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# Effect of *Achillea millefolium* Distillate on Recovery Time in Patients with Gastroenteritis

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## Abstract

**Background:** Some animal studies have reported that *Achillea millefolium* (*A. millefolium*) extract can affect intestinal movements in rats. However, no study is available on the effect of *A. millefolium* on recovery from gastroenteritis in human subjects.
**Objectives:** This study aimed to investigate the effect of *A. millefolium* on recovery from gastroenteritis in patients over 12 years old.
**Patients and Methods:** A randomized controlled trial was conducted on 44 patients with gastroenteritis. The patients were randomly assigned to two groups of 22 each. The control group received the usual treatments. In addition to the usual treatments, the intervention group received 0.5 mL/kg of *A. millefolium* distillate every 8 hours. The duration of recovery was recorded for both groups. Descriptive statistics, Chi-square, Fisher's exact test, and the t-test were used to compare the two groups.
**Results:** The mean duration of recovery in the group receiving *A. millefolium* distillate was 1.31 $\pm$ 0.71 days, while it was 1.86 $\pm$ 0.71 days in the control group (P = 0.015).
**Conclusions:** Adding *A. millefolium* distillate to the usual treatment for simple gastroenteritis was effective in shortening the recovery time.

*Keywords:* Gastroenteritis, Diarrhea, Vomiting, Recovery, *Achillea millefolium*

## 1. Background

Acute gastroenteritis is a major public health problem and one of the most common diseases worldwide (1). According to the world health organization (WHO), about 2 billion cases of diarrheal disease occur annually (2).

Symptoms of gastroenteritis may be self-limiting or may require medication to resolve. The main symptoms may include fever, abdominal pain, lethargy, diarrhea, and vomiting, which can cause electrolyte imbalance, dehydration, and shock (3-7). Medical and nursing treatments usually include monitoring intake and output, oral or intravenous fluids, and electrolyte replacement (8); administration of zinc (1, 3, 6, 9, 10); oral or intravenous antiemetic medications, such as ondansetron (3, 4); and antibiotics in bacterial cases (11, 12). Such treatments may have side effects; for example, ondansetron may increase the frequency of diarrhea (13). Excessive use of antibiotics might also increase the cost of treatment, lead to bacterial resistance, and prolong the diarrhea (14, 15).

Due to the side effects of synthetic drugs, herbal remedies are increasingly used, which also have lower costs and better patient compliance (16). One of the plants that has been commonly used is yarrow, or *Achillea millefolium*, which belongs to the asteraceae family. This herb is traditionally used to treat abdominal pain, stomach pain, acute gastritis, wounds, and uncomplicated diarrhea (17, 18). It contains certain active ingredients, such as camphor, 1 and 8-cineol, borneol, and $\beta$-pinene (17), which are used for medicinal properties including anti-inflammatory, antioxidant, anti-spasmodic, anti-hemorrhoidal, and disinfectant effects (19). Despite the historical background of using *A. millefolium* and reports on its antiviral (19), anti-inflammatory (20, 21), antibacterial (22, 23), and antispasmodic (24) effects, studies about its application for the treatment of diarrhea are rare.

In a study on the antispasmodic effects of *A. millefolium*, Moradi et al. reported that its alcoholic extracts could inhibit the acetylcholine and KCL-induced contractions in the smooth muscles of isolated ileum in rats (24). In an in vitro study, it was reported that the extract of *Achillea* had antirotaviral activity (19). Borrelli et al. have also reported that *A. millefolium* aqueous extract can affect and normalize contractions in mouse and human stomachs (25). In a study on the antidiarrheal effect of a methanolic extract of *A. millefolium* in rats, Bais et al. (26) attributed such effects to decreased bowel movements and support of the intestinal mucus against chemical changes (25). Another recent study showed that a mouthwash solution containing *A. millefolium* distillate could reduce the severity of stom-

atitis in cancer patients undergoing chemotherapy (20). In local observations, the first researcher has observed that people in Lorestan Province, Iran, have traditionally used boiled *A. millefolium* to treat or relieve diarrhea.

## 2. Objectives

This study aimed to investigate the effect of *A. millefolium* on recovery time from gastroenteritis.

## 3. Patients and Methods

This randomized controlled trial was conducted on gastroenteritis patients referred to Shahid Beheshti medical center and an infectious specialist's office in Kashan, Iran, over a six-month period during the year 2015.

The sample size was calculated using the results of a pilot study on two groups (five patients each) with simple gastroenteritis. The first group received *A. millefolium* distillate similar to that used in the present study, and the second group received routine treatment. In the group that received *A. millefolium* distillate, the mean recovery time was $1.20 \pm 0.55$ days, while it was $2.0 \pm 0.70$ days in the second group. Consequently, the sample size was determined to be 19 patients in each group [$\alpha = 0.05$, $\beta = 0.1$]. However, we recruited 22 patients for each group to compensate for probable attritions.

The inclusion criteria were age over 12 years, a diagnosis of simple gastroenteritis, the ability to eat by mouth, lack of sensitivity to any herbal products (i.e. herbal drugs and foods), lack of asthma or allergic rhinitis, willingness to participate in the study, and lack of any other comorbidity, such as heart disease, diabetes, malabsorption, coagulopathy, or eczema.

The exclusion criteria were receiving an order of nothing by mouth during the study, the patient's decision to withdraw from the study, any incident requiring specific treatments, the use of herbal remedies other than *A. millefolium* distillate, intolerance to *A. millefolium* (i.e. vomiting immediately after ingestion), using any antidiarrheal diet, developing an allergy to *A. millefolium*, and irregular use or overuse of *A. millefolium* distillate.

On arrival, all patients were visited by a specialist in infectious diseases or a general practitioner, and those meeting the inclusion criteria were recruited. A total of 44 such patients were consecutively recruited and randomly assigned to the study groups.

### 3.1. Intervention

The usual treatment consisted of oral rehydration therapy and antiemetic medications, such as oral ondansetron (4 mg every 8 hours), metoclopramide tablets (10 mg at the time of nausea), and antispasmodic drugs, such as hyoscine tablets (20 mg) or dicyclomine (20 mg). In bacterial cases, oral antibiotics, such as metronidazole (250 mg every 8 hours) or oral Bactrim (400 mg every 12 hours), were also used.

The control group received the usual treatment. In addition to the usual treatment, the intervention group received 0.5 mL/kg of *A. millefolium* distillate every 8 hours (40 ppm concentration, purchased from Gol Joush Pharmaceutical Co., Tabriz, Iran). The pasteurized *A. millefolium* distillate was prepared in 120 mL dark glass bottles. Three bottles of *A. millefolium* distillate were given to each patient in the intervention group at the end of the physician's visit, and the patients were instructed to drink the prescribed dosage of *A. millefolium* distillate before each meal (i.e. every 8 hours), with a glass of water. They also were instructed to discontinue use of the distillate and to inform the physician or the first researcher if they could not tolerate it, or if any symptoms appeared, such as itching, burning, or rash. The patients paid nothing for the *A. millefolium* distillate. The outpatients carried out the prescribed treatment at home and followed up through telephone calls for three days. The hospitalized patients were treated at the hospital and assessed through daily visits by the same nurse.

All patients in both groups were instructed to rest until recovery, and to not take any other medications. They were also instructed to eat a regular diet but to not use fatty or sweet foods for at least three days. The hospitalized patients received the regular hospital diet.

### 3.2. Data Collection

A two-part instrument was used. The first part included demographic information, such as age, gender, education level, living location, and financial status. There were also questions on the severity of diarrhea at admission (mild: 3 - 5 times/day, moderate: 6 - 9 times/day, and severe: $\geq$ 10 times/day), whether they had a high fever on arrival (body temperature $<$ 38°C), the date of admission, and the names and dosages of the drugs prescribed.

The second part of the questionnaire was a form consisting of two questions about the duration of the disease, from the initiation of diarrhea or vomiting to the time of admission, and the number of days until complete recovery (i.e. normal defecation $<$ 3 times/day). The first part of the instrument was completed upon the patient's arrival and the second section was completed through daily visits or telephone calls for three successive days. All patients and the nurse who assessed their recovery were blinded to the type of treatment each patient was receiving.

### 3.3. Ethical Considerations

This study was approved by the institutional review board and research ethics committee of Kashan University of Medical Sciences (ethics code: IR.KAUMS.REC.1394.55, issued on 06.07.2015). All of the patients were briefed on the study's aims, without specification of the exact type of intervention they may receive. They also were assured about the voluntary nature of their participation, their right to withdraw from the study at any point, and data confidentiality. All of the subjects signed written informed consent before participation. The research team was careful to preserve the participants' rights according to the Helsinki ethical declaration.

### 3.4. Data Analysis

Data were analyzed using SPSS version 13. Descriptive statistics were used to describe the data. Chi-square and Fisher's exact tests were used to compare the two groups in terms of nominal and categorical variables, such as gender, education level, economic status, place of residence, the drugs used, and the presence of a high fever or abdominal cramps at arrival. The Kolmogorov-Smirnov test was performed to examine the normality of the quantitative variables. The age distribution was normal, but the distribution of the duration of symptoms before admission, the recovery duration, and the doses of the drugs used were not normal. Next, the t-test was used to compare the mean age of the two groups, and the Mann-Whitney U test was used to compare the duration of disease before admission, the mean duration of recovery, and the mean dose of drugs used in the two groups. A P value $< 0.05$ was selected as the significance level for all tests.

## 4. Results

A total of 44 patients with a mean age of $28.62 \pm 2.20$ years participated in this study. No significant differences were observed between the two groups in terms of personal and clinical characteristics, including the severity of diarrhea (Table 1). However, a significant difference was observed between the mean recovery time in the two groups (P = 0.015) (Table 2). No allergic reaction to *A. millefolium* was observed during the study and no attrition occurred in the study sample.

Table 3 shows the usual drugs used over the course of treatment in the two groups. The amount of antiemetic drugs used was higher in the control group. However, in terms of antibiotics, the amount of metronidazole was higher in the control group, while Bactrim was used more in the intervention group. Moreover, the amount of hyoscine was higher in the intervention group, while dicyclomine was used more in the control group.

**Table 1.** Personal Characteristics of Intervention and Control Groups[a]

| Variable | Group | | P Value |
|---|---|---|---|
| | Intervention | Control | |
| **Gender** | | | 0.220[b] |
| Male | 7 (31.8) | 11 (50) | |
| Female | 15 (68.2) | 11 (50) | |
| **Fever** | | | 0.741[b] |
| Yes | 6 (27.3) | 7 (31.8) | |
| No | 16 (72.7) | 15 (68.2) | |
| **Living location** | | | 0.457[c] |
| Urban | 19 (86.4) | 16 (72.7) | |
| Rural | 3 (13.6 | 6 (27.3) | |
| **Education level** | | | 0.838[c] |
| Illiterate | 3 (13.6) | 2 (9.1) | |
| Semiliterate | 10 (45.5) | 9 (40.9) | |
| High school and over | 9 (40.9) | 11 (50) | |
| **Economic status** | | | 0.99[c] |
| Sufficient | 19 (86.4) | 18 (81.8) | |
| Insufficient | 3 (13.6) | 4 (18.2) | |
| **Drugs used** | | | 0.101 |
| All of the drugs | 12 (54.5) | 14 (63.6) | |
| Antiemetics | 5 (22.7) | 8 (36.4) | |
| None | 4 (18.2) | 0 | |
| **Abdominal cramps** | | | 0.233[c] |
| Yes | 22 (100) | 19 (86.4) | |
| No | 0 | 3 (13.6) | |
| **Severity of diarrhea** | | | 0.538[b] |
| Mild | 6 (27.3) | 3 (13.6) | |
| Moderate | 9 (40.9) | 12 (54.5) | |
| Severe | 7 (31.8) | 7 (31.8) | |
| **Age, y (mean ± SD)** | 29.22 ± 3.04 | 28.51 ± 3.37 | 0.874[d] |

[a] Values are expressed as No. (%) unless otherwise indicated.
[b] Chi square.
[c] Fisher's exact test.
[d] t-test.

## 5. Discussion

To the best of our knowledge, this was the first study on the effect of *A. millefolium* distillate on gastroenteritis in a sample of human subjects. In this study, the mean duration of recovery was significantly shorter in the group receiving *A. millefolium* distillate. This effect might be attributed not only to the disinfectant properties of *Achillea's* active ingredients but also to its antispasmodic ef-

**Table 2.** Comparison of Mean Duration of Symptoms Before Admission and Mean Recovery Time

| Variable | Group | | P Value |
|---|---|---|---|
| | Intervention | Control | |
| **Duration of symptoms before admission, days** | 1.77 ± 0.81 | 1.54 ± 0.67 | 0.603 |
| **Duration of recovery, days** | 1.31 ± 0.71 | 1.86 ± 0.71 | 0.001 |

**Table 3.** Comparison of Drugs Used[a]

| Drug, mg | Group | | P Value |
|---|---|---|---|
| | Control | Intervention | |
| **Metronidazole** | 863.63 ± 993.21 | 272.72 ± 455.84 | 0.027 |
| **Co-trimoxazole** | 145.45 ± 486.70 | 436.36 ± 739.72 | 0.080 |
| **Ondansetron** | 9.09 ± 11.65 | 5.45 ± 6.23 | 0.615 |
| **Metoclopramide** | 15.45 ± 21.54 | 4.09 ± 10.53 | 0.019 |
| **Hyoscine** | 9.09 ± 11.91 | 15.90 ± 21.74 | 0.314 |
| **Dicyclomine** | 12.72 ± 23.33 | 2.72 ± 8.82 | 0.062 |
| **Diphenoxilate** | 0 | 0.77 ± 2.72 | 0.153 |

[a]Values are expressed as mean ± SD.

fects, which cause decreased bowel movements. Although no significant differences were observed between the two groups with regard to the antibiotics received, the amount of antiemetic drugs used was significantly higher in the control group. This finding might also be attributed to the beneficial effects of *A. millefolium* distillate on vomiting due to gastroenteritis. An animal study also reported that alcoholic extract of *A. millefolium* could inhibit the smooth muscle contractions of isolated ileums in rats (24). Bais et al. have also reported that methanolic extract of *A. millefolium* showed antidiarrheal activity in rats (26). Some previous studies have also reported that *A. millefolium* has antiviral (19) and antibacterial (24) effects, which might also have contributed to the shorter recovery time of the patients in the intervention group.

When considering the results of this study, some limitations should be kept in mind. Firstly, this was the first human-subject study using *A. millefolium* distillate for gastroenteritis, and the study was conducted on a small sample, which might limit the generalizability of the findings. In addition, we did not perform any laboratory examinations to exactly distinguish between viral and bacterial diarrhea. The present study was conducted on a mix of hospitalized and outpatient subjects. There was telephone follow-up for the outpatients; however, monitoring their strict adherence to medical advice was not possible. Given these limitations, further studies with larger sample sizes are recommended. Finally, studies to identify the exact active ingredients that are effective against diarrhea and vomiting are suggested.

The present study showed that adding *A. millefolium* distillate to the usual treatments for simple gastroenteritis was effective in reducing the time of recovery. We observed no side effects in the patients during this study. Adding *A. millefolium* distillate to the usual treatments for simple cases of gastroenteritis can therefore be recommended.

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## Footnotes

**Authors' Contribution:** Mohsen Adib-Hajbaghery and Masoumeh Abdi were responsible for the study conception and design. Masoumeh Abdi performed data collection and preparing the first draft of the manuscript. Mohsen Adib-Hajbaghery did the data analysis, made critical revisions to the paper for important intellectual content, and supervised the study. Mohammad Reza Sharif helped in data collection.

**Conflict of Interest:** The authors have no conflict of interest to declare.

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