Respiratory Physiology & Neurobiology 235 (2017) 45–51

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

Alveolar gas composition during maximal and interrupted apnoeas in ambient air and pure oxygen

Nazzareno Fagoni[a,b,*], Anna Taboni[c], Giovanni Vinetti[c], Sara Bottarelli[a], Christian Moia[d], Aurélién Bringard[d], Guido Ferretti[a,d]

[a] Dipartimento di Medicina Molecolare e Traslazionale, Università di Brescia, Italy
[b] Dipartimento di Specialità Medico-chirurgiche, Scienze Radiologiche e Sanità Pubblica, Università di Brescia, Italy
[c] Dipartimento di Scienze Cliniche e Sperimentali, Università di Brescia, Italy
[d] Département des Neurosciences Fondamentales, Université de Genève, Switzerland

ARTICLE INFO

Article history:
Received 27 June 2016
Received in revised form 5 October 2016
Accepted 6 October 2016
Available online 6 October 2016

Keywords:
Interrupted apnoea
Maximal apnoea
Oxygen apnoea
P_ACO_2
Alveolar gas
Diaphragmatic contraction

ABSTRACT

Introduction: We tested the hypothesis that the alveolar gas composition at the transition between the steady phase II (φ2) and the dynamic phase III (φ3) of the cardiovascular response to apnoea may lay on the *physiological breaking point* curve (Lin et al., 1974).
Methods: Twelve elite divers performed maximal and φ2-interrupted apnoeas, in air and pure oxygen. We recorded beat-by-beat arterial blood pressure and heart rate; we measured alveolar oxygen and carbon dioxide pressures (P_AO_2 and P_ACO_2, respectively) before and after apnoeas; we calculated the P_ACO_2 difference between the end and the beginning of apnoeas (ΔP_ACO_2).
Results: Cardiovascular responses to apnoea were similar compared to previous studies. P_AO_2 and P_ACO_2 at the end of φ2-interrupted apnoeas, corresponded to those reported at the *physiological breaking point*. For maximal apnoeas, P_ACO_2 was less than reported by Lin et al. (1974). ΔP_ACO_2 was higher in oxygen than in air.
Conclusions: The transition between φ2 and φ3 corresponds indeed to the *physiological breaking point*. We attribute this transition to ΔP_ACO_2, rather than the absolute P_ACO_2 values, both in air and oxygen apnoeas.

1. Introduction

Beat-by-beat analysis of the cardiovascular responses to maximal apnoeas at rest (Costalat et al., 2013; Fagoni et al., 2015; Lemaître et al., 2008; Perini et al., 2008, 2010; Sivieri et al., 2015) allowed identification of three distinct phases: (i) a short dynamic phase, phase I (φ1), lasting less than 30 s, characterised by rapid changes in blood pressure and heart rate (HR); (ii) a steady state phase, phase II (φ2), lasting about two min, in which the values attained by each variable at the end of φ1 stay invariant; and (iii) a further subsequent dynamic phase, phase III (φ3), characterised by a continuous decrease in HR and increase in blood pressure, until the *volitional breaking point* is reached.

At the beginning of φ1, there is a sudden fall of stroke volume (SV) and of arterial blood pressure (Andersson and Schagatay, 1998; Palada et al., 2007; Perini et al., 2008), which may be generated by an immediate increase in central venous pressure related to the high lung volumes at which apnoeas are carried out (Andersson and Schagatay, 1998). The ensuing increase in HR in the initial part of φ1 was seen as a baroreflex attempt at controlling blood pressure (Fagoni et al., 2015). The duration of φ1 is invariant and independent of the metabolic rate (Sivieri et al., 2015) and of the size of lung oxygen stores (Fagoni et al., 2015).

Conversely, the meaning of φ2 and φ3 is still unclear. According to Perini et al. (2008, 2010), the end of φ2 might correspond to the end of the so-called *easy going phase* (Hong et al., 1971; Lin et al.,

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; MBP, mean blood pressure; P_ACO_2, alveolar pressure of carbon dioxide; P_AO_2, alveolar pressure of oxygen; $\dot{Q}$, cardiac output; SBP, systolic blood pressure; SpO_2, peripheral oxygen saturation; SV, stroke volume; TPR, total peripheral resistance; ΔP_ACO_2, difference in the alveolar carbon dioxide pressure between the end and the beginning of apnoea; φ1, phase I: first dynamic phase of the cardiovascular response to apnoea; φ2, phase II: steady-state phase of the cardiovascular response to apnoea; φ3, phase III: last dynamic phase of the cardiovascular response to apnoea.

* Corresponding author at: Dipartimento di Medicina Molecolare e Traslazionale, Università di Brescia, Viale Europa, 13, 25123 Brescia, Italy.
E-mail address: nazzareno.fagoni@unibs.it (N. Fagoni).

http://dx.doi.org/10.1016/j.resp.2016.10.002
1569-9048/

1974). If this hypothesis is correct, then the alveolar gas composition at the end of φ2 should lie, on an O_2-CO_2 diagram (Rahn and Fenn, 1955), around the *physiological breaking point* curve (Hong et al., 1971; Lin et al., 1974). Coherently with these concepts, the duration of φ2 is prolonged when lung oxygen stores are increased (Fagoni et al., 2015) and reduced at exercise, when the metabolic rate is increased (Sivieri et al., 2015).

A detailed analysis of the alveolar gas composition at the end of φ2 was never carried out in humans so far. The purpose of the present study was to demonstrate that the alveolar gas composition at the end of φ2 corresponds indeed to that reported at the *physiological breaking point*. In order to expand the range of investigated alveolar gas composition, experiments were carried out in air and in pure oxygen.

2. Methods

2.1. Subjects

Twelve competitive divers (9 males and 3 females) volunteered for this study. They were 42 ± 7 years old, 72 ± 11 kg heavy and 176 ± 9 cm tall. All participants refrained from apnoea training and from strenuous exercise on the days of the measurements. All divers were healthy non-smokers. None had previous history of cardiovascular, pulmonary or neurological diseases, or was taking medications at the time of the study. All gave their informed consent after having received a detailed description of the methods and of the experimental procedures. The study conformed to the Declaration of Helsinki and was approved by the local ethical committee.

2.2. Experimental design

Experiments were carried out in Lignano Sabbiadoro, Italy, in an air-conditioned room at 23 °C, with relative humidity between 60 and 65%, on two different days. On the first day, upon arrival in the laboratory and after instrumentation, the subject took the supine posture. Five min were allowed to achieve steady state conditions before starting the recordings. Then 10 min of resting recordings were obtained during spontaneous normal breathing; in this period, all the cardiovascular parameters were collected and were retained as control values (control). Then the subject performed two maximal apnoeas, the first of which was systematically shorter than the second: the first apnoea was thus taken as a training apnoea, the second as the experimental apnoea in air. These apnoeas were separated by a recovery interval of two min, as described elsewhere (Fagoni et al., 2015; Sivieri et al., 2015). At the end of the second apnoea, after further two min of recovery, the subject started breathing pure oxygen. Oxygen was administered from high-pressure, high-precision cylinders, via a Douglas bag that was used as pressure buffer. After 10 min of normal breathing to clear nitrogen from the airways, and further five min of resting recordings, the subject performed the third maximal apnoea. After the end of this apnoea, the subject kept breathing pure oxygen for further two min during the recovery period.

Both in air and in oxygen, the subject underwent his/her predive routine breathing before breath-holding, consisting of a couple of deep respiratory acts. A deep inspiration preceded the apnoeas, so that the lung volume at which the apnoeas started was close to the subject's total lung capacity. As a consequence, the first breathing movement at the end of the apnoeas was an expiration, which the subject performed as deep as possible, in order to allow analysis of alveolar gases from the alveolar plateau.

The cardiovascular time courses of the apnoeas carried out on the first day were immediately analysed, in order to identify φ1, φ2 and φ3 for each apnoea. The identification of the time, at which the transitions between φ2 and φ3 occurred, defined the duration of φ2-interrupted apnoeas to be performed on the following day. The procedure for the φ2-interrupted apnoeas was the same as on the first day, the unique difference being the shorter duration of the apnoeas. Each diver performed three apnoeas, two in air and one in oxygen.

2.3. Measurements

Arterial blood pressure profiles (PortaPres®, TNO-TPD, Amsterdam, The Netherlands) were continuously recorded throughout the experiments. Peripheral blood O_2 saturation (SpO_2) was also continuously monitored by infrared spectroscopy (BioPac System Inc., Goleta, CA, USA) at an earlobe. Cardiac output ($\dot{Q}$) was continuously measured on a beat-by-beat basis by impedance cardiography (ACKICG module, BioPac System Inc., Goleta, CA, USA). The signals were sampled at 100 Hz by using a 16-bit A/D converter (MP100 VS, BioPac System Inc., Goleta, CA, USA) and stored on a personal computer for subsequent analysis.

The time course of oxygen and carbon dioxide partial pressures throughout the respiratory cycles were calibrated against a gas mixture of known composition and continuously monitored by rapid gas analysers (O2100C and CO2100C respectively for O_2 and CO_2, BioPac System Inc., Goleta, CA, USA). The inspiratory and expiratory ventilations were measured by an ultrasonic flowmeter (Spiroson, Ecomedics, Duernten, Switzerland) calibrated with a 3 l syringe. The traces alignment was corrected for the time delay between the flowmeter and the gas analysers.

The breath-by-breath recording of respiratory data was obviously interrupted during the apnoeas. The time with flat gas flow signals provided the duration of apnoeas. The deep expiration at the end of apnoea was analysed and the alveolar partial pressures of O_2 and CO_2 determined on the alveolar plateau (P_AO_2 and P_ACO_2, respectively) were retained as representative of the mean alveolar gas composition at the end of the breath-holding.

2.4. Data treatment

Arterial pressure profiles were analysed off line, to obtain beat-by-beat values of HR, SBP, diastolic and mean blood pressure (DBP and MBP, respectively), using the Beatscope™ software (TNO-TPD, The Netherlands). SV was computed on a beat-by-beat basis by dividing each $\dot{Q}$ value by the corresponding HR value. The ratio between MBP and $\dot{Q}$ provided an estimate of total peripheral resistances (TPR).

The beat-by-beat data were analysed off-line to identify the three phases of apnoeas. An automated procedure implemented under Matlab (version 7.6.0.324, MathWorks, Natick, MA, USA) was used to this aim. The procedure was based on linear regression analysis, allowing detection of changes in slope between successive phases; linear regression was also used to verify steady state of investigated variables in φ2, as described elsewhere (Sivieri et al., 2015).

Control values were computed from the resting recordings as the mean value over one min for each cardiovascular parameter (SBP, DBP, HR, SV, $\dot{Q}$, and TPR), for both maximal and φ2-interrupted apnoeas. For each cardiovascular variable, in the analysis of the time course of apnoeas, the following values were highlighted: "Start", referring to the single value just before the beginning of apnoeas; "MSP", i.e. the single value when SBP reached its minimum during φ1; "Last 10 beats φ2", i.e. the average of the last 10 beats during φ2; and "Last 10 beats φ3", i.e. the average of the last 10 beats during φ3.