JOURNAL OF HERBAL MEDICINE 5 (2015) 71–76

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The effect of *Matricaria chamomilla* (chamomile) extract in Orabase on minor aphthous stomatitis, a randomized clinical trial

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ARTICLE INFO

Article history:
Received 22 September 2014
Received in revised form
7 February 2015
Accepted 5 May 2015
Available online 27 May 2015

Keywords:
Chamomile
Aphthous stomatitis
Triamcinolone

ABSTRACT

Recurrent aphthous stomatitis (RAS) is a common and painful oral mucosal disease, however, its aetiology and pathogenesis is not entirely clear. Many therapeutic protocols have been tried, but effectiveness remains an issue. The aim of this study was to compare *Matricaria chamomilla* (chamomile) extract and triamcinolone in Orabase on oral mucosal minor aphthous stomatitis. The study was a randomized, double-blind clinical trial. 45 patients participated in the study; randomly divided into three groups. The first group received placebo, the second group triamcinolone in Orabase and the third group chamomile in Orabase. Four variables were assessed in the study, including, size of the ulcer, intensity of pain, time required to complete resolution of the ulcer and satisfaction of patients. Triamcinolone and chamomile in Orabase reduced ulcer size by day 3 and pain by days 3 and 6 similarly with a significant difference from the placebo group. But triamcinolone in Orabase was superior to both chamomile in Orabase and placebo at reducing size of the ulcers by day 6 and the time taken to complete resolution of the ulcers. In addition, chamomile in Orabase produced patient satisfaction. According to this study, chamomile decreased the pain of the ulcers and provided satisfaction for the patients.

1. Introduction

Recurrent aphthous stomatitis (RAS) is one of the most common oral mucosal lesions and affects approximately 20% of the general population (Pourahmad et al., 2010). In a study by Davatchi et al. in Tehran, out of 10,291 interviewed people, 25.2% were affected by RAS (Davatchi et al., 2008). In another study performed by Shirzaei in Zahedan, of 1105 patients examined in Zahedan Health Centres, 18% suffered from RAS

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http://dx.doi.org/10.1016/j.hermed.2015.05.001
2210-8033/

(Shirzaei, 2011). According to these studies, prevalence of RAS is rather high in Iran.

RAS is more common in women than men and usually appears first in childhood or adolescence (Samet et al., 2007). RAS is divided, on morphological criteria, into three groups: minor ulcers, which are the most prevalent form (80% of all RAS), smaller than 1 cm in diameter and resolve within 10–14 days without scarring; major ulcers, which are characterized by painful ulcers, larger than 1 cm in diameter and lasting several weeks; and, herpetiform ulcers, a rare type of RAS with a bunch of small pinpoint ulcers (Babaee et al., 2010; Chattopadhyay and Shetty, 2011; Huling et al., 2012; Liu et al., 2012; Yasui et al., 2010). While the exact cause of RAS is still unknown, some aetiological factors such as genetics, allergies, medication, menstruation period, stress, excitement, fatigue, immune system dysfunction, bacterial or viral agents, chemical agents and vitamin deficiency have been suggested (Babaee et al., 2010; Chattopadhyay and Shetty, 2011; Huling et al., 2012; Kolseth et al., 2005; Liu et al., 2012; Messier et al., 2012; Wardhana and Datau, 2010). Of these factors, genetic is the most significant factor (Koybasi et al., 2006). The probability of someone suffering from RAS is 90% when both parents are affected, but only 20% when neither parent has RAS (Scully et al., 2003). Despite their self-limiting nature, many patients suffer from persistent ulcers, so that before an ulcer is healed, a new one appears. Ulcers can make speech, eating and swallowing uncomfortable for patients. Therefore may have a negative influence on patients' quality of life (Wardhana and Datau, 2010).

Treatments suggested for RAS are often palliative to relieve pain, promote healing and prevent secondary infection. These treatments include corticosteroids, antibiotics, local anaesthetics, analgesics and immune modulators (Femiano et al., 2007; Liu et al., 2012; Messier et al., 2012). Corticosteroids such as triamcinolone are the mainstay of RAS treatment (Scully and Porter, 2008). The major concern here is adrenal suppression caused by systemic steroids and local adverse effects associated with topical therapy, including oral candidiasis (Gorsky et al., 2007). Chuanxia Liu and colleagues studied the efficacy and safety of a topical corticosteroid on RAS. In their study no important side effects were detected, except perioral rashes and burning at the site the corticosteroid was administered (Liu et al., 2012). Bakhtiari performed a study to evaluate patients' satisfaction of medicinal plants in Isfahan. 37% of patients knew herbal drugs well and better than chemical drugs. 21% believed that chemical drugs are better and 67% did not give an opinion. In fact due to the side effects of some chemical drugs, many patients would prefer to use herbal treatment. Considering the side effects of chemical drugs and patients' interest in using herbal medicines, medicinal plants have received increasing attention (Bakhtiari, 2010). Some herbs like *Alchemilla vulgaris*, *Matricaria chamomilla* and *Aloe barbadensi* have been reported to be used in the management of RAS (Mekseepralard et al., 2010). There have also been some trials on the effect of these substances on RAS, for example, in one, a paste containing *Myrtus communis* was compared to placebo in 45 patients with RAS and as a result the researchers declared that the herbal substance was effective in reduction of pain severity, ulcer size, erythema and exudates. They also found it effectively improved the quality of life of the patients (Babaee et al., 2010).

Chamomile is a widely available herb with diverse therapeutic uses that has been used for centuries as a medicinal plant (Srivastava et al., 2010). The components of the essential oil extracted from chamomile flowers possess anti-inflammatory, anti-allergic, anti-spasmodic, anti-bacterial, anti-pyretic, ulcer-protective, anti-fungal, sedative, analgesic and anti-oxidant properties (Ghavimi et al., 2012; Shrafzadeh and Alizadeh, 2011; Srivastava et al., 2010; Srivastava and Gupta, 2009; Zeggwagh et al., 2009). Some of these principle components are terpenoids, flavonoids, bisabolol and chamazulene (Shrafzadeh and Alizadeh, 2011; Srivastava and Gupta, 2009). Cimen et al. studied oxidant/antioxidant status in patients with RAS; they demonstrated that enzymatic and non-enzymatic antioxidant defence systems are impaired in patients with RAS (Cimen et al., 2003). Holbrook et al. demonstrated that the amount of antioxidant vitamins such as A, C and E is decreased in the saliva and serum of RAS patients (Holbrook et al., 1998). Therefore, the antioxidant potential of chamomile may promote healing of the ulcers. Hamalainen et al. demonstrated the inhibitory effect of kaempferol, daidzein, genistein and quercetin on STAT-1 and NF-κB, while naringenin, flavone and isorhamnetin inhibited only NF-κB activation and inducible nitric oxide synthase (iNOS) expression. While nitric oxide (NO) is induced in inflammatory processes, compounds that have an inhibitory effect on NO production can have an anti-inflammatory effect (Hamalainen et al., 2007). According to these studies, the anti-inflammatory mechanisms of the flavonoids in chamomile can play a role in healing of the ulcers. Chamomile tea has been recommended for mouth inflammation (Srivastava et al., 2010). In folk medicine, chamomile has been suggested for mouth ulcers (Amin et al., 2011). To our knowledge, there is one study about the effect of chamomile extract on aphthous ulcers. Ramos-e-Silva et al. evaluated the safety and effectiveness of a fluid extract of chamomile on pain relief in RAS. They evaluated two parameters, analgesic effect and tolerance. The analgesic effect was considered excellent by 82% and good by 18% of patients. Tolerance was excellent according to 97% and good by 3% of the participants (Ramos-e-Silva et al., 2006). In order to determine the efficacy of chamomile extract when applied topically for the treatment of RAS, a new Orabase containing chamomile extract was developed and a randomized, double-blind, placebo-controlled clinical trial was performed. The purpose of this study was to assess the clinical efficacy of Orabase containing Chamomile extract in treating RAS.

2. Materials and methods

The study was a randomized, double-blind, placebo-controlled clinical trial and was conducted at Shiraz University of Medical Science in Iran. 45 patients of both genders were enrolled for participation in the study. Patients were selected from September 2012 till May 2013. The inclusion criteria were that patients should have a clear history of RAS, be aged 18–60 years, have adequate motivation and understanding to participate in the study, and provide informed consent. The patients also had had only one minor aphthous stomata, initiated in