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The Effect of Parsley in the Treatment of UTI in Iraqi Patients

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ABSTRACT

Background: *Urinary tract infections (UTI) are a common worldwide problem that affects the life of 150 million patients. As the problem of antibacterial resistance is rising, there is a growing and a continuous need for additional antimicrobial agents which could be from herbal sources. Parsley is a well-known herbal agent used in folk medicine in a variety of conditions.* ***Aim:*** *This study aimed to investigate the role of parsley in the treatment of UTI.* ***Method:*** *Total 37 patients were recruited and diagnosed as having UTI after taking a detailed history, performing a clinical examination, conducting GUE (general urine exam), and abdominal ultrasonography (U/S). They were prescribed parsley powder containing capsule 500 mg twice daily for 10 days. Patients were re-evaluated after 14 days for the same parameters.* ***Results:*** *The patients have expressed marked improvement after completing their course of treatment with parsley in terms of frequency, urgency, dysuria, suprapubic pain, and loin pain with high statistical significance. Moreover, the parameters of GUE have shown a strong decline in terms of acidity, pus cells, RBCs, crystals, and epithelial cells with high statistical significance.* ***Conclusions:*** *Parsley is a promising agent that could be implemented in the treatment of UTI. Further studies are required to explore the possibility of extracting its antimicrobial constituents for the preparation of new antimicrobials at an industrial level.*

Keywords: Parsley, UTI, GUE, pH, Clinical, Urolithiasis

INTRODUCTION

Urinary tract infections constitute the second most common infections presentation in community practice. Annually, about 150 million people worldwide were diagnosed with UTI [1]. Management of UTI requires investigating the possible site of infection and the responsible pathogen which could involve both the upper and/or lower urinary tract [2]. Lower urinary tract infections 'cystitis' is characterized by a spectrum of dysuria, urgency, frequency, and suprapubic pain [3].

The etiology of UTI may vary according to age, sex, contamination within or outside the hospital, and previous antibiotic usage [4]. The causative microorganisms are usually gram-negative bacteria, most commonly, *E. coli* followed by other bacteria, such as *Klebsiella spp., Enterococcus spp., Pseudomonas spp., and Proteus spp*. In addition, *Staphylococcus saprophyticus*, a gram-positive bacterium, has shown to be the second most frequent cause of uncomplicated UTI [5].

Candida is a common pathogen in hospitalized patients, especially those with predisposing factors like diabetes or indwelling urinary catheters [6].

In addition to the clinical findings, diagnosis requires GUE. The presence of pus cells in urine is an accompaniment of significant bacteriuria and their absence may exclude UTI [7]. Patients who are suffering from symptomatic UTI are usually prescribed empiric antimicrobial treatment while the culture and sensitivity results are pending.

Antimicrobial resistance is an expanding global problem. Nowadays, the choices of effective antibiotics that may be used in UTI are limited, particularly as new resistant strains emerge [8]. Thus, there is an urgent need for newer antimicrobial agents to be used empirically or as a definitive therapy. Medicinal plants may offer an alternative for the management of UTI [9,10]. Hence, they are attracting much research to develop new antimicrobial agents.

Parsley: [(*Petroselinum crispum*. Synonym: *Petroselinum sativum*), checked on http://www.theplantlist.org [11]],

is a member of the Umbelliferae family. It is regarded as an aromatic, culinary, herbal medicine, which has been utilized in the pharmaceutical industry. In traditional medicine, it is considered to be a diuretic, uterine stimulant, emollient, and anti-parasitic agent. It is commonly employed for the treatment of chronic bronchitis and dyspepsia [12]. Its leaves and stems are indicated in the cases of menstrual problems, cystitis, oedema, kidney stones, and prostatitis [13,14]. The constituents of parsley, which include flavonoids, ascorbic acid, carotenoids, myristicin, apiole, various terpenoid compounds, phthalides, phenylpropanoids, coumarins, furanocoumarins, and tocopherol, have been chemically investigated [15,16].

To the best of our knowledge there is no clinical study for the effect of parsley in the treatment of UTI, therefore, our objective was to evaluate the clinical advantages of parsley in the treatment of UTI.

PATIENTS AND METHODS

Patients and Samples

This is a prospective clinical study on patients with UTI who were attending a private GP clinic from January 2017 to May 2017. Total 44 patients with UTI symptoms who attended a private GP clinic were recruited after giving an informed written consent approval. The study was approved by the scientific and ethical committees in Al-Kindy College of Medicine/University of Baghdad and has followed the guidelines of the Declaration of Helsinki and Tokyo for humans.

Inclusion Criteria

Patients who included complaints of symptoms consistent with UTI, including increased frequency of urination, urgency, dysuria, suprapubic pain, and loin pain were included in the study.

Exclusion Criteria

Patients were excluded if they were currently on antibiotics, previously treated for a UTI within the past month, had severe comorbidities (end-stage renal disease or immunocompromised), had a recent urologic procedure, had an indwelling catheter or congenital genitourinary problems, or pregnancy.

UTI was diagnosed based on case history, clinical examination, GUE and abdominal U/S. The severity of symptoms was graded as follows: (none (-), mild (+), moderate, (++) and severe (+++). For these criteria, the sum symptoms score was calculated and recorded out of 20 (by giving a score from 1 to 4 for each of the 5 previously mentioned symptoms according to the severity and then adding all the scores to get the sum symptoms score) at each time interval. Sum symptoms scores for patients were calculated as similar to those used in other UTI trials [17].

GUE was conducted routinely using a 10 ml sample. Microscopically, GUE findings (RBCs, pus cells, crystals and epithelial cells)/high power field (HPF) were graded in a similar way as 0-4 as (-), 5-9 as (+), 10-14 as (++), and 15-19 as (+++). For these criteria, the sum GUE score was calculated and recorded as out of 16 at each time interval (by giving a score of 1 to 4 for each of the 4 previously mentioned GUE parameters according to severity and then adding all the scores to get the sum GUE score).

Patients with clinical and laboratory-confirmed UTI were prescribed parsley powder containing capsule 500 mg twice daily for 10 days. Symptoms and GUE parameters for each patient were reviewed after 14 days.

Parsley Powder Preparation

Parsley leaves and stalks were dried in a dry room for 1 week. Then, the leaves, and stems were grinded using an electric grinder. Finally, the resultant powder was packed into capsules (500 mg each).

Statistical Analysis

Graph pad 5 software package was utilized for statistical analysis. The results were expressed as mean ± SD. The statistical significance was calculated using Fischer's exact test and Wilcoxon signed rank test implementing *$p<0.05$ as a significance level. The analysis was conducted in June 2017.

RESULTS

Total 44 patients were recruited, with a mean age of 32.4 ± 9.9 years. Most of them were females 40 (90.9%), while

the males were 4(9.1%) (Table 1). According to the age group, the highest incidence of UTI was in 41-45 years old (10 patients, 27%) followed by 16-20 years old age group (8 patients, 21.6%). Regarding the marital status, most of them were single (24 patients, 54.5%), while the rest were married (20 patients, 45.5%). After commencing the treatment, 7 out of 44 (16%) patients failed to come at the second assessment and therefore we were left with 37 patients.

Table 1 Patients demographics distribution by age, sex, and marital status

Variable	N (%)
Sex	
Male	4 (9.09%)
Female	40 (90.91%)
Marital status	
Single	24 (54.55%)
Married	20 (45.45%)
Age groups	
16-20 years	8 (21.6%)
21-25 years	3 (8.1%)
26-30 years	6 (16.2%)
31-35 years	0 (0%)
36-40 years	7 (18.9%)
41-45 years	10 (27%)
46-50 years	0 (0%)
51-55 years	3 (8.1%)
56-60 years	0 (0%)

Evaluation of the patients after 14 days of treatment with parsley powder capsules showed marked improvement in their baseline symptoms and GUE parameters as compared with day 0. As Table 2 demonstrates, 11/17 patients ($p=0.011$) reported improved frequency, 17/20 ($p<0.0001$) reported improved urgency, 100% ($p<0.0001$) were recovered from dysuria and suprapubic pain, and 23/31 patients ($p<0.0001$) reported improvement in their loin pain. Sum symptoms score showed a significant decline to 3 ± 0.54 in the second assessment as compared with baseline scores of 5.94 ± 0.14 ($p=0.0313$). However, this comparison did not consider the severity of symptoms as shown in Table 2 (Figure 1).

Table 2 Patients presentations in terms of symptoms and signs, abdominal U/S findings

Symptoms	**Day 0**										**Day 14**										
	-	**%**	**+**	**%**	**++**	**%**	**+++**	**%**	**Total affected**	**%**	**-**	**%**	**+**	**%**	**++**	**%**	**+++**	**%**	**Total affected**	**%**	**p- value**
Frequency	20	54.10%	14	37.80%	0	0.00%	3	8.10%	17	45.90%	31	83.80%	6	16.20%	0	0.00%	0	0.00%	6	16.20%	0.0111
Urgency	17	45.90%	17	45.90%	0	0.00%	3	8.10%	20	54.10%	34	91.90%	3	8.10%	0	0.00%	0	0.00%	3	8.10%	< 0.0001
Dysuria	18	48.60%	16	43.20%	3	8.10%	0	0.00%	19	51.40%	37	100%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	< 0.0001
Suprapubic pain	0	0.00%	37	100%	0	0.00%	0	0.00%	37	100%	37	100%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	< 0.0001
Loin pain	6	16.20%	27	73.00%	4	10.80%	0	0.00%	31	83.80%	29	78.40%	8	21.60%	0	0.00%	0	0.00%	8	21.60%	< 0.0001
U/S findings	**-**		**%**		**+**		**%**		**Total affected**	**%**	**-**		**%**		**+**		**%**		**Total affected**	**%**	
	3000.00%		81.10%		700.00%		18.90%		700.00%	18.90%	3000.00%		81.10%		700.00%		18.90%		7	18.90%	
GUE	**-**	**%**	**+**	**%**	**++**	**%**	**+++**	**%**	**Total affected**	**%**	**-**	**%**	**+**	**%**	**++**	**%**	**+++**	**%**	**Total affected**	**%**	**p-value**
Pus cells	0	0.00%	9	24.30%	28	75.70%	0	0.00%	37	100%	30	81.10%	7	18.90%	0	0.00%	0	0.00%	7	18.90%	< 0.0001
RBCs	6	16.20%	21	56.80%	10	27.00%	0	0.00%	31	83.80%	21	56.80%	16	43.20%	0	0.00%	0	0.00%	16	43.20%	0.0006
Crystals	0	0.00%	30	81.10%	3	8.10%	0	0.00%	33	89.20%	19	51.40%	18	48.60%	0	0.00%	0	0.00%	18	48.60%	< 0.0001
Epithelial cells	11	29.70%	13	35.10%	10	27.00%	3	8.10%	26	70.30%	25	67.60%	12	32.40%	0	0.00%	0	0.00%	12	32.40%	0.0023
Ph	**Acidic**		**%**		**Alkaline**		**%**				**Acidic**		**%**		**Alkaline**				**%**		**p-value**
	34 patients		91.90%		3 patients		8.10%				29 patients		78.40%		8 patients				21.60%		0.1898

GUE findings on day 0 (the commencement of the study) and on day 14 after starting the treatment. Symptoms were graded according to severity to (-): none, (+): mild, (++): moderate, and (+++): severe. GUE findings/HPF were also graded as 0-4 as (-), 5-9 as (+), 10-14 as (++), and 15-19 as (+++). Statistical analysis was performed using Fisher's exact test implementing $p<0.05$ as a significance level.

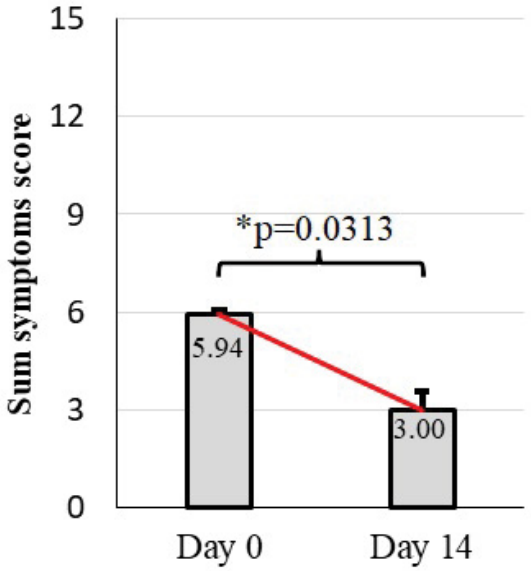

Figure 1 Time course change of sum symptoms score in UTI patients. Sum symptoms score was calculated on day 0 and on day 14 after starting treatment. Statistical analysis was done using Wilcoxon signed rank test which shows statistical significance at *p=0.0313

There was no change in abdominal U/S findings; renal stones were persistent in 7 patients (18.9%) after treatment on day 14. Conversely, marked improvement was seen in GUE parameters of the patients as compared to the baseline test. The GUE at day 14 showed absent pus cells in 30/37 ($p<0.0001$), absent RBC in 15/31 ($p=0.0006$), absent crystals in 15/33 ($p<0.0001$) and absent epithelial cells in 14/26 ($p=0.0023$) as shown in Table 2. Sum GUE parameters score showed a decline in day 14 (4 ± 0) compared with day 0 (5.79 ± 0.29), however, this was statistically not significant ($p=0.0625$) and this comparison did not consider the score of parameters as shown in Table 2 (Figure 2). In terms of urine pH, 5 patients (13.5%) have their urine pH changed from acidic to alkaline, however, this was statistically not significant ($p=0.1898$) (Table 2). The patients didn't complain of a side effect that draws attention.

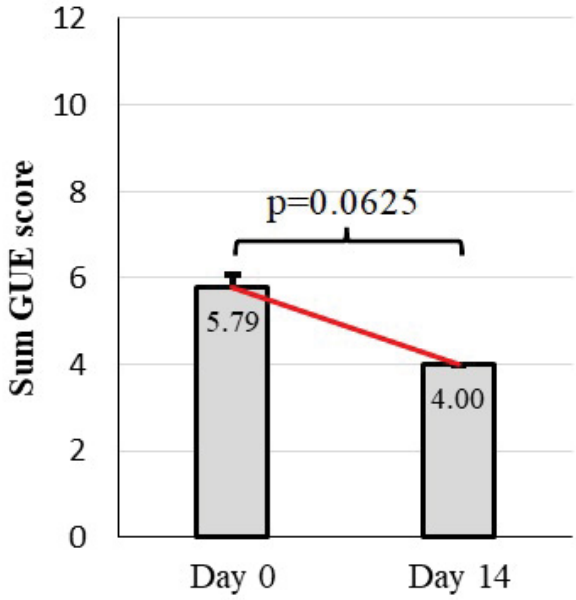

Figure 2 Time course change of sum GUE score in UTI patients. The score was calculated on day 0 and on day 14 of treatment. Statistical analysis was done using Wilcoxon signed rank test which shows no statistical significance at p=0.0625

DISCUSSION

Parsley is a herbal agent this is used in folk medicine for the treatment of UTI. However, its precise role has not been investigated through a clinical study. Thus, our study is the first clinical trial study trying to explore the role of parsley in the treatment of UTI.

The results show the effective role of parsley in improving the symptoms of UTI and urine examination findings. This role could be attributed to its chemical constituents and their physiological and chemical properties. Parsley is rich with apigenin, which was shown to possess a diuretic effect in addition to anti-inflammatory properties. Both effects are vital in the treatment of UTI [18,19]. The diuretic effect could be explained by the inhibition of Na-K pump activity [18]. Moreover, this would explain the shift of urine pH towards the alkaline side. Urine alkalinization is vital in the management of calcium- and phosphate-containing crystals/stones which are the most prevalent types [20,21].

The analgesic effect of parsley has been reported in traditional medicine as well as in animal studies [22,23]. It has been proposed that parsley constituents interfere with the analgesic paths like opioidergic, GABAergic, cholinergic and glutamatergic systems [24]. This effect is important to relieve the classical symptoms of UTI involving dysuria, suprapubic, and loin pain.

The alkalinizing effect of parsley together with a diuretic, lowering urinary calcium excretion, and decreasing urinary protein excretion have contributed to the recommendation of parsley as a safe and effective anti-urolithiasis remedy [25-27]. Failure to resolve renal stones in our study could be attributed to the short duration of the treatment course. Antibacterial effect of parsley has been under focus during the last decade. The essential oil extracted from parsley seeds and aerial parts is shown to have antibacterial activity against *Escherichia coli*, *Staphylococcus saprophyticus*, and *Klebsiella spp.* which are the most common pathogens in uncomplicated UTI in addition to its effect on *Listeria monocytogenes*, *Salmonella enterica*, *Enterobacter cloacae*, and *Pseudomonas aeruginosa* [5,28-30]. The antibacterial effect could be mediated by several constituents; namely: carotenoids via boosting immune response whether humoral or cell-mediated and ascorbic acid due to its induction of cell-mediated immunity [31,32]. Another constituent with antimicrobial effect is coumarins which are known to activate macrophages and furanocoumarins by disrupting DNA replication and thus inhibiting bacterial growth [33,34].

In addition to the antibacterial effects, parsley essential oil has shown antifungal activity against *Candida* [35]. Antifungal properties have been attributed to the coumarins compounds [36].

CONCLUSION

Parsley is a promising agent that can be used in the treatment of UTI symptoms. Further studies are required to investigate the possibility of the production of antimicrobial and/or antifungal agents derived from parsley chemical constituents.

DECLARATIONS

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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