of ureteral and renal stones smaller than 10 mm.

**Patients and Methods**

**Study design**
In this randomized clinical trial study conducted from March 2018-2019, eighty patients over 18 years old that referred to a urology clinic with kidney and ureteral stones sized between 4 to 10 mm were studied. Patients did not have any indications for immediate intervention and no severe pain. First, we conducted a complete history and physical exam. Then basic serum samples including Na, K, CBC, PT, PTT, renal function tests (BUN, creatinine) along with their analysis and urine cultures were taken. Pregnant women were excluded from the study, additionally other diseases, including cardiovascular or pulmonary disease, coagulopathy, uncontrolled hypertension, and those with contraindication for the use of sedatives or opioid drugs and also individuals with a history of herbal or drug allergies, were excluded from the study. After the ethics committee's approval, eligible patients were assigned to two groups by the simple random sampling method. All participants must drink 10-12 cups of water every day.

In group 1, after performing ultrasonography and confirming the presence of 4 to 10 mm stones, one 0.4 mg capsule of tamsulosin was prescribed for each night for two weeks.

Group 2, the _Nigella_ seeds were prepared from seeds harvested from the Dena region of Southern Iran. The seeds were dried in shadow after determining herbarium number. The blinded seeds were prepared in the form of capsules with a dose of 2 g/d, 2 capsules every 12 hours, after each meal with a cup of water for 2 weeks (1). In both groups, diclofenac sodium was prescribed for pain sedation. In the case of unresponsiveness or any indication of intervention, standard treatment and lithotripsy was conducted. Moreover, they were advised to do a minimum of daily exercise (30 minutes), especially walking (2). After 2 weeks, patients were tested by urinary ultrasound to exam renal stones. The pain severity was measured through the visual analog scale (VAS) by the patient. Data was gathered and analyzed throughout treatment and correspondingly at the end of the present study.

**Statistical analysis**
All the data was gathered and analyzed by the SPSS v. 21 software. For analyzing the data, descriptive statics tests including frequency, mean, and standard deviation was used. At that point, for between-intergroup assessments, the chi-square test and _t_ test were applied. The level of significance was fixed at 0.05%.

**Results**
The patients' demographic specifics such as gender, age, mean size, the number of stones, and stone location were similar between the two groups. This study showed no significant differences between the two groups regarding the mean age of patients (_P_ = 0.53) and stone location (_P_ = 0.07). Before treatment, the mean size of stones in nigella versus tamsulosin groups were 10.03±1.81 and 9.41 ± 1.68 millimeters, respectively (_P_ = 0.06). The mean sizes of stones after treatment with _Nigella_ versus tamsulosin groups were 4.97±4.33 and 5.21 ± 3.63 mm, respectively (0.39). After treatment, the mean number of stones in both participants was 0.83 ± 0.59 and 1.18 ± 0.94, respectively. No significant difference between the two groups was observed while after treatment, the size and number of stones per patient were reduced in both groups (_P_ = 0.52). There were no marked differences between the two groups regarding the average pain score before treatment (Table 1; _P_ = 0.065); however, after the intervention, the pain score reduced meaningfully in the two groups that were more significant in the _Nigella sativa_ group (Table 2).

Regarding the effectiveness of treatments, the sum of whole and fractional responses in the two participants were more than 60 %, but there were significant differences between the two groups (Table 3; _P_ = 0.005).

**Discussion**
Today, with the advent of technology, there has been a great revolution in urinary tract stone treatment, but there are still no functioning and safe medicines that can lead to absolute management or prevention of urinary stone formation without surgical intervention (1-5). However, various herbal and synthetic drugs have been marketed to prevent and/or reduce urinary stone formation, and to treat them (6-8). With regard to the belief by native people of the southern and central part of Iran as to the preventive and therapeutic effects of black seed (black seed oil) in reducing and improving pain and also its diuretic effects (7,8). The aim of this study was to compare oral capsules of black seeds (black seed oil) with tamsulosin in the relief of pain and passage of renal and ureteral stones.

Demographic features such as gender, age, pain intensity, quantity, and size of stones have no meaningful difference between the two contributors and after treatment, the dimension and amount of stones diminished in the two groups of patients.

AL-Mamoori et al studied the effect of _Nigella sativa_ on the debarment and handling of nephrolithiasis in urinary tract stones. The researchers concluded that black
Table 1. Patients’ distribution frequency of according pain intensity in two groups prior treatment

| Pain intensity | Group | Nigella sativa No. (%) | Tamsulosin No. (%) | P value |
|---------------|-------|------------------------|-------------------|--------|
| Mild          | 24 (61.5) | 21 (53.8)             |                   | 0.065 |
| Moderate      | 14 (35.9)  | 16 (41.1)             |                   |        |
| Severe        | 1 (2.6)    | 2 (5.1)               |                   |        |
| Total         | 39 (100)   | 39 (100)              |                   |        |

Table 2. Patients’ frequency distribution according pain intensity in two groups after treatment

| Pain intensity | Group | Nigella sativa No. (%) | Tamsulosin No. (%) | P value |
|---------------|-------|------------------------|-------------------|--------|
| Painless      | 24 (61.5) | 10 (25.6)             |                   |        |
| Mild          | 11 (28.2)  | 15 (38.5)             |                   | 0.001 |
| Moderate      | 2 (5.2)    | 11 (28.2)             |                   |        |
| Severe        | 2 (5.1)    | 3 (7.7)               |                   |        |
| Total         | 39 (100)   | 39 (100)              |                   |        |

Table 3. Frequency distribution of patients regarding efficacy of treatment after intervention in two groups

| Efficiency     | Group | Nigella sativa No. (%) | Tamsulosin No. (%) | P value |
|---------------|-------|------------------------|-------------------|--------|
| Complete      | 16 (41)   | 9 (23.1)              |                   | 0.005 |
| Partial       | 15 (38.5) | 15 (38.5)            |                   |        |
| Failure       | 8 (23.1)   | 15 (38.5)            |                   |        |
| Total         | 39 (100)   | 39 (100)             |                   |        |

Conclusion
The present study indicated that the seed of Nigella sativa and tamsulosin decreased the urinary stones’ dimensions and numbers and pain intensity during the passage of stones without a significant difference. However, Nigella sativa seed efficacy is more in the treatment of stones. It seems that Nigella seeds reduced the pain and size of urinary stones and can be used as an alternative treatment in urinary stones without significant side effects.

Limitations of the study
This study was conducted on a limited number of patients and requires further investigation by larger samples.

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**Authors’ contribution**

SM; the concept, design, data analysis, manuscript preparation, manuscript review, and final revision. NS; data collection and providing first draft and submission. AP; statistical analysis, data collection, and first revision. All authors read and signed the final paper.

**Conflicts of interest**

The authors declare that they have no competing interests.

**Ethical Issues**

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Yasuj University of Medical Sciences approved the study (IR.YUMS.REC.1396.120). The study was also registered as a clinical trial at the Iranian Registry of Clinical Trials (identifier: IRCT20081011001323N23; https://irct.ir/trial/30508, ethical code #IR.YUMS.REC.1397.155). Consequently, the consent form was obtained from all the study participants in advance of all interventions. Moreover, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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