A single session of Acu-TENS increases FEV_1 and reduces dyspnoea in patients with chronic obstructive pulmonary disease: a randomised, placebo-controlled trial

Ken SL Lau[1] and Alice YM Jones[2]

[1]Kowloon Hospital [2]The Hong Kong Polytechnic University
Hong Kong

Questions: What is the immediate effect of a single 45-minute session of transcutaneous electrical nerve stimulation over acupoints (Acu-TENS) on lung function and dyspnoea in patients with chronic obstructive pulmonary disease? **Design:** Randomised, placebo-controlled trial with concealed allocation, participant blinding, assessor blinding, and intention-to-treat analysis. **Participants:** Forty-six ambulatory patients with a mean age of 75 years, with stage I or II chronic obstructive pulmonary disease, and with no previous experience of TENS or acupuncture. **Intervention:** The experimental group received 45 minutes of Acu-TENS over acupoint Ex-B1 bilaterally (0.5 'cun' lateral to the spinous process of the 7th cervical vertebra) while the control group received placebo-TENS with identical electrode placement but no electrical output despite a flashing light indicating stimulus delivery. **Outcome measures:** Lung function was measured as FEV_1 and FVC while dyspnoea was measured using a shortness of breath 100-mm visual analogue scale. **Results:** After 45 minutes of Acu-TENS, the experimental group had increased FEV_1 by 0.12 litres (95% CI 0.07 to 0.15) and decreased dyspnoea by 10.7 mm (95% CI –13.9 to –7.6) more than the control group. The effect on FVC was only small (mean difference 0.05 litres, 95% CI –0.01 to 0.10). **Conclusion:** Acu-TENS may be a useful non-invasive adjunctive intervention in the management of dyspnoea in patients with chronic obstructive pulmonary disease. This study suggests that the effect of long-term Acu-TENS warrants further investigation. **[Lau KSL, Jones AYM (2008) A single session of Acu-TENS increases FEV_1 and reduces dyspnoea in patients with chronic obstructive pulmonary disease: a randomised, placebo-controlled trial. *Australian Journal of Physiotherapy* 54: 179–184]**

Key words: Acupuncture points, Acupressure, TENS, Chronic obstructive pulmonary disease, Forced expiratory volume, Dyspnoea

Introduction

Chronic obstructive pulmonary disease is a progressive condition characterised by airflow limitation which is not fully reversible (WHO). Dyspnoea, excessive sputum production, and chronic cough are the most common symptoms. It is estimated that 3 million people died of chronic obstructive pulmonary disease in 2005 and WHO predicts that it will be the fourth leading cause of death world wide by 2030 (WHO). Management of stable chronic obstructive pulmonary disease includes pharmacotherapy for relief of symptoms, pulmonary rehabilitation programs for health education, and exercise to improve exercise tolerance and dyspnoea (GOLD 2007). Adverse effects of medications have encouraged alternative approaches to management of patients with chronic illness. Acupuncture has been reported as an alternative mode of management for breathlessness (dyspnoea) in oncology patients (Cohen et al 2005, Pan et al 2000) as well as in patients with respiratory disease (Davis et al 2001, Jobst et al 1986, Lewith et al 2004). A review of 16 randomised control trials, involving 2937 participants, concluded that acupuncture is a safe and potentially-effective intervention for patients with asthma and chronic obstructive pulmonary disease (Jobst 1995).

Acupuncture is invasive and therefore carries some risk of injury (Lao et al 2003, Peuker and Gronemeyer 2001, Vilke and Wulfert 1997). Application of transcutaneous electrical nerve stimulation, a non-invasive modality, over specific acupoints (Acu-TENS) is believed to elicit similar responses to manual acupuncture in pain relief (Grant et al 1999, Kerr et al 2003, Ng et al 2003). Acu-TENS can be administered by the patient or their carers and if proven to be effective, may assist control of dyspnoea and thereby promote quality of life in patients with chronic obstructive pulmonary disease. The effect of Acu-TENS on dyspnoea has not been reported for any population.

The research question in this study of patients with stable chronic obstructive pulmonary disease was:

> What is the immediate effect of a single 45-minute session of Acu-TENS on lung function and dyspnoea?

Method

Design

A randomised, placebo-controlled, pre-test and post-test design was carried out and the STRICTA recommendations were followed (MacPherson et al 2002). Ambulatory elderly (over 60 years of age) citizens with a medical diagnosis of chronic obstructive pulmonary disease and attending pulmonary rehabilitation programmes at community centres were referred by social workers. Eligible participants were then randomly assigned to either the experimental (Acu-TENS) or control (placebo-TENS) group. Randomisation was by block mode to ensure even numbers between groups. Numbers were placed in sealed opaque envelopes before the

beginning of the trial so that randomisation was concealed from the recruiter. A sealed opaque envelope was given to the patient and opened by the investigator who applied the interventions. Participants rested for 30 minutes after which lung function and dyspnoea were measured. All participants then received 45 minutes of either Acu-TENS or placebo-TENS. Participants in the control group were told that the stimulation frequency selected was not perceivable by humans so participants were blind to group allocation. One investigator was responsible for the application of both interventions. Then, lung function and dyspnoea were measured again. Data collection and entry was performed by a person blinded to group allocation.

Participants

Patients were included if they had a diagnosis of stage I or II chronic obstructive pulmonary disease according to the GOLD classification (GOLD 2001), an ability to communicate, and were independent in mobility with or without a walking aid. They were excluded if they had co-existing ischaemic heart disease, a cardiac pacemaker, diabetes mellitus, a neurological deficit, poor perception and/or cognitive function, an acute exacerbation of obstructive airways disease within one month prior to data collection, or had previously received TENS or acupuncture. Participants were also excluded from the study if they had received a bronchodilator less than 6 hours prior to data collection. Demographic data such as age, gender, smoking history and medication were recorded.

Intervention

The experimental group received 45 minutes of Acu-TENS at bilateral acupoints Ex-B1 (known as Ding Chuan in Traditional Chinese Medicine), located at 0.5 'cun' lateral to the spinous process of 7th cervical vertebra, where 1 cun is the distance between the medial creases of the interphalangeal joints of an individual's middle finger. Ex-B1 was chosen since it is the point most commonly reported in the Chinese literature for management of shortness of breath (Ngai et al 2006). Once determined, each acupoint was cleaned with an alcohol swab to reduce resistance to passage of current and marked. A non-conductive plastic film 50 x 50 mm^2 was punctured in the middle creating a pore of diameter 0.79 mm. This film was then placed over the participant's skin, with the pore directly over the marked acupoint. A 50 x 50 mm^2 electrode was then placed over each plastic film (Figure 1). This configuration restricts electrical stimulation to the acupoint only. The bilateral electrodes were attached to a TENS machine[a]. Stimulation was at a frequency of 4 Hz and pulse width 200 microseconds. Intensity was set at the highest tolerable by the participant short of discomfort. Reliability of voltage output of the machine was tested using a laboratory oscilloscope prior to data collection.

The control group received 45 minutes of placebo-TENS. A plastic film with no central pore was placed on the skin over each marked acupoint. Participants could see the output light flashing but no current was transmitted to the acupoint throughout the 45 minutes. Prior to data collection, the absence of electrical stimulation employed by this method was affirmed in five participants.

Outcome measures

Lung function was measured as forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) according to the American Thoracic Society recommendations

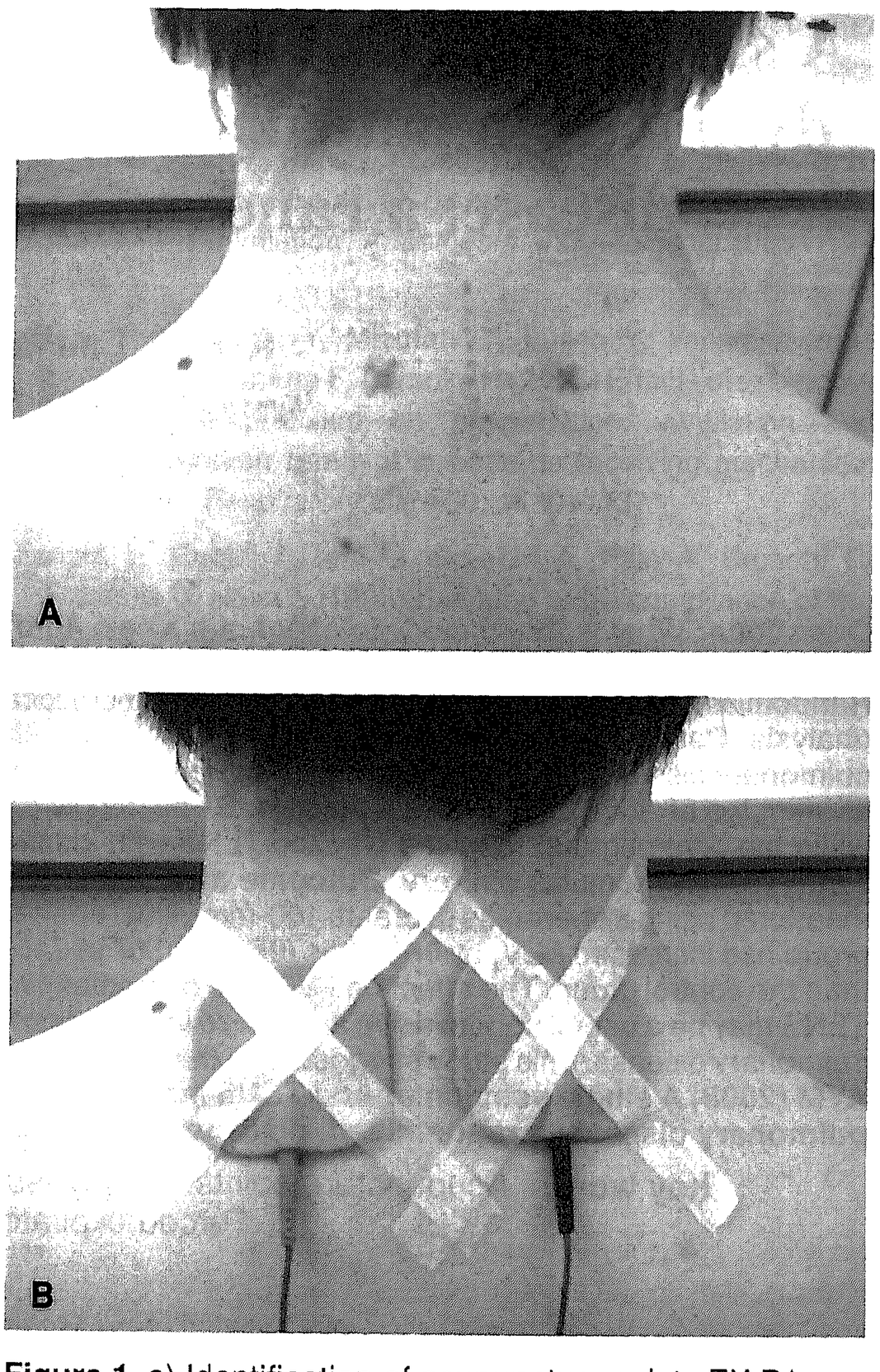

Figure 1. a) Identification of acupuncture points EX-B1. b) Placement of the electrodes over the acupuncture points EX-B1.

(American Thoracic Society 1995) using a spirometer[b] calibrated with a 3-litre super syringe. All measurements were performed in the sitting position and the best of 3 trials was recorded. Dyspnoea was measured using a shortness of breath 100-mm visual analogue scale (Martinez et al 2000) where zero represented 'not breathless at all' and 100 mm represented 'the worst breathless sensation you ever experienced'.

Data analysis

The clinical significance of the effect of Acu-TENS is reported as mean difference (95% CI) while the statistical significance is reported as p values from independent t-tests. Analysis was by intention-to-treat. A statistical significance level was set at $p < 0.05$.

Results

Flow of participants through the trial

A total of 46 participants (31 male and 15 female) from 4 community centres for the elderly met the inclusion criteria. The mean age was 75 years (SD 7), mean BMI was 23.6 kg/m^2 (SD 4.4); predicted FEV_1 was 69% (SD 14) and predicted FVC was 73% (SD 13). Fifteen participants (33%) were ex-smokers (ie, they had stopped smoking for over 12 months), 22 (48%) were current smokers, and 9 (20%) were non-smokers. Age, BMI, % predicted FEV_1 and FVC

Table 1. Characteristics of participants.

Characteristic	Exp (n = 23)	Con (n = 23)
Age *(yr)*, mean (SD)	77.5 (6.5)	73.7 (6.8)
Gender, n males (%)	19 (83)	12 (52)
BMI *(kg/m²)*, mean (SD)	23.7 (4.7)	23.5 (4.2)
FEV_1 *(% pred)*, mean (SD)	68 (16)	74 (8)
FVC *(% pred)*, mean (SD)	70 (13)	77 (12)
Smoking status, n (%)		
Smokers	11 (48)	11 (48)
Ex-smokers	9 (39)	6 (26)
Non-smokers	3 (13)	6 (26)

BMI = body mass index; FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity, Exp = experimental, Con = control

were similar between the two groups (Table 1). Medications prescribed were: Beclazone (250 mcg), theophylline (200 mcg/300mg), Ventolin (1–4 puffs), and/or Atrovent/ Combivent (1–2 puffs) as required. Medication for both groups was similar and none of the 46 participants received bronchodilators less than 6 hours prior to lung function measurements.

Compliance with trial method

All participants who met the inclusion criteria completed the trial. There was no report of adverse effects. All participants completed the post-intervention measurements, and all participants' data were included in the intention-to-treat analysis.

Effect of intervention

Group data as well as within- and between-group data are presented in Table 2 while individual data are presented in Table 3 (see eAddenda for Table 3). After 45 minutes of Acu-TENS, the experimental group had increased their FEV_1 by 0.12 litres (95% CI 0.07 to 0.15, $p < 0.001$) more than the control group. They had increased their FVC by 0.05 litres (95% CI –0.01 to 0.10, $p = 0.09$) non-significantly more than the control group. Their shortness of breath had decreased by 11 mm on the 100-mm visual analogue scale (95% CI –14 to –8) more than the control group.

Discussion

Comparison with previous studies

This study showed that a single session of bilateral application of TENS to acupoint EX-B1 (Ding Chuan) for 45 minutes in patients with chronic obstructive pulmonary disease increased FEV_1 and decreased dyspnoea. Positive effects of acupuncture and acupressure on dyspnoea management have been reported previously. Maa and colleagues (1997) showed that self-administered acupressure (kneading and pressure) over 7 acupoints (1 to 2 minutes per point) for 6 weeks reduced dyspnoea in patients with chronic obstructive pulmonary disease. Wu and colleagues (2004) showed that, compared to sham acupressure, acupressure over 5 acupoints (different from those reported in Maas's study) for 3 minutes, 5 sessions per week for 4 weeks decreased dyspnoea (measured by the Modified Pulmonary Function Status and Dyspnoea Questionnaire), improved walking capacity, and reduced anxiety. Maa's group (2003) also compared the effect of acupuncture and acupressure on dyspnoea and quality of life in participants with chronic obstructive asthma and found that patients who received acupuncture reported an 18-fold improvement in the St George's Respiratory Questionnaire score compared with a 6-fold improvement in patients who received acupressure. While our findings of decreased dyspnoea are similar to previous studies, direct comparison is not possible because previous studies investigated the effect of needle acupuncture, acupressure, and even moxibustion (burning of herbs over certain acupuncture points) (Jobst et al 1986) as part of the intervention. Furthermore, acupuncture points were not standardised in many of the studies and duration of intervention varied between studies. A combination of points was used in many studies as some points were believed to improve the flow of energy (Qi) as well as decrease dyspnoea whereas in our study, the stimulation of Ex-B1 was standardised.

St George's Respiratory Questionnaire (Lewith et al 2004), the Pulmonary Function Status and Dyspnoea Questionnaire (Wu et al 2004), the Shuttle Test (Davis et al 2001) and the 6-min Walk Test (Maa et al 2003) have all been used to evaluate the effect of acupuncture on dyspnoea in patients with chronic obstructive pulmonary disease. Most studies reported a positive effect of acupuncture on dyspnoea, but whether acupuncture improved quality of life in patients with chronic obstructive pulmonary disease remains controversial. While Maa's group (2003) showed that the St George's Respiratory Questionnaire score improved significantly more after acupuncture than acupressure, Lewith and colleagues (2004) reported that the improvement in St George's Respiratory Questionnaire scores did not differ significantly from the effect of sham TENS (no electrical output). Davis and colleagues (2001) commented that the Shuttle Test was 'impractical in a domiciliary environment' because most patients lacked a 10-m flat space at their residence (Davis et al 2001). Furthermore, while these measures may be appropriate for evaluation of the effect of long-term acupuncture, they may not be sufficiently sensitive to evaluate the effect of a single acupuncture session.

Mechanism of effect of acupuncture on dyspnoea

According to traditional Chinese medicine, dyspnoea results from a deficiency in the flow of 'Qi' (energy) in the lungs (Xu and Tan 1988) and application of an appropriate acupuncture technique is thought to restore the 'Qi balance'. This concept led to the use of a combination of points including those that were believed to restore energy and improve the flow of Qi (Maa et al 1997). However a satisfactory explanation of Qi flow and balance according to western medicine, has not yet been described (Tan and Horn 1998). Western medicine hypothesises that signals from stimulation of peripheral nerve fibres (possibly through acupuncture points) can influence hypothalamic functions via the dorsal periaqueductal grey fibres, and thereby influence the respiratory centre in the medulla, modifying respiration (Takeshige et al 1993). Investigation of the relationship between acupuncture and neural activity has been reported. Stimulation of vision-related acupoints has been shown to be associated with activation of the occipital lobe using functional magnetic resonance imaging (Cho et al 1998). Electroencephalography has been used to demonstrate a relationship between acupuncture and brain

Table 2. Mean (SD) for each group, mean (SD) difference within groups, and mean (95% CI) difference between groups for lung function and dyspnoea for the experimental group (n = 23) and the control group (n = 23).

Outcome	Groups				Difference within groups		Difference between groups
	Pre		Post		Post minus pre		Post minus pre
	Exp	Con	Exp	Con	Exp	Con	Exp minus Con
Lung function							
FEV_1 (*l*)	1.24 (0.46)	1.39 (0.43)	1.37 (0.47)	1.41 (0.43)	0.13 (0.09)	0.01 (0.03)	0.12 (0.07 to 0.15)
FVC (*l*)	1.70 (0.44)	1.75 (0.53)	1.77 (0.44)	1.77 (0.52)	0.07 (0.09)	0.02 (0.09)	0.05 (–0.01 to 0.10)
Dyspnoea							
SOB VAS (*0 to 100 mm*)	81 (5)	77 (7)	67 (6)	74 (7)	–14 (5)	–3 (5)	–11 (–14 to –8)

FEV1= forced expiratory volume in 1 second; FVC = forced vital capacity; SOB VAS = shortness of breath visual analogue scale; Exp = experimental, Con = control

activity (Rosted et al 2001). There is also speculation that the decrease in dyspnoea resulting from acupuncture is mediated by endogenous opiate release as a consequence of hypothalamic stimulation (Jobst et al 1986). Indeed, opiates are prescribed as respiratory depressants to modulate the sensation of breathlessness (Bellofiore et al 1990).

Dyspnoea in patients with chronic obstructive pulmonary disease has been associated with increased bronchial and systemic inflammation (Bhowmik et al 2000, Hill et al 1999, Roland et al 2001) and changes in levels of inflammatory mediators such as tumour necrosis factor and interleukin-8 have been associated with airflow limitation (Wouters 2002). Inflammation leads to a rise in cytokine levels, which are transmitted to the hypothalamus via sensory nerve transmission (Maier et al 1998). An efferent signal from the hypothalamus via parasympathetic nerves causes a release of acetylcholine at the parasympathetic nerve endings, evoking a suppressive effect on the release of the inflammatory cytokines (Tracey 2002). Increased levels of cytokines may also directly activate the hypothalamus-pituitary-adrenal axis via the vagus nerve, inducing the release of glucocorticocoids, further suppressing cytokine synthesis (Cho et al 2006, Maier et al 1998, Tracey 2002). Acupuncture is thought to evoke a suppressive effect on inflammatory mediator levels either via afferent (pre-synaptic) or efferent (post-synaptic) vagus nerve stimulation (Cho et al 2006) thereby decreasing dyspnoea. However, a direct effect of acupuncture on inflammatory markers in patients with chronic obstructive pulmonary disease has yet to be shown.

Mechanism of effect of Acu-TENS on dyspnoea

Application of TENS, at a tolerable intensity in humans, has been shown to stimulate Aα and Aβ nerve fibres (Levin and Hui-Chan 1993). We hypothesised that the application of TENS over acupoints may induce signal transmission similar to acupuncture, influencing vagal afferents via hypothalamic stimulation. However, determining whether the decrease in dyspnoea was a result of hypothalamic activity associated with endorphin release was beyond the scope of our study. The physiological mechanism underlying dyspnoea is complex and further investigation of the association between Acu-TENS and endorphin levels on dyspnoea is warranted.

Clinical implication of the application of Acu-TENS on lung function

This study found that FEV_1 increased by 10% (ie, 120 ml) more after Acu-TENS than placebo-TENS. While there is no complete agreement on standard criteria for evaluation of a short-term response to a bronchodilator (Tashkin et al 2008), the common indicators used to express a positive response to a bronchodilator are ≥ 15% improvement over pre-bronchodilator FEV_1 (ACCP 1974); ≥ 12% improvement plus an absolute volume increase of ≥ 200ml (Pellegrino et al 2005) and an absolute improvement over pre-bronchodilator FEV_1 of ≥ 10% predicted value (Anthonisen and Wright 1986). The improvement of FEV_1 in this study did not reach these standards, however direct comparison between effects of bronchodilators and Acu-TENS may not be appropriate. It is believed that bronchodilators decrease dyspnoea by reducing residual volume (air-trapping) (Price et al 2004). Bronchodilators are chemicals that specifically target reversible bronchoconstriction through neuromuscular transmission at receptors over the airways, inducing relaxation of airway smooth muscle. The proposed effect of Acu-TENS on FEV_1 is through central processing of neural signals whereas its action on airways, if any, is indirect. Furthermore, acute dyspnoea ratings and changes in FEV_1 are not necessarily linear, and a decrease in dyspnoea does not correlate with an increase in FEV_1 (O'Donnell et al 1997). Although the improvement in FEV_1 demonstrated in this study did not reach the gold standard set for 'bronchodilator' evaluation, this study revealed that Acu-TENS improved FEV_1 by 10% more than placebo-TENS, which is very close to the '≥ 10% predicted value' standard proposed (Anthonisen and Wright 1986). Furthermore, a decrease in dyspnoea score by 13% more than placebo-TENS should not be underestimated.

This study found Acu-TENS improved FVC by only 3% (ie, 50 ml) over placebo-TENS which was statistically insignificant. The total volume of air exhaled during forced expiration should increase when airway narrowing is less, but with one session of Acu-TENS, a clinically-significant change in FVC was not expected.

Limitations of the study

This study has several limitations. First, the severity of chronic obstructive pulmonary disease of the participants

was moderate. Even though the participants reported a mean dyspnoea score as high as 80 on a 100-mm visual analogue scale, the high end anchor of our visual analogue scale was 'the worst breathless sensation ever experienced'. Our predictive values were based on Lam's sample of Chinese participants (Lam et al 1982). If our predictive values were based on a European data base (Roca et al 1986), the predicted FEV_1 of our participants would be 50% which would categorise them very close to severe (GOLD 2007). Most participants travelled to the centre by bus and had to walk some distance to the community centre. Participants who took part in the study were those who did not take their bronchodilator on the day of assessment. Although they were allowed 30 minutes of rest before measurement of lung function, this may not have been sufficient for their dyspnoea to return to normal resting levels. Therefore, it may not be appropriate to extrapolate our findings to patients with mild chronic obstructive pulmonary disease and moderate dyspnoea. It should however be noted that if the expected effect of acupuncture is to maintain homeostasis, the effect of Acu-TENS on patients might be more dramatic on patients with high but not low level of dyspnoea. Second, this study focused on the effect of a single session of Acu-TENS in chronic obstructive pulmonary disease patients and the potential long term effects of Acu-TENS on dyspnoea were not explored. Third, we compared the effect of TENS or placebo-TENS over acupuncture points rather than TENS applied over non acupuncture points and therefore we are unable to draw conclusions on whether the positive effect of Acu-TENS was in fact acupoint-specific or a general effect of TENS. Fourth, we did not measure quality of life, although function is related to dyspnoea and determines quality of life.

This study demonstrated that, compared to placebo-TENS with no electrical stimulation, bilateral application of Acu-TENS at acupuncture point EX-B1 for 45 minutes in ambulatory patients with chronic obstructive pulmonary disease lead to an improvement in dyspnoea and FEV_1. TENS is a non-invasive, user-friendly, low cost, electrotherapy modality, and the application of Acu-TENS may assist dyspnoea management in patients with chronic obstructive pulmonary disease with the potential to improve activity levels and quality of life. The encouraging effect of Acu-TENS in our patient cohort suggests that Acu-TENS may be a useful adjunctive intervention in the management of dyspnoea in patients with chronic obstructive pulmonary disease. The effect of Acu-TENS on endorphin levels, its combined effect with medication on dyspnoea, its effect on frequency or intensity of disease exacerbation, and its long-term effect on the quality of life in patients with chronic obstructive pulmonary disease, warrant further investigation.

Footnotes: [a]NeuroTrac, model CE 0120, Verity Medical LTD, England, UK. [b]Pony spirometer graphic, COSMED, Italy.

eAddenda: Table 3 available at www.physiotherapy.asn.au/AJP.

Ethics: The Human Subjects Ethics Committee of Hong Kong Polytechnic University approved this study. Informed consent was gained from all subjects before data collection began.

Competing interests: None declared.

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Correspondence: Professor Alice Jones, Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong. Email: rsajones@polyu.edu.hk

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