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CLINICAL STUDY

Evaluation of anti-aphthous activity of decoction of Nicotiana tabacum leaves as a mouthwash: a placebo-controlled clinical study

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Abstract

OBJECTIVE: To determine the effects of decoction derived from the leaves of Nicotiana tabacum (L.) as a mouthwash on minor recurrent aphthous.

METHODS: A randomized double-blinded placebo-controlled clinical trial was conducted on 60 patients with minor recurrent aphthous. Treatment comprised of application of tobacco or placebo mouthwash (10 mL 3 times a day) for 5 days. Clinical evaluation included pain level using a visual analog scale and ulcer size on days 1, 3, and 5 were measured. Adverse effects after mouthwash application were recorded, and the oral mucosa was examined by the investigator at each visit.

RESULTS: A total of 54 subjects with the mean age (38 ± 10) years fulfilled the study. No minor and major adverse effects were observed. In the treatment group, ulcer pain score was decreased by 79.2% and 93.8% and ulcer size was reduced by 69.1% and 92.2% (days 3 and 5, respectively), which was significantly greater than the control group ($P < 0.01$).

CONCLUSION: The decoction prepared with of Nicotiana tabacum leaves, used as mouthwash are well-tolerated and safe, and can be used for the management of recurrent aphthous.

Key words: Stomatitis, aphthous; Tobacco; Pain; Ulcer; Medicine, Traditional; Complementary therapies; Mouthwashes

INTRODUCTION

Recurrent aphthous ulcers (also termed canker sores) are currently one of the most common inflammatory ulcerative disorders of the oral mucosa.[1,2] This condition is characterized by painful, recurrent and single or multiple ulceration of the oral cavity that affect nearly 10%-20% of the general population.[2,3] The ethiopathogenesis of aphthae is unclear but some factors such as heredity, immune dysregulation, hematinic deficiency (like iron, folic acid, vitamin B6 and B12), stress, local trauma, infections and systemic diseases (Behcet's syndrome) have been proposed as causative factors.[4,5] Despite the multi-factorial etiology of the disease, most of the treatments for aphthae are designed to reduce pain and inflammation. However, in order to eliminate or reduce the symptoms, we need to search safer and more effective agents with multi-bioactivities.[6] Nowadays, there is an increasing tendency to use herbal med-

icines for the treatment of aphthae and several herb's extracts have been evaluated for this propose.[7-11]

The genus Nicotiana (L.) (Family: Solanaceae) comprises about 100 species and natively distributed in tropical America.[12-16] Three species of this genus, Nicotiana gluaca, Nicotiana rustica and Nicotiana tabacum are cultivated in Iran with the common Persian name of "Tanbakoo".[17] Nicotiana tabacum, of the most commercially valued agricultural herbs in the world, has half hardy annual subshrubs with rose-coloured flowers and elliptic-ovate leaves.[12-14] In folk medicine, the leaves of tobacco have been used in the treatment of backache, toothache, lumbago, gastrosis, ulcers and wounds.[12-14] As a medicinal plant, leaves have been used due to their sedative, narcotic, emetic and antispasmodic activities and applied for the rheumatic swelling and skin disorders.[12,14,15] According to the literature, different biological compounds, such as, isoflavones,[13] phenolic acids,[15] sesquiterpenes,[16,18] diterpenoids,[19,20] and alkaloids were isolated from tobacco but alkaloid constituents, chiefly nicotine, are the most important part of these components due to their main pharmacological and biological activities.[21,22] Moreover, several reports revealed that smoking has potential inhibitory effects on the occurrence of aphthous ulcers.[3,23-25] In the light of above findings, it is reasonable to assess the anti-aphthous activity of tobacco leaves extract against aphthous ulcers. In the present study, anti-aphthous activity of the leaf decoction from Nicotiana tabacum as a mouthwash was evaluated on patients with recurrent aphthous ulcers.

MATERIALS AND METHODS

Preparation of decoction and formulation (Sample preparation)

Dried leaves of Nicotiana tabacum were purchased from local bazaar market, Kermanshah, Iran.

500 grams of Nicotiana tabacum leaves was ground and decocted with 10-folded mass of water (5000 mL) for 30 min, filtered, and then let the decoction be cooled down to room temperature. For preparation of a mouthwash, 3000 mL of filtrated decoction was mixed with 3 grams of a mixture of methylparaben and propylparaben (9∶1) as preservatives. In addition, placebo was prepared in similar container including distilled water with approved color additives which looked the same as the tobacco mouthwash. The placebo mouthwash also had similar label as the tobacco mouthwash preparation.

Subjects and study design

In this randomized double-blinded placebo-controlled clinical study, 60 patients were assigned into group of placebo (n = 30) and group of tobacco treatment (n = 30). Patients were seen at the Infectious Diseases Clinic, Kermanshah University of Medical Sciences, Kermanshah. Randomization of equal number of subjects to placebo or treated group was achieved using a simple random allocation strategy, using block randomization method according to CONSORT Statement (2010). The participants were instructed to apply 10 mL of mouthwash, 3 times a day for 5 days. Likewise, the patients in placebo group were instructed to use the placebo mouthwash the same as treatment group (10 mL of mouthwash, 3 times a day for 5 days). The baseline factors were taken and recorded on the day of the first visit. All of the subjects were free to withdraw at any time during the course of study. All participants signed a written informed consent before recruiting in the study. The Ethics Committee of Kermanshah University of Medical Sciences approved this clinical study (approval number: KUMS. REC.1394.14).

To exclude potentially confounding systemic diseases, all patients underwent careful examination by dermatologists, gastroenterologists, and ophthalmologists before enrollment. The clinical diagnosis was made by infectious medicine specialists based on clinical appearance, location, and patient history. All patients were selected according to specific inclusion and exclusion criteria. The inclusion criteria were as follows: (a) men and women (males and females) aged 15-65 years old who can follow the doctor's advice; (b) Willingness to participate and sign the informed agreement forms; (c) patients with 1 to 5 aphthous ulcers (less than 48 hours' duration); (d) an anticipation that their ulcers normally take 5 or more days to resolve without treatment; (e) ulcers must be in positions simply accessible for evaluation and treatment, such as the labial mucosa, buccal mucosa, or the tongue; and (f) patients with normal sense of pain. Exclusion criteria were the following: (a) a known history of severe drug hypersensitivities, particularly allergies to tobacco or nicotin; (b) pregnancy or lactation; (c) ulcers as a manifestation of a systemic disease process, including Behçet disease, serious anemia Crohn's disease, ulcerative colitis, or acquired immune deficiency syndrome; (d) simultaneous clinical conditions which represent a health risk to the subjects, such as severe heart, liver, or kidney disorder; (e) treatment with systemic non-steroidal anti-inflammatory drugs, systemic steroids or other immunomodulatory agents, oral antihistamines, or systemic antibiotics within 2 weeks study entry; (f) treatment of the ulcer with any medication within 72 h before study entry; and (g) attendance of any clinical studies within 2 months before trial entry.

Measurement

In all studies, the size and number of ulcers were calculated by the investigator, and the pain was assessed by the subjects before the first mouthwash application and at each subsequent evaluation. For patients who had more than 1 ulcer, only the ulcer that occurred lately and was easy for evaluation was selected. Periodic telephone interviews were performed to supervise the