European Journal of Oncology Nursing xxx (2014) 1–10

Contents lists available at ScienceDirect

European Journal of Oncology Nursing

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

Nevasic audio program for the prevention of chemotherapy induced nausea and vomiting: A feasibility study using a randomized controlled trial design

Saeed Moradian [a, *], Catherine Walshe [b], Soodabeh Shahidsales [c], Mohammad Reza Ghavam Nasiri [c], Mark Pilling [a], Alexander Molassiotis [a, d]

[a] School of Nursing, Midwifery and Social Work, University of Manchester, Manchester, UK
[b] International Observatory on End of Life Care, Division of Health Research, Lancaster University, UK
[c] Cancer Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
[d] School of Nursing, The Hong Kong Polytechnic University, Hong Kong

Keywords:
Chemotherapy-induced nausea and vomiting
Nevasic
Music therapy
Feasibility

A B S T R A C T

Purpose: Pharmacological therapy is only partially effective in preventing or treating chemotherapy induced nausea and vomiting (CINV). Therefore, exploring the complementary role of non-pharmacological approaches used in addition to pharmacological agents is important. Nevasic uses specially constructed audio signals hypothesized to generate an antiemetic reaction. The aim of this study was to examine the feasibility of conducting a randomized controlled trial (RCT) to evaluate the effectiveness of Nevasic to control CINV.

Methods: A mixed methods design incorporating an RCT and focus group interviews. For the RCT, female breast cancer patients were randomized to receive either Nevasic plus usual care, music plus usual care, or usual care only. Data were analysed using descriptive statistics and linear mixed-effects models. Five focus group interviews were conducted to obtain participants' views regarding the acceptability of the interventions in the trial.

Results: 99 participants were recruited to the RCT and 15 participated in focus group interviews. Recruitment targets were achieved. Issues of Nevasic acceptability were highlighted as weaknesses of the program. This study did not detect any evidence for the effectiveness of Nevasic; however, the results showed statistically significant less use of anti-emetics ($p = 0.003$) and borderline non-significant improvement in quality of life ($p = 0.06$).

Conclusions: Conducting a non-pharmacological intervention using such an audio program is feasible, although difficulties and limitations exist with its use. Further studies are required to investigate the effectiveness of Nevasic from perspectives such as anti-emetic use, as well as its overall effect on the levels of nausea and vomiting.

Introduction

Nausea and vomiting are frequently experienced toxicities associated with chemotherapy (Roscoe et al., 2000; Schwartzberg, 2007). These symptoms have a negative effect on nutritional status, physical functioning and quality of life (Farrell et al., 2013). The standard management of chemotherapy induced nausea and vomiting (CINV) involves the use of pharmacological agents. Despite advances in pharmacological management, approximately 50% of patients receiving chemotherapy still experience (primarily) nausea and/or vomiting (Pirri et al., 2011). Since pharmacological therapy is only partially effective in preventing or treating CINV, there is a need for additional methods to reduce these symptoms (Ezzo et al., 2006).

Mind and body medicines are based on interactions among the brain, mind, body, and behaviour, with the intent to use the mind to affect physical functioning and promote health (NCINIH, 2012). Several mind-body techniques, in addition to conventional anti-emetics, have been examined over the years for the treatment of CINV. For example, during the last decade several trials examining the efficacy of acupressure/acupuncture for alleviating CINV have

* Corresponding author. 61 Steeles Ave E. Toronto, Ontario, M2M 3Y3, Canada. Tel.: +1 647 858 9755; fax: +1 416 519 9694.
E-mail address: dr.smoradian@gmail.com (S. Moradian).

http://dx.doi.org/10.1016/j.ejon.2014.10.016
1462-3889/

been a focus of research (Ezzo et al., 2006; Taspinar and Sirin, 2010; Suh, 2012). In addition, the impact of psychological factors on nausea and vomiting has been widely acknowledged, and the efficacy of inducing these psychosomatic aspects, e.g. by relaxation training, coping preparations, imagery, music therapy, distraction techniques or hypnosis, has been demonstrated in a number of studies (Schneider and Hood, 2007; Tipton et al., 2007; Gimeno, 2010). Nevertheless, many patients still experience nausea and vomiting in relation to chemotherapy. The need to evaluate additional ways to reduce these symptoms is still, therefore, a priority.

Nevasic, which is an audio program, is a technical innovation that proposes using specially constructed audio signals to generate an antiemetic reaction. Nevasic was originally developed as an audio tape over a decade ago (branded as TravelWell and MorningWell for motion and pregnancy sickness), and is now available in a number of formats including as a CD and App. Nevasic has been registered as a Medical Device in the UK, the USA, and in Australia (as an exempt product under the Therapeutic Goods Act) (http://nevasic.com/nevasic/).

The process of emesis is complex, believed to involve different organs such as the brain, intestines and vestibular labyrinths. Nevasic is theorized to work by emitting specific constructed tones, frequencies and pulses which disrupt the normal auditory signal chain at the vestibular level, and thus having an effect on the experience of nausea and vomiting.

No studies have examined the Nevasic effect(s) on chemotherapy-related nausea and vomiting. Only one study was conducted to compare the effectiveness of controlling breathing and listening to the Nevasic on increasing tolerance to nauseogenic motion. The results showed that mean (±SD) motion exposure time in minutes tolerated before the onset of moderate nausea was significantly longer ($p < 0.01$) for controlling breathing (10.7 ± 5.6 min) and longer ($p < 0.01$) for the music audiotape (10.4 ± 5.6 min) compared with control (9.2 ± 5.9 min) (Yen Pik Sang et al., 2003).

The objectives of this study were to examine the feasibility of implementing and conducting a randomized controlled trial (RCT) using the Nevasic program. We sought to determine feasibility of recruitment and randomization, acceptability of the interventions, adherence to the trial and to evaluate potential effect of Nevasic on cancer patients undergoing chemotherapy.

Methods

Study design

We conducted a pilot, multicenter, randomized controlled trial with three parallel arms (intervention, attention, and control) in Mashhad, Iran. The attention arm was used to assess the feasibility of using the three arms and include one (control) group that mimics the intervention as closely as possible to determine the "true" effects of the intervention over the placebo effects (Dowrick and Bhandari, 2012) and also to control for the potentially therapeutic effects of the placebo (Noll et al., 2004), as it has been stated that placebos may improve outcomes in up to 30–40% of patients with a wide range of clinical conditions (Wilcox, 2008).

Participants' perspectives regarding the burden of completing this study and the acceptability of the intervention and attention arms of the trial were obtained by conducting semi-structured focus groups.

Participants

Female breast cancer patients were the target population for the study, as they are likely to experience the symptom of interest (Levin et al., 2009). Eligibility criteria for participants were: diagnosed with breast cancer, chemotherapy naïve, scheduled to receive moderately high emetogenic chemotherapy, aged over 18 years, and able to read and write in Persian. Patients, who had any other disease, were undertaking any concomitant treatment which might affect the severity of their nausea and vomiting, had any condition resulting in them not being able to listen to Nevasic or relaxation music, were excluded.

Ethical considerations

Ethical approval of the study was obtained from the ethics committees in Mashhad University of Medical Sciences (MUMS) and University of Manchester. The participants gave informed verbal and written consent.

Sample size

A sample size for a pilot study is usually based on pragmatic issues and the necessity of examining feasibility (Leon et al., 2011). For this pilot feasibility study, therefore, no formal sample size calculation was conducted. Lancaster et al. (2004) suggest that 30 participants per group is an adequate sample size for a feasibility RCT. Hertzog (2008) suggests that 30 per group may be required for a good estimation of the recruitment and attrition rate. For this study, 30 participants seemed feasible in terms of time and resources. Assuming a 20% attrition rate, it was planned to randomize 114 participants equally to one of three groups, with 38 per group.

Recommendations for both the number of focus groups and sample size vary. It is emphasized that both too few and too many groups can affect the quality of focus group studies; therefore, quantity must be balanced against quality (Bryant and Charmaz, 2007). For this study, 4–8 participants per group and 3–4 focus groups was planned to allow us to examine themes common across groups.

Randomization and allocation

The participants were randomly assigned to one of the three treatment groups using a list (generated by nQuery Advisor program), done by a Statistician who was independent of this study.

Trial participants were invited to participate in the focus groups based on the criteria that they had something to state on the mentioned topics and were comfortable talking to the interviewers and each other and prepared to engage in the discussion. Limited the number of specific questions (6–8 questions regarding issues with questionnaires, listening to music or Nevasic, practical ability to use them and adherence to the study and ended with any suggestions or questions) were designed and asked participants to freely talk about them. The sessions were run by the researcher and an oncologist from cancer research center affiliated to MUMS.

Study settings

Participants were recruited from three cancer centers in Mashhad, Iran from March 2011 to February 2012. Two of these centers were affiliated to MUMS and the third center was a radiation and oncology center run by a charity. These centers are among Iran's leading cancer centers and serve a population of 7 million across Khorasan province.

Health system in Iran

Iran's health care system is managed primarily by the government. Health care and public health services are provided through a

Please cite this article in press as: Moradian, S., et al., Nevasic audio program for the prevention of chemotherapy induced nausea and vomiting: A feasibility study using a randomized controlled trial design, European Journal of Oncology Nursing (2014), http://dx.doi.org/10.1016/j.ejon.2014.10.016