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ACUPOINT TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IN HOSPITALIZED COPD PATIENTS WITH SEVERE DYSPNOEA: STUDY PROTOCOL FOR A RANDOMIZED CONTROLED TRIAL

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Study protocol

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Abstract

Background Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a major cause of hospital admissions and dyspnoea is its main symptom. Some studies have concluded that a new modality of acupuncture called Acupuncture transcutaneous nerve stimulation (acuTENS) could reduce dyspnoea in COPD patients by increasing beta-endorphin levels, however those trials have mainly been conducted on patients with stable condition. This study aims to determinate if the administration of acuTENS can reduce dyspnoea in patients hospitalized for AECOPD. Methods A multicentric randomized control trial with patient- and assessor-blinded will be conducted. A sample of 60 patients will be randomised to receive 45 minutes of either real acuTENS or sham acuTENS treatment once a day during 5 consecutive days. The trial will be conducted at the “Hospital del Mar” of Barcelona (Spain) and the “Hospital Sant Joan de Déu de Manresa” in Manresa (Spain). The Borg scale at baseline, and day 1 to 5 will be the primary outcome. Secondary outcomes will be the duration of the hospitalization, quantity of drugs administrated, expiratory peck flow adverse effects and mortality and readmissions at 3 months. Discussion AcuTENS is non-pharmacological, non-invasive and cheap intervention. This trial will help to understand acuTENS potential role in the treatment of AECOPD.

Background

Chronical obstructive pulmonary disease (COPD) is characterized by persistent and progressive airflow limitation associated with a chronic inflammatory response in the airways and the lung parenchyma to noxious particles or gases. (1) COPD is a major cause of morbidity and mortality worldwide and its prevalence is expected to increase over the next decade due to continuous exposure to risk factors and the aging of the population (2). It is estimated that in 2030 COPD will be the fourth leading cause of death globally (3). Currently, the prevalence of the disease in Spain is 10.2% of the population between 40 and 80 years (4).

Dyspnoea, along with chronic cough and sputum production, is one of the main symptoms of COPD. Its severity and magnitude increase as the disease progresses being the main cause of disability and reduced quality of life in COPD patients (5).

Patients may experience periods of acute exacerbation of COPD (AECOPD) defined as " a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, which is acute in onset and necessitates a change in regular medication in a patient with underlying COPD "(6). These can be particularly severe exacerbations requiring hospitalization. In Spain it is estimated that hospitalizations for AECOPD have an average cost of 344.96 euros per person per day (7), most of which is due to stays in hospital. These exacerbations are associated with a 12% of mortality and a 35 % of readmissions up to 3 months after discharge (8).

Treatment of AECOPD includes bronchodilators, corticosteroids, antibiotics, oxygen therapy and non-invasive mechanical ventilation (9). In the case of severe dyspnoea oral or parenteral administration of

opioids are recommended, although these have side effects and can cause respiratory depression (5). However, dyspnoea remains a major symptom in patients hospitalized for an AECOPD (7).

The acupoint transcutaneous electrical nerve stimulation (AcuTENS) is a modern technique based on traditional acupuncture. It consists in the stimulation of acupuncture points using transcutaneous electrical nerve stimulation (TENS) instead of needles, which makes it a very easy to learn, non-invasive method without the traditional acupuncture adverse effects such as infections or puncture of internal organs (10).

Several clinical studies using AcuTENS in patients with COPD have recently been published. All studies have used the stimulation of the acupuncture point named Dingchuan (EX-B1), traditionally used to treat dyspnoea. In those studies, a decrease in dyspnoea and an increase in FEV 1, β-endorphin level and quality of life have been observed (11-13). However, these studies have been conducted on patients in stable conditions and little is known about the possible effect of this technique in patients with an AECOPD. Only one case study has been published to the date suggesting possible benefits on the shortness of breath besides an increase in the level of oxygen saturation and β-endorphins (14).

The objectives of this study are to determine if the use of AcuTENS at the Dingchuan point (EX-B1) could be beneficial for patients hospitalized for AECOPD by reducing dyspnoea, days of hospitalization and consumption of regular medication. Moreover, we will assess possible adverse effects of this technique and its effect on mortality and readmissions at 3 months after discharge.

Trial Design

Multicentric, randomized controlled trial with blinded patients and assessors with a 1:1 allocation and two parallel groups.

Methods

Study setting:

The study will be performed at the “Hospital del Mar” in Barcelona (Spain) and the “Hospital de Sant Joan de Déu de Manresa” in Manresa (Spain).

Participants:

The study subjects will be patients admitted at the study centres for an AECOPD.

Participants will be recruited at the time of their admission by the pulmonology service and hospital emergency staff using the following inclusion: (1) patients aged between 45 and 75 years, with a diagnosis of COPD according to the GOLD guidelines, (2) patients with one episode of hospitalization for COPD exacerbation in the past year, but not more than three episodes, (3) smoking habit history of more

than 10 packages-year, (4) patients able to correctly understand and answer the modified Borg scale, (5) patients with an initial degree of dyspnoea with a score of at least 5 in the modified Borg scale at recruitment, (6) patients recruited for the study during the first 48 hours of their hospitalization, (7) patients who agree to participate in the study and sign the informed consent.

Exclusion criteria will be: (1) patients with any contraindication for transcutaneous electrical stimulation (patients with pacemakers, skin injury in the application area ...), (2) patients with any cardiovascular, neurological or psychiatric disease that may affect the perception of dyspnoea.

Interventions:

In both groups the Dingchuan point (EX-B1) will be localized bilaterally at 0.5 "cun" from the midline between the posterior spinous processes of C7 and T1. Afterwards a conductive plastic sheet between the skin and the electrodes will be placed. These sheets have a hole of about 0.5 cm in diameter, which will coincide with the point above. Finally, the electrodes will be fixed with tape.

AcuTENS group (experimental): The stimulation is performed using a portable TENS electrostimulation device (Sale & Sevice TN23) that uses a biphasic rectangular wave with a frequency of 2Hz and a pulse width of 200 mS. The stimulation will be achieved using the highest intensity tolerated by the patient without pain.

TENS simulated group (control): This group will have electro stimulators of the same make and model as the experimental group, but that have been modified to have no electrical outlet, even though the screen will light up and display the same data as in the unmodified device. Patients in this group will be informed that, due to the frequency of stimulation, it is unlikely that they will feel the electric stimulation.

In both groups, the session will last 45 minutes and will take place during a maximum of five consecutive days or until the patient is discharged.

If the acuTENS stimulation produces any kind of discomfort, the intensity of the current being applied to the patient will be reduced. If for any reason a treatment cannot be administered or is administered differently from the original protocol (example: only 30 min treatment because the electrostimulation device had no battery) this will be reported. Any discomfort or skin reaction will be reported as an adverse event.

The interventions will be performed by physiotherapists or physicians with a minimum of one year of clinical experience, who have been trained in the handling of the two treatment protocols. There will be a pre-pilot test to detect potential problems and ensure the adequacy of the implementation of the protocols.

Adherence to the treatment will be reported. No special stages for improving adherence will be taken since all patients will be hospitalized in the participating centres.

Both groups will receive the standard treatment for patients with AECOPD (bronchodilators, steroids ...) according to medical criteria, as well as the treatment with acuTENS or simulated acuTENS. No treatment is prohibited.

Outcomes

The primary outcome of this trial will be dyspnoea using the modified Borg Scale. Evaluators will show a printed Borg scale to patients and explain the meaning of each punctuation, then patients will be asked to rate their dyspnoea. Data will be assessed at baseline and after each treatment session (day 1 to day 5). The modified Borg Scale is a valid and reliable assessment tool for dyspnoea in patients with an AECOPD (16).

Secondary outcomes will be (1) number hospitalization days, (2) quantity of drugs administered during hospitalization, (3) adverse events during the 5-day treatment, (4) peak expiratory flow at each day (day 1 to day 5) and difference from baseline to day 5 using a peak flow meter, (5) blood gas analysis (PaO_2, $PaCO_2$, arterial blood pH, bicarbonate and SaO_2) at each day (day 1 to day 5) and difference from baseline to day 5 and (6) mortality, relapses and readmissions during the first three months after discharge.

Data will be collected using a standard form.

Participant timeline

Participant timeline is described in figure 1.

Randomization and allocation:

Participants will be randomly assigned to the acuTENS or sham acuTENS group with a 1:1 allocation using a computer-generated randomisation list. A blocked randomisation list will be generated for each centre by the main author, who will not be involve in the recruitment or assessment.

Randomisation lists will be kept using electronic key and only will be available to the persons responsible for administering the treatments.

Once participants give consent for participation a consecutive number will be assigned by the head of recruitment, the staff responsible of administrating the treatment will match the patient's number with the randomization list to define patient's allocation.

Blinding

Trial participants, outcome assessors and usual care providers will be blinded during the trial, only the physiotherapists who will perform the acuTENS or sham acuTENS procedure will know patient's allocation. The medical staff will not be present during the application of technology to ensure that they remain blinded to allocation.

Sample size

Given that the significant difference in clinical minimally dyspnoea measured by the Borg scale for patients with COPD exacerbation is 2 (15), a common standard deviation of 2.6 and assuming an α error of 0.05, a β error of 0.2 and a 10% of losses, it is calculated that we will need to recruit 60 patients for this study.

Statistical methods

There will be a descriptive analysis of the demographic data using means and standard deviations (mean ± SD) for continuous variables and absolute values and percentages for qualitative outcomes.

For the comparative analysis between the two groups, continuous outcomes will be analysed using mean differences with a 95% confidence interval with a t' Student test or Mann-Whitney U depending on the distribution of these. For qualitative outcomes risk ratio will also be used with a confidence interval of 95% and test $\chi 2$.

The main analysis will be done by intention to treat, but there will be another per-protocol analysis for patients who have received at least three interventions. Significant difference will be considered as a value of $p < 0.05$.

In the case of significant baseline differences between the two groups there will be an adjusted analysis for these outcomes.

Discussion

This protocol describes the design of a clinical trial investigating the effectiveness of adding acuTENS stimulation to usual treatment on dyspnoea, in patients hospitalized with an AECOPD. If the results of this trial are positive, a new non-pharmacological and cheap intervention could be used in cases of intense dyspnoea. Moreover, dyspnoea improvement could also lead to a reduction in medication and hospitalization days, reducing hospitalization costs. It is also important to highlight that this is a quit simple intervention to learn and TENS devices are usually available in any health centre, this is important as it would facilitate the technique's implementation and generalization.

Abbreviations

AcuTENS: Acupuncture transcutaneous nerve stimulation

AECOPD: Acute exacerbation of chronic obstructive pulmonary disease

COPD: Chronical obstructive pulmonary disease

TENS: Transcutaneous electrical nerve stimulation

SD: Standard deviations

Declarations

Ethics approval and consent to participate

This protocol was approved by the research ethics committee of each centre (identification codes 2018/8153/I and CEI 17/97). All protocol modifications will be informed to all lead investigators and reported in the final manuscript.

All patients will be informed about the nature of the study, its objective, and the possible adverse effects of the treatments, as well as their voluntary participation. All patients must sign an informed consent document. The patients will be able to leave the study whenever they want without any detriment to their health care.

The data collected during the study will be treated in accordance with the LOPD, Regulation (EU) nº2016 / 679 of the European Parliament and European Council on data protection (RGPD) that came into force on May 25, 2018.

Data monitoring is not needed as the treatment used is expected to have low safety risk. For the same reason, no interim analysis or stopping guidelines are considered. No additional insurance was needed for this trial since the TENS device is regularly used in the rehabilitation department.

Results of the trial will be disseminated via publication.

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

Competing interests

Authors declare no financial or competing interests.

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Funders had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Authors’ contributions

CF has been responsible for writing the protocol of the study, and the submission of the manuscript. JV helped with the study design and the sample size calculation. All authors contributed to refinement of the study protocol and approved the final manuscript.

Trial Status

Protocol Admen Number: 02

Issut Date: 20 March 2018

Recruitment start day: 1 April 2018

Estimated recruitment completion date: June 2019

Acknowledgments

Not applicable

References

1. Vestbo J, Hurd SS, Agusti AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2013; 187 (4): 347-65.

2. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL Held LS, et al. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J. 2006; 27 (2): 397-412.

3. World Health Organization. The global burden of disease: 2004 update. Geneva, Switzerland: World Health Organization; 2008. 146 p.

4. Miravitlles M, Soriano JB, García-Río F, Muñoz L, Duran-Tauleria E, Sanchez G, et al. Prevalence of COPD in Spain: impact of undiagnosed COPD on quality of life and daily life activities. Thorax. 2009 Oct;64(10):863–8.

5. Marciniuk DD, Goodridge D, Hernandez P, Rocker G, Balter M, Bailey P, et al. Managing dyspnea in patients with advanced chronic obstructive pulmonary disease: a Canadian Thoracic Society clinical practice guideline. Can Respir J. 2011 Apr;18(2):69–78.

6. Rodriguez-Roisin R. Toward a consensus definition for COPD exacerbation. Chest. 2000;117 (5 Suppl 2): 398S-401S. 7. Miravitlles M, García-C Polo, Domenech A, G Villegas, Conget F, the Roza C. Clinical outcomes and cost analysis in exacerbation of chronic obstructive pulmonary disease. Lung. 2013; 191 (5): 523-30.

8. JL López-Campos, Hartl S Pozo-Rodriguez F, CM Roberts, European COPD Audit team. European COPD Audit: design, Organisation of work and methodology. Eur Respir J. 2013; 41(2): 270-6.

9. Miravitlles M Soler-Cataluña JJ, Calle F, J Molina, Almagro P Quintano JA, et al. Guide Spanish COPD (GesEPOC). Update 2014. Arch Bronconeumol. 2014; 50 (Suppl 1): 1-16.

10. Xu S, Wang L, Cooper E, Zhang M, Manheimer E, Berman B, et al. Adverse events of acupuncture: a systematic review of case reports. Based Complement Altern Med-evident ECAM. 2013; 2013: 581203.

11. Alice J Lau KSL and YM. A single session of Acu-TENS increasi you reduce dyspnoea and FEV1 in Patients with chronic obstructive pulmonary disease: a randomised, placebo-controlled trial. 2008; 54 (3): 179-84.

12. AYM Jones and Shirley N PC and Hui-Chan, Christina WY and Yu, Homer PM. Acute Effects of Acu-TENS on FEV1 and Blood B-Endorphin Level in Chronic Obstructive Pulmonary Disease. 2011; 17 (5): 8-13.

13. Ngai SPC and Alice J YM and Hui-Chan, Christina WY and Ko, Fanny and WS Hui, David SC. Effect of 4 weeks of Acu-TENS on functional capacity and beta-Endorphin level in subjects with chronic obstructive pulmonary disease: a randomized controlled trial. January 1, 2010; 173(1): 29-36.

14. SPC Ngai, AYM Jones, Hui-Chan CWY, FWS Ko Hui DSC. An adjunct intervention for management of acute exacerbation of chronic obstructive pulmonary disease (AECOPD). J Altern Complement Med NY N. 2013; 19 (2): 178-81.

15. Kelly AM. The minimum clinically significant difference in visual analogue pain scale score does not Differ with severity of pain. EMERG Med J. 2001; 18 (3): 205-7.

16. Kendrick KR, Baxi SC, Smith RM. Usefulness of the modified 0-10 Borg scale in assessing the degree of dyspnea in patients with COPD and asthma. J Emerg Nurs. 2000 Jun;26(3):216–22.

Figures

	STUDY PERIOD							
	Enrolment	Allocation	Post-allocation					Close-out
TIMEPOINT**	$-t_1$	0	day_1	day_2	day_3	day_4	day_5	3 months
ENROLMENT:								
Eligibility screen	X							
Informed consent	X							
Allocation		X						
INTERVENTIONS:								
AcuTENS			X	X	X	X	X	
Sham AcuTENS			X	X	X	X	X	
ASSESSMENTS:								
Dyspnea	X		X	X	X	X	X	
Duration of hospitalization								X
Quantity of drugs administrated	X		X	X	X	X	X	
Adverse effects or disadvantages	X		X	X	X	X	X	
Peak expiratory flow	X		X	X	X	X	X	
Blood gas analysis	X		X	X	X	X	X	
Mortality								X
Readmissions								X

Figure 1

Schedule of enrolment, interventions, and assessments.