Complementary Therapies in Medicine (2013) 21, 195—199

Available online at www.sciencedirect.com

SciVerse ScienceDirect

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

A randomised double-blind comparability study of a placebo for Individualised Western Herbal Medicine

S. Berkovitz[a,*], P. Bassett[b], J.G. Hughes[a]

[a] Royal London Hospital for Integrated Medicine, UCLH NHS Trust, United Kingdom
[b] UCL Research Support Centre, United Kingdom
Available online 11 April 2013

KEYWORDS
Individualised Western Herbal Medicine;
Placebo;
Randomized double blind comparability study

Summary
Objectives: To determine the non-inferiority of placebo Individualised Western Herbal Medicine (IWHM) tinctures compared with true IWHM tinctures.
Design: Randomised double blind comparability study.
Setting: Pharmacy department of an NHS integrated medicine hospital.
Interventions: The IWHM intervention consisted of mixed tinctures of five herbs from a list of eleven herbs for which chronic knee pain is an established indication. Placebo IWHM tinctures contained food and colouring extracts, designed to mimic as closely as possible the taste, smell and appearance of true IWHM.
Main outcome measures: The primary outcome of the study was the proportion of patients who indicated that they believed they were taking true IWHM. Secondary outcomes included the palatability of the true and placebo tinctures.
Results: 64% of the placebo group indicated that they believed they had consumed true IWHM, compared with 60% of the true IWHM group. The palatability of the placebo IWHM was also acceptable to participants, and similar to the palatability of true IWHM.
Conclusions: The findings from the present study indicate that the placebo tinctures were non-inferior to the true IWHM tinctures in terms of participants' ability to correctly identify them as herbal tinctures by their taste, smell and appearance. The placebo tinctures could be utilised in future double blind, placebo controlled randomised trials of IWHM

Introduction

The use of herbal interventions for the treatment of medical conditions is widespread. In 2002 the World Health Organisation estimated that up to 80% of people in developing countries rely on herbal medicines for their primary healthcare needs.[1] Within the developed world herbal medicines continue to be a popular treatment option. A recent large UK survey of complementary and alternative medicine use by patients with cancer, for example, found herbal medicine was the most popular treatment modality with 22.3% of patients having consumed one or more herbal medicines since their diagnosis.[2]

The widespread global use of herbal medicines has led to demands for scientific evidence of their efficacy and

* Corresponding author at: Royal London Hospital for Integrated Medicine, University College London Hospital NHS Trust, 60 Great Ormond Street, London WC1N 3HR, United Kingdom.
Tel.: +44 0 20 3488 8975; fax: +44 0 20 7391 8869.
E-mail address: saul.berkovitz@uclh.nhs.uk (S. Berkovitz).

0965-2299/$ — see front matter © 2013 Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.ctim.2013.03.006

safety.[3] The de facto gold standard for evaluating efficacy is the randomised placebo controlled trial. However, there are significant difficulties associated with the use of placebos in herbal medicine clinical trials. Herbal medicines have distinctive aromas and tastes which are difficult to mimic with therapeutically inert ingredients.[4] One approach to this problem has been to develop herbal extracts which can be prepared as tablets or capsules, and for which a convincing placebo is readily producible. Examples of placebo controlled clinical trials of herbal extracts for medical conditions include digestive disorders,[5,6] allergic disorders[7,8] and musculoskeletal disorders.[9,10]

However, for many herbal practitioners in the UK, the use of standardised herbal extracts does not reflect their normal clinical practice. Despite many positive trial results, standardised herbal extracts may lack the resultant potency of individualised herbal preparations.[4] Practitioners of Individualised Western Herbal Medicine (IWHM) frequently combine several herbal tinctures (liquid alcohol-based extracts) in an individualised manner according to traditional as well as scientific knowledge of their properties. The mixture is often changed at successive appointments according to patient response, which can alter the taste and smell each time. This presents a considerable problem for those intending to evaluate the efficacy of IWHM in placebo controlled clinical trials. The challenge for research into the practice of IWHM is to evaluate what practitioners actually do, not to change practice to fit into an acceptable research design at the expense of external validity.

A recently conducted pilot randomised, double blind, placebo controlled trial of IWHM in 19 patients appeared to show promise for treating knee osteoarthritis and began to develop a feasible method for assessing this complex intervention.[11] However the placebo was unsatisfactory, leading to five out of nine participants in the placebo group dropping out due to palatability problems. Before attempting further randomised controlled trials, it appears essential that a convincing placebo be developed and validated by testing for comparability to ensure adequate blinding and palatability.

Population sample

The sample consisted of 102 adult general outpatients attending the pharmacy of the Royal London Hospital for Integrated Medicine. 52 participants were allocated to receive true IWHM and 50 placebo IWHM. The sample consisted of 82 female and 20 male participants. The mean age was 53 (age range from 18 to 83).

Methods

A randomised double blind comparability study was conducted to determine the non-inferiority of placebo tinctures compared with true IWHM tinctures. Patients were recruited from the pharmacy department of the Royal London Hospital for Integrated Medicine. Patients were approached directly by a member of the research team (SB or JH), using a standardised recruitment script. Patients were excluded if they had previously used IWHM; were pregnant or lactating; were currently using warfarin or other drugs which suppress the immune system; had gallstones, stomach ulcers or liver disease; or if they had an allergy to any herbal medicines, celery, aspirin or similar drugs. Patients were provided with a copy of the patient information sheet, and written informed consent obtained. Patients were recruited between 5th September 2011 and 29th November 2011. Participants were allocated to receive either true or placebo IWHM by computer randomisation. A study pharmacist dispensed the true and placebo IWHM and both the participants and study researchers were blind to allocation until the end of the study. Participants were left alone in a room adjoining the pharmacy to taste or swallow two vials of tinctures (as much or as little as required to reach a decision), either neat or diluted in water, and complete the study questionnaire. The procedure took up to fifteen minutes to complete, and each participant completed the procedure on just one occasion.

The primary outcome was the proportion of participants who indicated that they believed they were taking true IWHM. The study questionnaire asked participants to indicate whether they believed the tinctures they had received were real or placebo. Participants were additionally asked to indicate on a 100 mm visual analogue scale how sure they were of their answer (0 = complete guesswork, 100 = complete certainty). If participants felt sure of their answer they were asked to explain why in a free response section. Participants were additionally asked to rate the palatability of the tinctures on a 100 mm visual analogue scale (0 = totally unpalatable, 100 = pleasant).

The study was approved by the North London Research Ethics Committee.

Study treatments

True IWHM consisted of 10 ml bottles of two different IWHMs. These were mixed tinctures of five herbs from a list of eleven herbs for which chronic knee pain is an established indication in Western herbal practice (see Table 1). These eleven herbs were identical to those used in a previous pilot study,[11] and had been selected after discussion with senior herbal practitioners. The five herbs in each mix were determined by random draw from an envelope containing labels corresponding to the eleven herbs, performed by the study pharmacist. The herbal medicines, in everyday use at the Royal London Hospital for Integrated Medicine Herbal Medicine Clinic, were sourced from routine hospital stock. All herbal medicines were manufactured by Mediherb Pty, Australia and distributed in the UK by Balance Healthcare Ltd. The manufacturer has a current Australian TGA certificate which is reciprocally equivalent to EU Good Manufacturing Practice. The distinctive taste of the herbal medicine was masked by adding 15% by volume of a chocolate-based flavouring mixture (chocolate flavour R196).

A placebo controlled trial of IWHM would have to overcome the problem of the taste of the herbal tinctures changing as different herb combinations, or different proportions of the same herbs, were adjusted according to clinical response. For this reason two different tasting placebos were developed for the current study so that their taste may be changed in parallel with IWHM to maintain