European Journal of Cancer 61 (2016) 102–110

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

A randomised study comparing the effectiveness of acupuncture or morphine versus the combination for the relief of dyspnoea in patients with advanced non-small cell lung cancer and mesothelioma

A. Minchom [a,1], R. Punwani [a,1], J. Filshie [b], J. Bhosle [a], K. Nimako [a], J. Myerson [a], R. Gunapala [a], S. Popat [a], M.E.R. O'Brien [a,*]

[a] *Lung Unit, Royal Marsden Hospital, Sutton, UK*
[b] *Dept of Anaesthetics and Pain Management Royal Marsden Hospital, Sutton, UK*

Received 15 March 2016; accepted 21 March 2016

KEYWORDS
Lung cancer;
Acupuncture;
Dyspnoea

Abstract ***Background:*** Dyspnoea is one of the commonest symptoms of lung cancer. Opioids can reduce dyspnoea. This study investigates acupuncture for relief of breathlessness in lung cancer.

Methods: We performed a single-centre, randomised phase II study of 173 patients with non-small cell lung cancer or mesothelioma with dyspnoea score of ≥4 on visual analogue scale (VAS). Randomisation was to acupuncture alone (A), morphine alone (M) or both (AM). Acupuncture was administered at upper sternal, thoracic paravertebral, trapezius trigger points and LI4. Manubrial semi-permanent acupuncture studs were inserted and massaged when symptomatic. Arm A patients received rescue morphine. Primary end-point was proportion of patients achieving ≥1.5 improvement in VAS dyspnoea at 4 h. Measurements continued to day 14 and included VAS relaxation, line analogue rating (Lar) anxiety, hospital anxiety and depression and European Organisation for Research and Treatment of Cancer quality-of-life scores.

Results: Dyspnoea VAS improved ≥1.5 in 74%, 60% and 66% of arms A, M and AM, respectively, and was maintained in 45% at 2 weeks. There was no statistically significant difference between arms. VAS relaxation improved in arms A (1.06 points) and AM (1.48 points) compared to arm M (−0.19 points, $p < 0.001$). At 7 d, the Lar anxiety score improved in arm A (1.5 points), arm AM (1.2 points) and arm M (no change, $p = 0.003$). Fewer patients received at least one morphine dose in arm A compared with arm M or AM (21% versus 87%

* *Corresponding author*. Tel.: +44 02086426011x3278; fax: +44 02086430373.
E-mail address: mary.o'brien@rmh.nhs.uk (M.E.R. O'Brien).
[1] Equal contribution, joint first authors.

http://dx.doi.org/10.1016/j.ejca.2016.03.078

versus 87%, respectively, $p < 0.001$).
Conclusions: A, M and AM were effective in relieving dyspnoea. Acupuncture relieved anxiety and was morphine sparing, providing an alternative to morphine.

1. Introduction

Dyspnoea is one of the commonest symptoms of lung cancer [1]. Though unlicensed for treating dyspnoea, oral and parenteral morphine are commonly used [2]. Unfortunately, patients may develop toxicities such as constipation, nausea and respiratory depression.

One study of cancer patients reported that 64% used complementary therapy [3]. Patients use acupuncture to manage pain, side-effects and stimulate the immune system [4–7]. Acupuncture is widely provided in oncology units and hospices [8].

The majority of trials of acupuncture for breathlessness have been performed in a non-cancer setting. A trial of traditional Chinese acupuncture in chronic obstructive pulmonary disease (COPD) demonstrated improved breathlessness and 6-min walk test compared to placebo [9]. Others have shown superiority of acupuncture over placebo in COPD on Borg dyspnoea scores and 6-min walk [10]. Trial of Wu *et al.* [11] in COPD randomised to active acupressure (non-needle pressure to acupuncture points) or sham acupressure and showed that the former significantly improved pulmonary function, dyspnoea and 6-min walk. A Cochrane review of non-pharmacological interventions for breathlessness included five trials of acupuncture, though only one of these included cancer patients. The trials were heterogeneous and small and the review found insufficient evidence to recommend acupuncture [12].

A pilot study of 20 cancer patients by Filshie *et al.* [13] suggested that acupuncture gave short-term benefit. Seventy percent of patients reported symptomatic improvement, with a significant reduction on dyspnoea visual analogue scale (VAS) score 6 h post-acupuncture. To prolong response, the authors proposed acupuncture studs. These indwelling upper-sternal needles can be massaged by the patient when dyspnoeic or prior to exercise.

Data are accumulating on acupuncture mechanisms of action. Endogenous endorphin release is important and some effects of acupuncture are inhibited by naloxone [14,15]. Zhao [16] summarised other mechanisms of action, including serotonin release.

This study investigates acupuncture for relief of breathlessness in patients with advanced lung cancer.

2. Methods

2.1. Trial design

Eligible participants recruited from out-patient clinics had a histological diagnosis of non-small cell lung cancer (NSCLC) or mesothelioma and were breathless at rest with a score ≥4 on VAS. The patient makes a mark on a 100-mm line with descriptors at each end corresponding to the extent of their symptom [17]. The line analogue rating (Lar) scale comprises 100 mm lines, with extremes of feeling at each end and a central section representing normal state of mind [18]. Inclusion criteria were Eastern Cooperative Oncology Group performance status (PS) 0–3 and no change in treatment (chemotherapy/radiotherapy) in the previous 4 weeks or change of steroids in the previous 1 week. Exclusion criteria included acupuncture in the previous 4 weeks, acupuncture contraindications, current morphine use or reversible causes of breathlessness (including anaemia or pleural effusion).

Subjects were randomised using permuted blocks with stratification factors of PS and steroid use in a 1:1:1 ratio by telephone to acupuncture alone (arm A), morphine alone (arm M) or acupuncture in combination with morphine (arm AM). In Arm A, acupuncture was administered to two upper sternal midline points (12), five paraspinal points from T1 to T5, two to three trigger points in the trapezius muscle bilaterally and LI4 (acupuncture point near the base of thumb) bilaterally (Fig. 1). Thirty-millimetre-long 36-gauge stainless steel acupuncture needles (Seirin) were inserted and left *in situ* for 10 min. At sternal points, needles were inserted to the level of the periosteum and gently 'pecked' twice. No attempt was made to elicit needling sensation ('de qi') at other sites. After needle removal, stainless steel press needle studs (Seirin/Acumedic) were inserted in the upper 6 cm of the midline sternum to 0.6 mm and covered with a dressing. Treatments were given between 12 and 2 pm to avoid diurnal variation. Patients were instructed to massage studs for 1 − 2 min when symptomatic or prior to exercise whilst documenting in a diary. The ethics committee advised against using a placebo and that arm A should have access to rescue morphine. Therefore, all patients were given a supply of morphine with anti-emetics and laxatives. In arm M, patients were prescribed oral morphine solution