

Inhaled furosemide does not alleviate respiratory effort during flow-limited exercise in healthy subjects

Pierantonio Laveneziana^a, Andrea Galarducci^a, Barbara Binazzi^a, Loredana Stendardi^b,
Roberto Duranti^a, Giorgio Scano^{a,b,*}

^a*Dipartimento di Medicina Interna, Sezione di Immunologia e Malattie dell'Apparato Respiratorio, Università degli Studi di Firenze, Viale G.B. Morgagni 85, 50134 Firenze, Italy*

^b*Fondazione Don C. Gnocchi, Sezione di Riabilitazione Respiratoria, Via Imprunetana 124, 50020 Pozzolatico, Italy*

Received 29 November 2005; received in revised form 2 February 2007; accepted 20 February 2007

Abstract

Expiratory muscle loading results in increased perception of respiratory effort; this response is mediated by non-vagal reflexes originating in the chest wall. Furosemide, due to its vagal effect, might not affect the perception of respiratory effort during expiratory flow-limited incremental exercise. In this study, we compared in nine healthy subjects the following determinants of exercise performance such as respiratory effort (Borg), workload (W'), ventilation (V_E), tidal volume (V_T), respiratory frequency (f), and mean inspiratory flow (V_T/T_I), an index of central respiratory drive, during either standard incremental cycling exercise, or expiratory flow-limited incremental exercise. In addition we examined the effect of inhaled placebo, furosemide (40 or 80 mg) on the perception of respiratory effort following standard incremental cycling exercise and expiratory flow-limited incremental exercise. Compared with standard incremental cycling exercise, expiratory flow-limited incremental exercise increased the Borg score and V_T/T_I , and decreased W' , V_E , V_T , and f in all subjects at iso-workload. Neither placebo nor furosemide modified peak ventilatory variables, slopes, or intercepts of the relationships of the Borg score with W' , V_E , V_T/T_I and V_T during expiratory flow-limited incremental exercise. We conclude that (a) compared with standard incremental exercise, expiratory flow limited exercise increases central respiratory drive and perception of respiratory effort, and (b) furosemide does not affect the sensation of respiratory effort under the present conditions of increased drive to the respiratory muscles.

© 2007 Elsevier Ltd. All rights reserved.

Keywords: Dyspnea; Breathing pattern; Hyperinflation; Furosemide; Exercise; Flow-limitation

1. Introduction

It has been recently shown that inhaled furosemide alleviates dyspnea induced by a combination of inspiratory resistive loading and hypercapnia in healthy subjects [1]. Nishino et al. [1] have attributed the effect of inhaled furosemide on dyspnea to a predominant altered activity of sensory airway vagal receptors that transmit afferent information to the central nervous system (CNS): i.e.,

decreased activity of irritant receptors and increased stimulation of stretch receptors.

Expiratory muscle loading is associated with increased respiratory muscle force not mediated by vagal afferents [2–4]. This response is a reflex arising in the respiratory muscles as a result of the load imposed upon them by the distended thorax [2], and is mediated by reflexes originating in the chest wall [2,4–6].

Because the combined drive to inspiratory and expiratory muscles, and/or receptors within these muscles are thought to be the prime mechanisms for generating respiratory-effort sensation during incremental expiratory flow-limited exercise [7], we hypothesized that under these circumstances, when vagal activity is thought to play a minor role [2–4], furosemide might not affect the

*Corresponding author. Dipartimento di Medicina Interna, Sezione di Immunologia e Malattie dell'Apparato Respiratorio, Università degli Studi di Firenze, Viale G.B. Morgagni 85, 50134 Firenze, Italy.
Tel.: +39 55 4296414; fax +39 55 412867.

E-mail address: gscano@unifi.it (G. Scano).

perception of respiratory effort. To validate this hypothesis we carried out the present investigation on nine normal subjects who underwent expiratory flow-limited exercise before and after medication with either placebo or furosemide.

2. Materials and methods

2.1. Subjects

We studied nine healthy subjects (4 females and 5 males) whose combined ages, anthropometric characteristics, baseline lung volume subdivisions and pulmonary function are shown in Table 1. All subjects were free of cardiovascular and neuromuscular diseases. All were trained in respiratory maneuvers and were naïve to the purpose of the study. Spirometry and FRC ($V_{\max}$ 22, SensorMedics, Yorba Linda, CA) were assessed in accordance with recommended standards [8]. The study was approved by a Local Ethics Committee and each subject gave informed consent.

2.2. Exercise testing

Symptom-limited incremental cycling exercise was assessed using an electronically braked cycle ergometer (Ergometrics 800S; SensorMedics). After 3 min of spontaneous resting breathing, subjects performed an inspiratory capacity (IC) maneuver. After this, they started pedaling at a rate of 60 revolutions per min, first at zero load. After 1 min, the workload (W') was increased in 15–20 W steps every minute until exhaustion. Subjects breathed through a mouthpiece and a mass flowmeter ($V_{\max}$ 29c; SensorMedics) which was attached to a Hans–Rudolph valve, which separated the inspiratory and expiratory lines. Maximum power output ($W'_{\max}$) was defined as the highest level of exercise that could be sustained. The output of CO_2 ($\dot{V}\text{CO}_2$), O_2 consumption ($\dot{V}\text{O}_2$), end tidal CO_2 tension ($P_{\text{ET},\text{CO}_2}$), respiratory frequency (f), minute ventilation ($\dot{V}_E$), tidal volume (V_T), inspiratory time (T_I) and mean inspiratory flow ($\dot{V}_T/T_I$), as a rough index of central

respiratory drive, were measured at rest and for each breath throughout exercise ($V_{\max}$ 29c; SensorMedics). IC was assessed at rest and at 2 min interval during exercise. Data were averaged during the last 30 s of each workload, including the subject's assessment of breathing. During exercise runs, the subjects were asked to rate difficulty in breathing using a 10-point modified Borg scale [9]. The precise wording used with the subjects was the following: please rate the respiratory work/effort in breathing during exercise using the scale where zero indicates no sensation at all and 10 an intolerable sensation. ECG and SpO_2 by ear lobe sensor (RAD-9; Masimo Corporation, Irvine, CA) were monitored throughout the test.

2.3. Study design

The subjects performed a standard incremental cycling exercise in order to determine $W'_{\max}$ under control conditions, and a flow-limited exercise by exhaling through a Starling resistor that limited expiratory flow to about 1 l/s. Flow-limitation was achieved by inserting the Starling resistor into the expiratory port of the valve [10].

The pharmacological arm of the study was conducted in a double-blind, randomized, crossover design (Fig 1). Baseline spirometry was assessed before and 15 min after inhalation of placebo. Four and eight milliliters of furosemide (Aventis; Frankfurt am Main, Germany) as a 10 and 20 mg/mL solution, respectively, containing NaCl 7 mg plus NaOH at pH 9 and H_2O to make up 1 and 4 mL of placebo (0.9% saline solution, the diluent solution of furosemide) were given by means of ultrasonic nebulizer (ULTRA-NEB 2000; De Vilbiss; output: 0.3 mL/min) with the subject breathing tidally over a period of 15 min. Exercises were done after completion of nebulization.

2.4. Data analysis

Values are means $\pm$ SD. The highest W' achieved by each subject during flow-limited exercise ($W'_{\max}$) was used as an iso-workload to compare responses at identical levels of exercise during standard incremental exercise, and before and after medication with either furosemide or placebo. Correlations among variables were performed with the Pearson test. Borg rating (in arbitrary units, a.u.) of

Table 1

Ages, anthropometric characteristics, baseline lung volume subdivisions, and pulmonary function of the nine healthy subjects

Age	31 $\pm$ 10
BMI (Kg/m^2)	21.1 $\pm$ 2.5
TLC, L	6.5 $\pm$ 0.8 (102 $\pm$ 5)
VC, L	5 $\pm$ 0.6 (107 $\pm$ 10)
IC, L	3.2 $\pm$ 0.6 (103 $\pm$ 15)
FRC, L	3.2 $\pm$ 0.6 (102.6 $\pm$ 6)
FEV ₁ , L	4.2 $\pm$ 0.5 (110 $\pm$ 12)
FEV ₁ /VC (%)	85 $\pm$ 4

Values are means $\pm$ SD with predicted values in parentheses. BMI: body mass index; TLC: total lung capacity; VC: vital capacity; IC: inspiratory capacity; FRC: functional residual capacity; FEV₁: forced expiratory volume in one second.

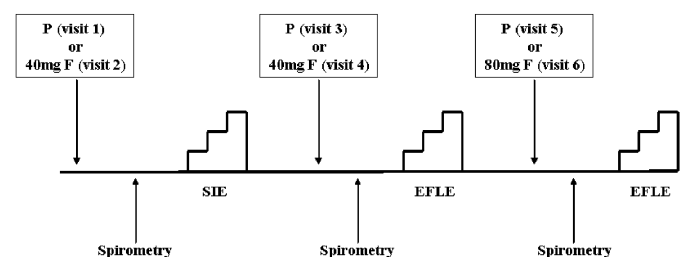


Fig 1. Events and measurements of the study. Abbreviations: P = Placebo; F = Furosemide; SIE = Standard incremental exercise; EFLE = Expiratory flow-limited exercise.

Download English Version:

<https://daneshyari.com/en/article/2567644>

Download Persian Version:

<https://daneshyari.com/article/2567644>

[Daneshyari.com](https://daneshyari.com)