Complementary Therapies in Medicine 27 (2016) 58–64

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevierhealth.com/journals/ctim

Sage tea–thyme–peppermint hydrosol oral rinse reduces chemotherapy-induced oral mucositis: A randomized controlled pilot study

Ezgi Mutluay Yayla [a,*], Nur Izgu [a], Leyla Ozdemir [a], Sinem Aslan Erdem [b], Murat Kartal [b]

[a] Nursing Faculty, Hacettepe University, 06000 Sihhiye, Ankara, Turkey
[b] Department of Pharmacognosy, Faculty of Pharmacy, Ankara University, 06000 Tandogan, Ankara, Turkey

ARTICLE INFO

Article history:
Received 21 October 2014
Received in revised form 4 May 2016
Accepted 24 May 2016
Available online 25 May 2016

Keywords:
Oral mucositis
Oral rinse
Sage tea
Thyme
Peppermint
Nursing

ABSTRACT

Objective: This pilot study aimed to investigate the preventive effect of sage tea–thyme–peppermint hydrosol oral rinse used in conjunction with basic oral care on chemotherapy-induced oral mucositis.
Design: An open-label randomized controlled study.
Setting: Two oncology hospitals in Ankara, Turkey.
Interventions: Patients receiving *5-fluorouracil*-based chemotherapy regimens were divided into the intervention group (N = 30) and control group (N = 30). Basic oral care was prescribed to the control group, while the intervention group was prescribed sage tea–thyme–peppermint hydrosol in addition to basic oral care. All patients were called to assess their compliance with the study instructions on day 5 and 14.
Main outcome measures: Oral mucositis was evaluated using an inspection method or by assessing oral cavity photos based on the World Health Organization oral toxicity scale on day 5 and 14.
Results: Most of the patients in the intervention group did not develop oral mucositis on day 5. In addition, the incidence of grade 1 oral mucositis was statistically lower in the intervention group (10%) than the control group (53.3%) on day 5. By day 14, the majority of patients in both the groups had grade 0 oral mucositis.
Conclusions: Sage tea–thyme–peppermint hydrosol oral rinse has promising results in alleviating oral mucositis. This hydrosol can be recommended for clinical use as it is well tolerated and cost-effective. However, further randomized controlled trials are needed to support the study.

1. Introduction

Oral mucositis, an inflammatory and potentially ulcerative process, adversely affects the mucous membrane of the oral cavity in patients undergoing chemotherapy. Specifically, chemotherapy drugs facilitate the infiltration of microorganisms that disrupt the function of serous mucous glands.[1] Oral mucositis may cause erythema, edema, and atrophy of the oral mucosal epithelium.[2] Although the incidence of oral mucositis is reported to be 5%–15% overall among patients, the observed incidence varies depending on the treatment and risk factors.[3,4] The incidence of oral mucositis can increase significantly with the use of high-risk drugs such as *5-fluorouracil* (*5-FU*). Approximately 40%–60% patients receiving *5-FU* develop oral mucositis. Along with high incidence, the grades of *5-FU* induced oral mucositis can reach 3–4 with a ratio of 10–15%.[5,6]

Oral mucositis is one of the most debilitating and troublesome toxicities, causing mouth discomfort, pain, nutritional deficits, weight loss, and the delay of treatment, leading to a low quality of life in patients undergoing chemotherapy.[2,7,8] In addition, oral mucositis poses a serious risk for the development of life-threatening infections such as bacteremia and septicaemia.[9,10] Therefore, to prevent any occurrence of this condition, clinically effective prophylactic procedures should be developed and employed. Within this scope, there are several different approaches to mouth care which might prevent oral mucositis. Despite the lack of supporting evidence, basic oral care has been recommended in clinical guidelines.[11] In addition to basic oral care, a variety of treatments have been reported to prevent oral mucositis.[8,12–18] These preventive treatments include the use of solutions such as chlorhexidine, chamomile, black mulberry syrup, and honey; treatment modalities such as cryotherapy and low-energy helium–neon

* Corresponding author.
E-mail addresses: ezgmtly@gmail.com, akglnur@gmail.com (E. Mutluay Yayla).

http://dx.doi.org/10.1016/j.ctim.2016.05.010
0965-2299/

laser therapy; and supplements such as selenium, zinc sulfate, vitamins A and E, cytokine-like agents, and growth factors. However, despite the implementation of strict mouth care procedures, patients undergoing chemotherapy regimens frequently suffer from increased incidence of oral mucositis.[6,19,20] Therefore, it is necessary to develop additional methods that complement basic oral care for the prevention of oral mucositis.

In traditional medicine, patients with cancer used sage tea, thyme and peppermint for the prevention of oral mucositis.[14,21,22] These herbs have antiseptic,[23–25] anti-inflammatory,[23–25] antimicrobial,[23,24,26,27] antifungal,[23,27,28] and antiviral,[24,28] properties. In addition, these herbs are effective as a mouthwash or mouth rinse against stomatitis,[24,25] pharyngolaryngitis, and oral candidiasis.[29] However, to the best of our knowledge, no study has thus far evaluated the effects of these herbs on chemotherapy-induced oral mucositis. Therefore, considering the paucity of research on effective prophylactic approaches for the avoidance of oral mucositis and on the effects of sage tea, thyme, and peppermint on improving oral mucosal health, further studies investigating the prophylactic effect of these herbs on oral mucositis are warranted.

Extracts, essential oils or hydrosols of these plants can be used for medicinal purposes. Hydrosols, known as floral water, distillate water or herbal aromatic water, are the by-products of hydro and steam distillation of different parts of plant materials. In general, hydrosols comprise the water-soluble components of the extracted essential oil[30,31] and they demonstrate a longer shelf-life compared to other extracts.[32,33] Hence, the present study was designed to examine the effect of sage tea–thyme–peppermint hydrosol oral rinse combined with basic oral care on the prevention of chemotherapy-induced oral mucositis.

2. Materials and methods

2.1. Subjects and study design

The research was conducted in the outpatient chemotherapy units of two oncology hospitals in Ankara, Turkey. The study population comprised patients receiving *5-FU*-based chemotherapy regimens (bolus or infusion). The inclusion criteria were as follows: 18–65 years of age, receiving either bolus or infusion *5-FU*-based chemotherapy regimens, platelet counts over 20,000/μl, no oral mucositis upon inspection (according to the World Health Organization [WHO] oral toxicity scale), permission provided for photos to be taken of their oral cavity, and voluntary participation in the study. The criteria for exclusion included receiving head and neck radiotherapy and exhibiting an allergy to sage tea, thyme, or peppermint.

Of the 78 assessed individuals, 13 were excluded because of their ineligibility (>65 years of age) and 5 refused to participate because of their dislike of the hydrosol odor. Therefore, 60 patients were randomly allocated into the study groups. To accomplish this, the first patient was assigned to the control group and the next one to the intervention group and so on. The statistical power for our sample size was 0.95 and the margin of error was 0.05. The design was an open-label randomized controlled trial. A placebo was not used since the sage tea–thyme–peppermint hydrosol has a characteristic odor and taste.

2.2. Measurement tools

Data were collected using a patient questionnaire, the WHO oral toxicity scale, oral cavity photos of the patients, and intervention and control group compliance checklists. The patient questionnaire, which was developed from a questionnaire used extensively in previous studies,[6,7,19,34,35] contained questions on socio-demographic characteristics (age, gender, and educational level), patient-related risk factors (current smoking habits, daily liquid consumption, and dental prosthesis), and treatment-related risk factors (diagnosis, chemotherapy regimen, and dose). To grade oral mucositis, the WHO oral toxicity scale was utilized.[36] This tool categorizes grades of oral mucositis as follows: grade 0 (no mucositis); grade 1 (soreness and erythema, no further symptoms); grade 2 (ulcers present, but solid diet possible); grade 3 (ulcers present, required a liquid diet) and grade 4 (severe mucositis preventing oral nutrition and necessitating total parenteral nutrition).[36] Although the WHO oral toxicity scale has been widely used in many studies and clinical practices,[6,17,37,38,39] it has never been subjected to rigorous validation tests. Use of this empirical scale has been verified by 40 years of accumulated experiences (and the rationale for its use coincides with the opinions of most experts). However, several additional oral mucositis assessment scales have been derived based on the WHO oral toxicity scale.[40,41,42]

The inspection of oral mucosa and oral cavity photos was independently performed by two researchers. If the patients attended the hospital on days 5 and 14, oral mucositis was assessed using the manual inspection method, but if the patients did not attend hospital on the aforementioned monitoring days, oral mucositis was evaluated using photos taken by the patients' relatives. The presence of visible ulcers was the key feature to distinguish between grade 1 and grade 2 mucositis. The intervention and control compliance checklists included blank spaces to be completed during the 14-day study period. The control group compliance checklist comprised basic oral care instructions, while the intervention group compliance checklist, contained directions for the use of sage tea–thyme–peppermint hydrosol oral rinse in addition to basic oral care instructions.

2.3. Preparation of the sage tea–thyme–peppermint hydrosol

Sage tea, thyme and peppermint hydrosols were obtained from an essential oil producing company. After mixing equal amounts of these hydrosols, the mixture was analyzed at the Pharmacognosy Department, Ankara University Faculty of Pharmacy. Gas chromatography (GC) analysis using the Agilent 6890N Network GC system was used to check the quality of the hydrosol. According to the GC analysis, the major constituents of the hydrosol included 2-hexanone, eucalyptol, menthone, camphor, pulegone, menthol, α-terpineol, piperitenone, thymol and carvacrol. Following analysis, the mixed hydrosol was transferred to light-proof glass bottles using an aseptic technique. These bottles were then stored in cool, dark conditions. Instructions were provided to patients indicating that once the bottles were opened, the bottles were to be kept in a refrigerator.

2.4. Data collection and intervention

On the first day of chemotherapy, the patient questionnaires of both groups were filled out by the researchers; this process took approximately 10 min. Subsequently, patients in the control group were informed about basic oral care using a leaflet. Using another leaflet, the intervention patients were provided with information about basic oral care and with information about using sage tea–thyme–peppermint hydrosol oral rinse. Both leaflets were developed by the researchers based on literature.[14,16,23]

The leaflet for control patients included the following basic oral care instructions: rinse the mouth out with saline four times a day for 30 s and brush the teeth twice a day for 14 days starting on the first day of chemotherapy. The leaflet for intervention patients included the aforementioned basic oral care instructions and also