European Journal of Oncology Nursing 19 (2015) 207–213

Contents lists available at ScienceDirect

European Journal of Oncology Nursing

journal homepage: www.elsevier.com/locate/ejon

Effect of adding the herb *Achillea millefolium* on mouthwash on chemotherapy induced oral mucositis in cancer patients: A double-blind randomized controlled trial

Sedigheh Miranzadeh [a], Mohsen Adib-Hajbaghery [a, *], Leyla Soleymanpoor [a], Majid Ehsani [b]

[a] Department of Medical Surgical Nursing, Faculty of Nursing and Midwifery, Kashan University of Medical Sciences, Kashan, Iran
[b] Department of Internal Medicine, Shahid Beheshti Medical Center, Kashan University of Medical Sciences, Kashan, Iran

Keywords:
Achillea millefolium
Chemotherapy
Oral mucositis
Cancer
Mouthwashes

A B S T R A C T

Background: Oral mucositis (OM) is a debilitating side-effect of chemotherapy. It has different complications, including impairment of drinking, eating and even talking, sometimes so severe that physician stops the therapy.
Objective: Investigating the effect of *Achillea millefolium* distillate solution in the treatment of chemotherapy-induced OM.
Interventions/methods: In this randomized controlled trial, 56 cancer patients with chemotherapy-induced OM were randomly assigned into control and experimental groups in similar blocks based on the severity of OM. The experimental group gargled 15 mL of a mixture of routine solution and distilled *A. millefolium* 4 times a day for 14 days while the control group gargled 15 mL of routine solution. The severity of OM was assessed at three times before, 7 and 14 days after intervention. Data was analyzed using Wilcoxon, Kruskal–Wallis, Mann–Whitney U, Friedman, Chi-square and Fisher's exact tests.
Results: The mean severity score of OM was 2.39 ± 0.875 in both groups at start of the study that was changed to 1.07 ± 0.85 and 0.32 ± 0.54 in the intervention group in days 7 and 14 ($p < 0.001$). However, the severity of OM was increased to 2.75 ± 0.87 and 2.89 ± 0.956 in the control group respectively ($p < 0.001$).
Conclusions: A. millefolium distillate healed OM much more than the routine solution. Therefore, it is suggested to be used in patients with chemotherapy-induced OM.
The study was registered in the Iranian Registry of Clinical Trials, Number: IRCT2013092214729N1.

Introduction

Oral mucositis (OM) refers to mucosal damage secondary to cancer therapy occurring in the oral cavity. Mucositis can be caused by chemotherapy and/or radiation therapy (Lalla et al., 2014). It occurs in approximately 20%–40% of patients receiving conventional chemotherapy, 80% of patients receiving high dose chemotherapy as conditioning for hematopoietic stem cell transplantation, and nearly all patients receiving head and neck radiation therapy (Avritscher et al., 2004; Lalla et al., 2014; Vera-Llonch et al., 2007).

Pain induced by OM disturbs patients and makes it difficult to eat and drink, resulting in indigestion and dehydration (He, 2011; Pavesi et al., 2011; Potting et al., 2006). OM can also disturb speaking and communication with others, resulting in psychological and social stresses (Abedipour et al., 2006). In addition, OM is accompanied by a wide range of oral mucus alterations such as infection and bleeding, which could result in systemic infection (Abedipour et al., 2006; Potting et al., 2006). In severe cases, it can increase the length of hospitalization and even lead the physician to cease the chemotherapy (Pavesi et al., 2011; Potting et al., 2006).

A wide variety of agents have been tested to prevent OM or reduce its severity (Yarom et al., 2013; Lalla et al., 2014). The Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) has published evidence based clinical practice

* Corresponding author. Tel.: +98 3615550021; fax: +98 3615556633.
E-mail address: adib1344@yahoo.com (M. Adib-Hajbaghery).

http://dx.doi.org/10.1016/j.ejon.2014.10.019
1462-3889/

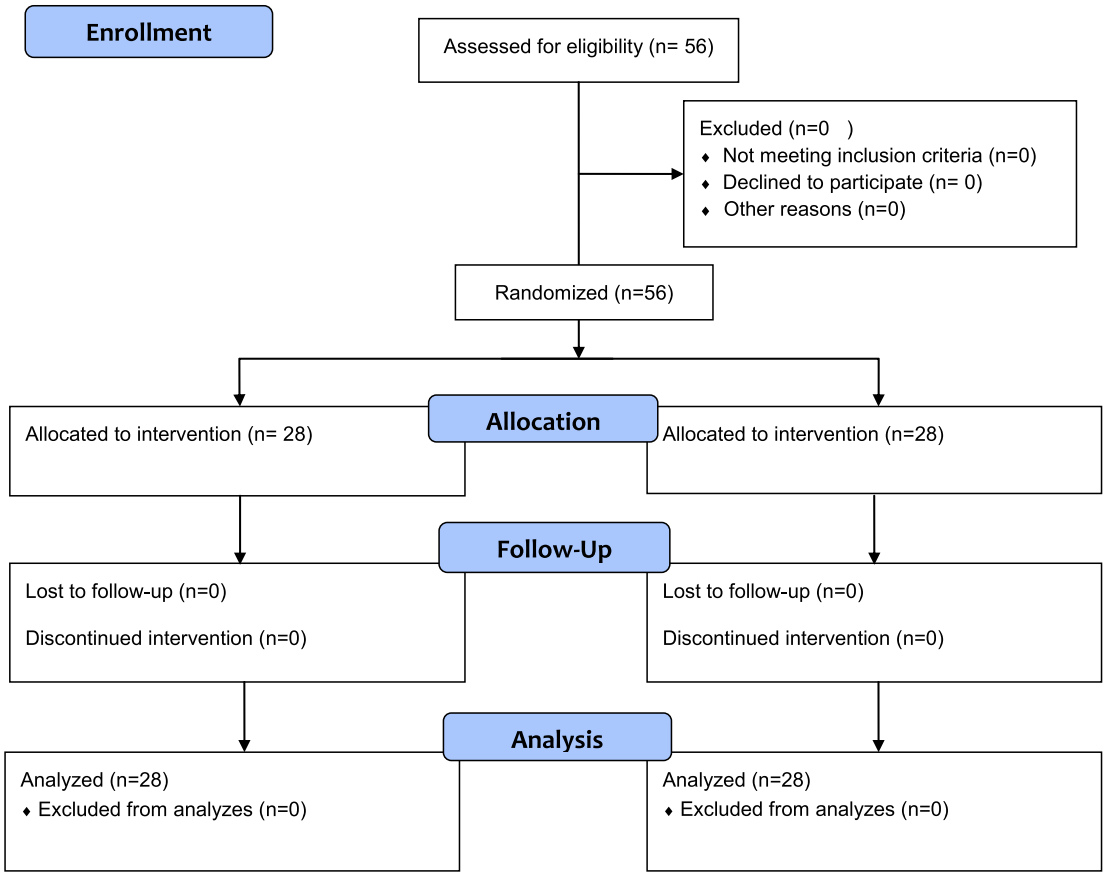

Fig. 1. Consort flow diagram.

guidelines for mucositis (Lalla et al., 2014), in order to facilitate evidence based patient care and improve outcomes. The current guidelines updated in 2013 examined the evidence for the following interventions: basic oral care, growth factors and cytokines, anti-inflammatory agents, antimicrobials, coating agents, anesthetics, analgesics, Laser and other light therapy, cryotherapy, natural and miscellaneous agents (Lalla et al., 2014). The most commonly used therapies often have no significant effect and sometimes cause additional side-effects (Arora et al., 2008).

Given the side-effects of chemical drugs, complementary therapies in the forms of herbal products are increasingly used all over the world (Adib-Hajbaghery and Hoseinian, 2014).

Most of ancient civilizations used different forms of herbal medicines. Among herbal plants, *Achillea millefolium* has attracted attentions due to its wide range of therapeutic effects. It is a well known herb from the asteraceae family, and has been extensively used in ancient medicine for treating different diseases in general and burns, injuries and infections in particular. One of the most important therapeutic effects of *A. millefolium* is its antibacterial effect on a wide range of pathogens (Aggarwal et al., 2011; Saeidnia et al., 2011; Tajik and Jalali, 2009). *A. millefolium* fresh flowers have been used to resolve respiratory problems (Düsman et al., 2013). It also was employed as anti-allergic (Aggarwal et al., 2011), anti-congestion, and expectorant (Nemeth and Bernath, 2008). Its flowers' distillates contain chamazulene, cineol, borneol (Orav et al., 2006), caffeic acid and salicylic acid with antibacterial, antispasmodic and anti-inflammatory effects (Aggarwal et al., 2011; Pires et al., 2009; Saeidnia et al., 2011; 2005). Some ingereduants of *A. millefolium* also exert beneficial effects on nervous, cardiovascular and digestive systems (Aggarwal et al., 2011). Despite historical background of this herb, reports about its application in treatment of wounds and injuries are rare (Tajik and Jalali, 2009). Aljancic et al. showed its significant inhibitory effect on candida albicans and bacillus subtilis in-vitro. They also reported that, the flavonoids existed in *A. millefolium* essence prevents the growth of aspergillus niger (Aljancic et al., 1999).

Sökmen et al. have also studied the antimicrobial effects of *A. millefolium* distillate on 12 bacterial species and 2 types of yeast. They have reported that though its aqueous extract had no antibacterial activity, the methanol one and the herb distillate had considerable antimicrobial activity (Sökmen et al., 2004). In another study, 32 separate ingredients have been extracted from *A. millefolium*, among which Comphor and Eucalyptol have significant inhibitory effects on candida albicens and clostridium perfringens. Also, Borneol and Piperitone in *A. millefolium* are two other compounds with considerable bacterial inhibitory activity (Sökmen et al., 2003).

During conversation with cancer patients, some revealed that to mitigate oral wounds, they gurgle *A. millefolium* distillate based on the recommendations received from some traditional groceries. Therefore, given the anti-inflammatory and antimicrobial effects of the plant, prevalence of chemotherapy-induced OM, and lack of studies on the effects of *A. millefolium* on chemotherapy induced oral muscositis, the present study was designed to investigate the effect of *A. millefolium* distillate-contained solution on the chemotherapy-induced OM.