



# 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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## ARTICLE INFO

**Article Type:**  
Original

### Article History:

Received: 26 June 2020

Accepted: 12 April 2021

Published online: 15 June 2021

### Keywords:

Urinary stone  
*Nigella sativa*  
Tamsulosin  
Treatment

## ABSTRACT

**Introduction:** Urinary stones are the third most common urinary tract disease after urinary tract infections and prostate diseases.

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

**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 sativa* 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 (VSA). 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  $10.3 \pm 1.81$  and  $9.41 \pm 1.68$  mm respectively ( $P=0.06$ ). Mean size of stones after treatment with *Nigella* versus tamsulosin groups were  $4.97 \pm 4.33$  and  $5.21 \pm 3.63$  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.

**Please cite this paper as:** Shakeri N, Mehrabi S, Paymard A. 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. J Nephropharmacol. 2022;11(1):e08. DOI: 10.34172/npj.2022.08.

## Introduction

Urinary stones are the third most common urinary tract disease after urinary tract infections and prostate diseases (1). Its 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).

The black seeds have a rich medical and religious history. This plant is native to Southern Europe, North Africa, and Asia (6-8). Ancient Egyptians knew the black seed, and Greek physicians prescribed black seeds for headaches, nasal congestion, asthma, allergies, immune system deficiency, toothache, and intestinal worms. It

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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  $10.03 \pm 1.81$  and  $9.41 \pm 1.68$  millimeters, respectively ( $P=0.06$ ). The mean sizes of stones after treatment with *Nigella* versus tamsulosin groups were  $4.97 \pm 4.33$  and  $5.21 \pm 3.63$  mm, respectively (0.39). After treatment, the mean number of stones in both participants was  $0.83 \pm 0.59$  and  $1.18 \pm 0.94$ , 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                     |                       | P value |
|----------------|---------------------------|-----------------------|---------|
|                | Nigella sativa<br>No. (%) | Tamsulosin<br>No. (%) |         |
| 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                     |                       | P value |
|----------------|---------------------------|-----------------------|---------|
|                | Nigella sativa<br>No. (%) | Tamsulosin<br>No. (%) |         |
| Painless       | 24 (61.5)                 | 10 (25.6)             | 0.001   |
| Mild           | 11 (28.2)                 | 15 (38.5)             |         |
| 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                     |                       | P value |
|------------|---------------------------|-----------------------|---------|
|            | Nigella sativa<br>No. (%) | Tamsulosin<br>No. (%) |         |
| 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)              |         |

seeds oil dissolved kidney stones or caused a significant excretion and therefore a reduction in size of the stones (18). Our findings are consistent regarding the effect of black seeds oil on renal stone size and excretion, although the excretion rate and decrement in size were more visible in our study.

Yun et al studied chemical constituents and pharmacological effects of the genus *Nigella sativa*. The urinary and tissue parameters results showed that calcium crystals formation and oxalate excretion were significantly reduced, indicating a therapeutic and prophylactic effect of these seeds on kidney stones (19). In our study, the drug's clinical efficacy in improving pain and excretion of kidney and ureteral stones was investigated. Tissue specimens and urinary parameters were not evaluated. However, regarding decreasing stone size that is secondary to crystal formation, this study is consistent with the above study. In Abdel-Aal et al, crystallization parameters of aqueous extract of black seeds on growth inhibition of calcium

oxalate monohydrate fragments are evaluated. According to their results, the oxalate excretion rate and the size of the black seeds were significantly reduced (20). Results of our study are consistent with the study by Abdel-Aal et al. However, two differing aspects are that black seeds were examined in capsule form and only stones larger than 6 mm in size were examined. In some studies, honey is added in combination with the black seed oil and used to treat a urinary stone that, in addition to its powerful antioxidant and anti-inflammatory properties, enhances black seeds efficiency (13,20).

In the study of Ali and Blunden, the pharmacological and toxic effects of black seed were investigated. The most significant biological compound was Timokin, a major component of volatile and stable oils. These compounds have anti-inflammatory, antimicrobial, and anti-tumor effects (21). There were no specific complications in our study. Only one patient in each group was excluded due to a lack of follow-up. Of note, is that our dose was lower than in some other studies.

In the studies of Yencilek et al, Georgiev et al, and Losek et al, the effect of tamsulosin on ureteral stone excretion was investigated. In their studies, tamsulosin facilitated the excretion of stones below 10 mm and also improved their movement to the distal part of the ureter (22-24). Tamsulosin reduced pain and facilitated the removal of ureteral stones, which is consistent with our study results (23,24).

Omar A et al studied the aqueous extracts of the *Nigella sativa* melanin; which experimental in vivo test and in vitro HEP-2 cell lines showed some cytotoxicity effects. In these studies, thymoquinone in black seed and butanol components and melanin were the most effective elements in treating and preventing kidney calculus and had anti-inflammatory and antioxidant effects (25).

## 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.

## Acknowledgments

We present our appreciation to the respected vice president's technical and research department of YUMS that provides the facility with material and ethical support. Additionally, we thank all staff of the medicinal plant

research centers of YUMS who assisted us in performing this project.

#### 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.

#### Funding/Support

The deputy of the YUMS research supported this project financially (Grant #960431).

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