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Original Article

The Effect of *Rosa damascena* on Children's Enuresis: A Randomized Pilot Study

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Abstract

Background and Aim: Enuresis is one of the common problems among children. The present pilot study was conducted to investigate the effect of Rosa damascene on nocturnal enuresis in children.

Materials and Methods: A randomized pilot study was performed from April 2017 to March 2018. The study participants were 40 children aged between 5-12 years with nocturnal enuresis. They were randomly divided to intervention and control groups using block randomization. The intervention group received *R. damascena* petals under the brand name Gole-Ghand (Barij- essence, Iran) as 5 cc orally, every 8 hours for one month. The control group received desmopressin as nasal spray (Sina Darou, Iran) 1-2 puffs for one month (maximum 20 mg daily). The primary outcome was complete or partial improvement in enuresis. The secondary outcome was frequency of side effects in patients.

Results: Twenty-two out of 39 patients 22 (56.4%) were male and 17 patients (43.6%) were female with the average age of 7.3±1.86 years. There was no noticeable distinction between the groups in age, sex, urbanity, history of treatment, and primary or secondary enuresis ($p>0.05$). Complete improvement was observed in 14 patients (70%) in the control group. Partial improvement was observed in four patients (20%) in the control group and in six patients (31.5%) in the intervention group ($p:0.001$). No side effect was reported during the study in the intervention group.

Conclusion: Based on the results of this pilot study, the use of R. *damascena* may lead to partial improvement against enuresis in some children. Further studies are required to evaluate this hypothesis.

Keywords: Enuresis, Child, Rosa damascene, Clinical study, Iran

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Introduction

Nocturnal enuresis (NE) is a prevalent health problem among children. Parents often worry over this disorder. Approximately 10% of children aged 6 years old and 5% of children aged 10 years old suffer from NE (1). It has been indicated that NE can cause psychosocial dysfunction in 20%-30% of children (2, 3).

There are several mechanisms responsible for enuresis. Each mechanism may be confirmed by some studies Nocturnal enuresis in some children is because of abnormal nocturnal plasma vasopressin release (4).

Some patients may have an overactive bladder and several other problems (5).

Pharmacological and non-pharmacological approaches are available for the treatment of NE. Pharmacological treatments include the use of anticholinergic drugs, smooth muscle relaxants, tricyclic antidepressants, and antidiuretics (6, 7). There are some non-pharmacological treatments for enuresis, including behavioral treatments and alarm therapy (7, 8). In some studies, the effect of non-pharmacological approaches was compared with pharmacological interventions (9).

In spite of the importance of enuresis, sometimes it is difficult to convince parents about the treatment of their children. Some parents do not consider enuresis as a serious problem in their children. Therefore, they persist for an alternative treatment or herbal treatment, and some parents are disinclined to take chemical medications for a long time to reduce side effects. On the other hand, an increasing interest in herbal treatments has been recently observed among people. Thus, the evaluation of the efficacy and safety of medicinal plants is necessary and logical.

In spite of the effectiveness of pharmacological treatments, their side effects are common and unpleasant for children and parents. Some parents are disinclined to take chemical medication for a long time because of probable side effects (10). Hence, treatment of some patients with herbal and alternative approaches is inevitable.

Desmopressin is the first treatment recommended for nocturnal enuresis (11). Unfortunately, its use is limited due to the occurrence of hyponatremia and seizure in some patients (12, 13). Anticholinergic drugs are routinely used in the treatment of enuresis. Common drugs are oxybutynin and tolterodine (14). They can improve enuresis via reducing uninhibited detrusor contractions, increasing the threshold volume at which an uninhibited detrusor contraction takes place, and enhancing the functional bladder capacity (15). Regarding the side effects of chemical medications, additional studies are required to discover effective medications with fewer side effects. Herbal medicines have been traditionally used to improve the NE. The mechanism of action is variable. They vary from anticholinergic (16) to spasmolytic (17), antispasmodic (18) and other sorts of medications. In many herbs, specific mechanism of action is unknown.

Rosa damascena is one of the most significant species of Rosacea family. *Rosa damascena* is mostly known for its perfume (19). However, it has many pharmacological properties, including antioxidant, anticonvulsant, anti-depressive, anti-inflammatory, and laxative properties. These results were reported in in vitro and in vivo studies (20-22). It has been shown that *R. damascena* can be effective on the cholinergic system, which may be useful in controlling enuresis. However, as far as we know, this has not been clinically examined. To offer new insight, the present randomized pilot study was conducted to evaluate the clinical effect of *R. damascena* on nocturnal enuresis of children.

Materials and Methods

This research was a pilot randomized clinical study with two parallel groups. It was performed in Dr. Sheikh Hospital, Mashhad University of Medical Sciences, Mashhad, Iran from April 2017 to March 2018. The study participants were 40 children, aged between 5-12 years with nocturnal enuresis. The diagnosis of enuresis was documented based on the patients' history, symptoms and physician examination. Enuresis was considered as primary if the patient had never been dry at night. Enuresis was considered as secondary if the patient had had a period of being dry for at least 6 months (23). Patients with mellitus diabetes, urolithiasis and urological abnormalities were excluded. Consort flowchart of the study has been shown in Figure 1. Patients were randomly assigned to the intervention and control groups via block randomization. Since this intervention involved aromatic compound, blinding was not an option. We opened the allocation list only after the groups were created. At the time of randomization, an expert who did not then contribute to the study gave each participant a sealed, opaque envelope.

Parental informed consent was obtained prior to the study. The information of all the patients remained anonymous, coded and confidential with the researchers. The intervention group received *R. damascena* petals under the brand name Gole-Ghand (Barij- essence, Iran) as 5 cc, every 8 hours orally for one month. The dose was selected according to the recommendation of manufacturing company. The

control group received desmopressin as nasal spray (Sina Darou, Iran) 1-2 puffs for one month (maximum 20 mg daily). The major outcome was complete or partial improvement in enuresis. Complete improvement was defined as bedwetting less than 2 times during 1 month. Partial improvement was defined as 50% bedwetting decrement. Secondary outcome was the side effect of the intervention. Moreover, age, gender, location, age of toilette training, type of enuresis, and history of treatment were evaluated and analyzed in the groups. All the patients were trained about how to consume the drugs accurately (time of use, exact amount of consumption and other recommendations). One of the researchers (RS) had an active relationship with all the patients for giving the medicine under supervision of an expert nephrologist (AA). No placebo was used during the study.

This study was approved by the Ethics Committee of Mashhad University Medical Sciences (code: IR.MUMS.fm.REC.1395.633) and registered in Iranian Registry of Clinical Trials (IRCT) (code: IRCT2017050233653N2).

Sample size

This research could be categorized as a pilot study. Twenty patients in each group were selected according to the reliable sample size in the pilot studies (24, 25), consultation of the statistician and available patients at the time of study.

Statistical Analysis

Statistical analysis was performed using SPSS windows program Version 16 (Chicago, IL, USA). All the experimental values were presented as means ± standard deviation (SD). Qualitative variables were presented as frequency and percentage of frequency. Normal distribution was checked via shapiro-wilk test. Due to normal distribution, the comparison between the groups was made using t-test. The relationship between qualitative variables was examined using chi-square test. P-value less than 0.05 was considered significant.

Results and Discussion

Among the included patients, 1 patient in the intervention group withdrew from the study. Therefore, 20 patients in the control group and 19 patients in the intervention group participated in the study. Twenty-two out of the 39 patients (56.4%) were male and 17 patients (43.6%) were female with the average age of 7.3±1.86 years. No remarkable difference was observed between the groups with regard to age and sex. Fourteen out of 39 patients (70%) in the control group and 13 patients (68.4%) in the intervention group lived in the city. No significant difference was observed (p: 0.91). In the control group, 10 patients (50%) were 3 years old or less. In the intervention group, 8 patients (42.1%) were 3 years old or less. No significant difference was observed (p: 0.66). The type of enuresis was primary in 14 patients (70%) in the control group and in 14 patients (73.7%) in the intervention group. No significant difference was observed (p: 0.79). There was a history of treatment in 11 patients in the control group (55%) and 11 patients (57.9%) in the intervention group. No significant difference was observed (p: 0.85). Baseline characteristics have been shown in Table 1.

Complete improvement was observed in 13 patients (65%) in the control group and 2 patients (10.54%) in the intervention group. Partial improvement was observed in 4 patients (20%) in the control group and in 6 patients (31.57%) in the intervention group. Significant differences were observed between the groups (p: 0.001). Thee data have presented in Table 2. No side effect was reported during the study in the intervention group.

Forty children with enuresis were studied in order to evaluate the effect of *R. damascena* on the improvement of enuresis. The use of *R. damascena* led to partial improvement in more than 30% of the patients.

As far as we know, this study is the first research that aimed to investigate the effect of *R. damascena* on children with enuresis. The present study indicated that the use *R.* damascena could lead to partial improvement in more than 30% of patients without any side effect. However, its effect was less than desmopressin.

The pharmacological impact of *R. damascena* are extensive. Antibacterial, antioxidant, antitussive, hypnotic, antidiabetic and relaxant effects on tracheal chains have been indicated for *R. damascena*. *R. damascena* was used in the treatment of cough in pediatrics as an effective and safe herb (20, 21). *R. damascena* contains various constituents such as terpenes, glycosides, flavonoids, and anthocyanins with

useful effects on human health. Lipid soluble (non-polar) components of this plant are primarily responsible for the bulk of of the above-mentioned impacts (19).

According to certain documents, *R. damascena* has some effects on the cholinergic system (26, 27), which may be responsible for its effect on enuresis. However, further studies are needed to recognize the mechanism of action. Anticholinergic drugs are common drugs in the treatment of enuresis. They decrease uninhibited bladder contractions and reduce bladder instability (15). The effect of anticholinergic drugs on enuresis has been frequently investigated. However, the results are inconsistent. In a study conducted by Friedman, beneficial effects of anticholinergicson enuresis were reported (28). In another study, the efficacy of oxybutynin in the treatment of enuresis was compared with desmopressin. It was reported in this study that oxybutynin could be used as second line in the treatment of enuresis (29). In another study, effects of oxybutynin were compared with the placebo and the authors stated that the effect of oxybutynin is not more than the placebo (28).

The efficacy of herbal treatment against enuresis has been frequently investigated (31-33). In a randomized clinical trial conducted by by Schloss on an herbal compound under the brand name Urox® it was reported that it could assist children to decrease bedwetting significantly (31). In another study on Radix Ephedrae it was reported that it could decrease the grade of NE significantly without correlation with the age of children (32). In a review on medicinal plants used in Iranian traditional medicinal, it was reported that most of them act via their anticholinergic and antispasmodic effects. However, more clinical trials are needed because of low valid clinical evidences confirming their effects (34). In a systematic review comparing the alarm therapy versus desmopressin, it was reported that enuresis alarm could lead to about 50% decrease in bedwetting and it is comparable with desmopressin (9). In a randomized clinical trial in which a comparison was made with regard to the efficiency of the topical use of Matricaria recutita L oil versus placebo in the treatment of enuresis in children it was reported that the use of chamomile oil could decrease the frequency of bedwetting in children with monosymptomatic nocturnal or daytime enuresis (35).

Limitations and Suggestions

Since children are vulnerable, there are more concerns concerning ethical issues in research on children. Thus, we were limited in choosing the dose and duration of treatment. More studies with add-on design, larger sample size and longer duration of treatment are required to be conducted.

Conclusion

Clinical effects of *R. damascena* in enuresis were investigated in the present study for the first time. The use of *R. damascena* could lead to partial improvement in more than 30% of the patients without any side effect. The present pilot research suggests that the use of R. *damascena* may lead to partial improvement against enuresis in some children. Further studies would be useful to evaluate this hypothesis.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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