



RESEARCH PAPER

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Evaluation of *Plantago major* aqueous extract in treatment of acute urticaria

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Abstract

Urticaria is one of the most common skin disorders that can markedly affect on patients' quality of life that is associated with multi strategy management in almost every case. The most important therapeutic method for urticaria is use of antihistamines such as cetirizine. This method has various side effects such as renal and hepatic complications. The best alternative for this method is use of traditional medicine and medicinal plants. In this way, *Plantago major* has been named in several references of Persian traditional medicine with effective properties in ameliorating urticarial symptoms. Thus, in this double-blind randomized clinical trial, 48 patients with urticarial were selected and divided into 2 groups, one group was treated with aqueous extract of *Plantago major* and another group with cetirizine syrup. According to data of this study, patients who treated with aqueous extract of *Plantago major* in comparison with another group, showed a better response to treatment. The rate of recovery was also higher in patients treated with aqueous extract of *Plantago major* with no side effects than cetirizine syrup group. In comparison with cetirizine syrup group, patients treated by extract of *Plantago major* had a better impact on patients' satisfaction. According to results of this study, *Plantago* extract could be applied for treatment of patients with urticaria with no side effects and duration of treatment.

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Introduction

Urticaria describes a group of skin disorders affecting adults and children. Transient pruritic, erythematous and edematous lesions of the skin are common symptoms of this disease (Kaplan and Greaves 2009). Urticaria disease has a significant negative effect on patients' quality of life and may result in psychopathological symptoms, such as anxiety (Barbosa *et al.* 2011). There are a range of methods for treatment. All of these therapeutic methods are developed to reduce the degranulation of mast cells and inhibit the vast flow of histamines to blood flow. The side effects of these methods as well as low response rate to treatment leads to investigate new approach for treatment of urticaria (Guldbakke and Khachemoune 2007, Morgan and Khan 2008). Different antihistamines like cetirizine are the first line of treatment in urticaria. However, these agents are associated with renal and hepatic complications (Bagenstose *et al.* 2004, Bonadonna *et al.* 2003, Townley 1991). By far, the most recognized mechanisms that trigger the progression of this condition are hypersensitivity reactions. Thus, development and introduction of new methods for treatment of this disease is necessary. Due to this, medicinal plant and traditional medicine are unique sources for investigation new approach. *Plantago major* is a species of *Plantago* that is member of family Plantaginaceae. The plant is native in most of Europe, Northern and central Asia (El-Bakatoushi 2011, Matsuura *et al.* 2014, Ren *et al.* 1999, Samuelsen 2000, Velasco-Lezama *et al.* 2006). This plant has approximately 250 species associated with benefit activities such as hypoglycemic effect, antiviral, cell proliferation, antioxidant, dendritic cells maturation, anti-inflammatory, cytotoxic activities and etc (Beara *et al.* 2012, Chiang *et al.* 2002, Huang Danfei *et al.* 2014, Ren *et al.* 1999, Velasco-Lezama *et al.* 2006, Zubair *et al.* 2012). *Plantago major* has also been named in several references of Persian traditional medicine with effective properties in ameliorating urticarial symptoms. According to this, the aim of this study was to investigate the effect of aqueous extract of *Plantago major* in treatment of urticaria according to

the current knowledge about the plant effects.

Materials and methods

Preparation of extract

The aqueous extract of urticaria was prepared using simple USP syrup with 63% glucose after boiling 10 gram seeds in water.

Treatment of patients

This study was double-blind randomized clinical trial. 48 patients with urticaria were selected. According to our previous study, these patients were divided into 2 groups, so that one group was treated with aqueous extract of *Plantago major* and another group with cetirizine syrup (Yazdian *et al.* 2014). For detection of improvement of patients, the conditions including itching, drug resistance and side effects on the days 15 by visiting a dermatologist at the clinic were investigated. These conditions were comprised in 2 groups. The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences. Informed consents were obtained from all the study participants at the initial visit and before administration of the drugs.

Statistical analysis

Statistical analysis was done by SPSS software (version 17.0). P value ≤ 0.05 was considered significant statistically.

Results

According to inclusion and exclusion criteria, totally 48 patients (20 male and 28 female) was evaluated in this study. Demographic data of 2 groups (age and sex) was summarized in Table 1. Based on Table 2, patients who treated with aqueous extract of *Plantago major* in comparison with another group showed a better response to treatment. There was one patient who was resistance to treatment although that was two in cetirizine syrup group with no significant changes statistically between two groups. Patients were compared in base of recovery rate and results were summerized in Table 3. The rate of recovery was higher in patients treated with aqueous extract of *Plantago major* than cetirizine syrup group. 21 and 17

patients were treated completely with aqueous extract of *Plantago major* and cetirizine syrup groups respectively after 7 days. Itching was tolerable in patients treated with aqueous extract of *Plantago major* group. Moreover, drowsiness was seen in

patients treated with cetirizine compared to another group. Totally, there was no side effects in patients treated with aqueous extract of *Plantago major* than cetirizine group in associated with better impact on patients satisfaction.(Figure 1,2 and 3).

Table 1. Information of patients in 2 groups (age and sex).

| | group | | p value |
|------------------|-------------------|-----------------------|---------|
| | cetirizine (n=24) | Plantago major (n=24) | |
| Age (year) | | | |
| Mean±SD | 34/7 ± 12/1 | 35/9 ± 12/6 | |
| Confidence limit | 29/6 -39/8 | 30/6-41/2 | 0.736 |
| Minimum- maximum | 15-56 | 16-59 | |
| Sex | | | |
| Male | 12 (50%) | 3/3%)38 (| 0.242 |
| Female | 12 (50%) | 16 (66/7%) | |

Table 2. Comparison of response to treatment and resistance to treatment into groups.

| | Group | | p value |
|---------------------------------|-------------------|-----------------------|---------|
| | cetirizine (n=24) | Plantago major (n=24) | |
| Appropriate response to therapy | 22 (91/7%) | 23 (95/8%) | 0.551 |
| Resistance to treatment | 2 (8/3%) | 1 (4/2%) | |

Table 3. Recovery rate of patients into two groups.

| Day of treatment | Group | | p value |
|------------------|-------------------|-----------------------|---------|
| | cetirizine (n=24) | Plantago major (n=24) | |
| first | 5 (20/8%) | 6 (25%) | 0.794 |
| third | 8 (33/3%) | 15 (62/5%) | 0.056 |
| 7 th | 17 (70/8%) | 21 (87/5%) | 0.060 |
| 14 th | 22 (91/7%) | 23 (95/8%) | 0.551 |

Discussion

Urticaria is one of the most common skin disorders that can markedly affect on patients' quality of life that is associated with multi strategy management in almost every case. The common symptoms related to urticarialinclude: transient pruritic, erythematous and edematous lesions of the skin that gradually disappear within a few hours (Deacock 2008). Hence, diagnosis is usually based on patients' history and clinical features of the disease. In this study, the effect of aqueous extract of urticaria on patients with urticaria was evaluated. Totally, 48 patients were treated with extract of urticaria and with cetirizine

syrup. *Plantago major* is a plant of the Plantaginaceae family. The articles showed that the extract of this plant generate active spot as an antibacterial (Najib *et al.* 2012). In addition, *Plantago major* has different activities such as anti-inflammatory, antiviral and antitumor effects as well as immunoenhancing properties (Chiang *et al.* 2002, Falcão *et al.* 2005, Gomez-Flores *et al.* 2000) that is used in Iranian traditional medicine and other countries for different proposes (Harput *et al.* 2012, Huang Dan-Fei *et al.* 2009, Li *et al.* 2014, Samuelsen 2000). The result of this study showed that the extract of *Plantago major* has potent activity on

patients with urticaria and was higher than cetirizine syrup. preparation of extract was done by water, although similar study with alcoholic extract of plantago leaves (with concentrations of 0.5 mg/ml) demonstrated that it can deploy high inhibitory activity more than 80% on IgE-dependent histamine release from RBL-2H3 cells, a tumor analog of mast cells. Results of this study indicated that active compounds of the extract inhibit mast-cell degranulation, and provide insight into the development of novel drugs for treating allergic skin manifestations (Ikawati *et al.* 2001).

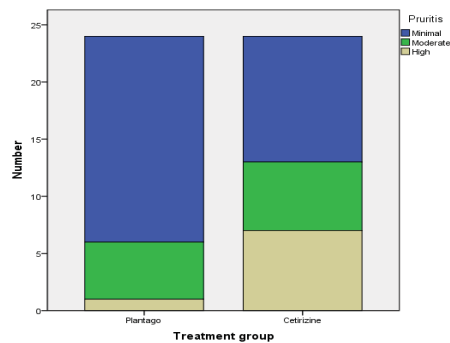


Fig. 1. Comparison of itching into two groups during treatment.

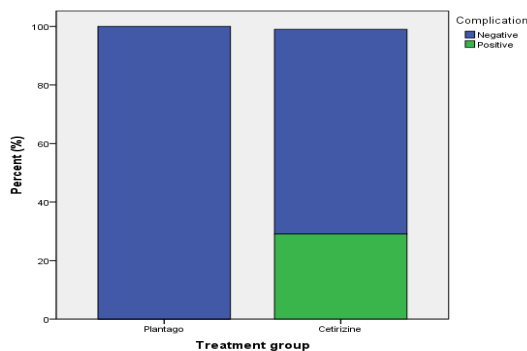


Fig. 2. Comparison of side effects into two groups during treatment.

One of limitations of antihistamine use for treatment of urticaria is side effects of these drugs such as drowsiness, renal and hepatic lesions (Gengo 1996, Walsh 2014). In this study, the results showed that the extract of *Plantago major* has no adverse side effect on patients. Moreover, drowsiness was seen in patients treated with cetirizine compared to another group. Many chemical compounds were identified and purified from *Plantago major* such as ursolic

acid, Luteolin and etc (Ringbom *et al.* 1998, Zembowicz *et al.* 2003). One of strategy for treatment of urticaria is inhibition of cyclooxygenase 2 (Hilário *et al.* 2006, Inomata *et al.* 2007, Sánchez-Borges *et al.* 2005, Zembowicz *et al.* 2003). Based on previous study, ursolic acid, a triterpenoid from plantago, can inhibit this enzyme and thus it can inhibit prostaglandin production. Regarding to this reason, the extract *Plantago major* can treat the urticaria disease (Ringbom *et al.* 1998). Itching is one of concern in patients with urticaria disease (Greaves Malcolm 2000, Greaves Malcolm W. 2014, Irfan and Honari 2014). In base of our study, itching was tolerable in patients treated with aqueous extract of *Plantago major* group. Totally, all measured factors were better in patients treated with aqueous extract of *Plantago major* than cetirizine group.

According to results of this study, *Plantago* extract could be applied for treatment of patients with urticaria with no side effects and duration of treatment.

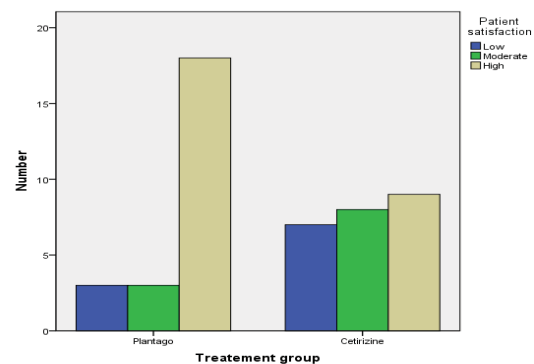


Fig. 3. Comparison of satisfaction of patients into two groups.

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