Respiratory Physiology & Neurobiology 219 (2015) 1–8

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

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

Cardiovascular responses to dry resting apnoeas in elite divers while breathing pure oxygen

Nazzareno Fagoni[a,b,*], Andrea Sivieri[a], Guglielmo Antonutto[c], Christian Moia[d], Anna Taboni[a], Aurélién Bringard[d], Guido Ferretti[a,d]

[a] Dipartimento di Scienze Cliniche e Sperimentali, Università di Brescia, Italy
[b] Dipartimento di Specialità Medico-Chirurgiche, Scienze Radiologiche e Sanità Pubblica, Università di Brescia, Italy
[c] Dipartimento di Scienze Mediche e Biologiche, Università di Udine, Italy
[d] Département des Neurosciences Fondamentales, Université de Genève, Switzerland

ARTICLE INFO

Article history:
Received 11 May 2015
Received in revised form 31 July 2015
Accepted 31 July 2015
Available online 4 August 2015

Keywords:
Oxygen apnoea
Dry static apnoea
Heart rate
Arterial blood pressure
Cardiac output
Baroreflexes

ABSTRACT

Purpose: We hypothesized that the third dynamic phase ($\phi 3$) of the cardiovascular response to apnoea requires attainment of the physiological breaking point, so that the duration of the second steady phase ($\phi 2$) of the classical cardiovascular response to apnoea, though appearing in both air and oxygen, is longer in oxygen.
Methods: Nineteen divers performed maximal apnoeas in air and oxygen. We measured beat-by-beat arterial pressure, heart rate (f_H), stroke volume (SV), cardiac output ($\dot{Q}$).
Results: The f_H, SV and $\dot{Q}$ changes during apnoea followed the same patterns in oxygen as in air. Duration of steady $\phi 2$ was 105 ± 37 and 185 ± 36 s, in air and oxygen ($p < 0.05$), respectively. At end of apnoea, arterial oxygen saturation was 1.00 ± 0.00 in oxygen and 0.75 ± 0.10 in air.
Conclusions: The results support the tested hypothesis. Lack of hypoxaemia during oxygen apnoeas suggests that, if chemoreflexes determine $\phi 3$, the increase in CO_2 stores might play a central role in eliciting their activation.

1. Introduction

In recent years, changes in blood pressure, heart rate (f_H), stroke volume (SV), cardiac output ($\dot{Q}$) and total peripheral resistance (TPR) in response to apnoea (cardiovascular response to apnoea) were determined beat-by-beat on elite divers during apnoeas prolonged to the volitional breaking point (Costalat et al., 2013; Lemaître et al., 2008; Perini et al., 2008, 2010; Sivieri et al., 2015). These studies described the cardiovascular response to apnoea as consisting of three distinct phases: (i) a short dynamic phase ($\phi 1$), that lasts less than 30 s, characterised by rapid changes in blood pressure and f_H; (ii) a steady state phase ($\phi 2$), of about 2 min, in which the values attained by each variable at the end of $\phi 1$ are maintained invariant; and (iii) a further subsequent dynamic phase ($\phi 3$), lasting about 1.5 min, characterised by a continuous decrease in f_H and increase in blood pressure, until the volitional breaking point was reached. According to Perini et al. (2008, 2010), the end of $\phi 2$ might occur at the attainment of the physiological breaking point of apnoea (Hong et al., 1971), which is characterised by a specific alveolar PO_2 and PCO_2 composition possibly capable of inducing the first diaphragmatic contraction (Agostoni, 1963; Cross et al., 2013; Lin et al., 1974; Whitelaw et al., 1981): the higher is the alveolar PO_2, the higher must be the concomitant PCO_2 eliciting diaphragmatic contractions, and vice versa. *Ceteris paribus*, the time necessary to reach that alveolar gas composition is directly proportional to the body oxygen stores at the beginning of the apnoea and inversely proportional to the body metabolic rate during apnoea. In fact, a beat-by-beat analysis of the cardiovascular responses to apnoeas carried out during light exercise demonstrated not only a reduction, but even a disappearance of $\phi 2$, with remarkable shortening of $\phi 3$ (Sivieri et al., 2015).

On the opposite side, an increase in oxygen stores would postpone the attainment of the condition determining the onset of

Abbreviation: DBP, diastolic blood pressure; f_H, heart rate; FIO_2, inspired oxygen fraction; MBP, mean blood pressure; $\dot{Q}$, cardiac output; SaO_2, arterial oxygen saturation; SBP, systolic blood pressure; SV, stroke volume; TPR, total peripheral resistance; $\dot{V}O_2$, oxygen uptake; $\phi 1$, first, dynamic phase of the cardiovascular response to apnoea; $\phi 2$, second, steady-state phase of the cardiovascular response to apnoea; $\phi 3$, third, dynamic phase of the cardiovascular response to apnoea.

* Corresponding author at: Dipartimento di Scienze Cliniche e Sperimentali, Università di Brescia, Viale Europa 11, 25123 Brescia, Italy.
E-mail addresses: nazzarenofagoni@gmail.com, nazzareno.fagoni@unibs.it (N. Fagoni).

http://dx.doi.org/10.1016/j.resp.2015.07.016
1569-9048/

ϕ3. The largest increase in oxygen stores before breath-holding is attained by having subjects breathe pure oxygen (inspired oxygen fraction, FIO_2, of 1) before the performance of maximal breath-holds. The investigations of breath-holding in hyperoxia are scanty and rarely using pure oxygen (Bjurström and Schoene, 1987; Breskovic et al., 2012; Klocke and Rahn, 1959; Lin, 1987; Otis et al., 1948). None of them studied the cardiovascular responses to apnoea on a beat-by-beat basis.

The general hypothesis of this study is that the onset of ϕ3 is related to the onset of diaphragmatic contractions, requiring the attainment of a specific alveolar gas composition and representing the so-called physiological breaking point of apnoea, as proposed by Perini et al. (2008, 2010). In the context of this hypothesis, we postulated that the three phases of the cardiovascular response to apnoea would be present both at $FIO_2 = 1$ and at $FIO_2 = 0.21$, but the duration of ϕ2 and ϕ3 would be longer in the former than in the latter condition. To this aim, we investigated the effects of breathing pure oxygen before the performance of maximal breath-holds on the cardiovascular response to apnoea.

2. Methods

2.1. Subjects

19 competitive divers (16 males and 3 females) volunteered for this study. Their age was 41.3 ± 9.9 years, and they were 71.5 ± 10.1 kg heavy and 175.1 ± 8.7 cm tall. All divers were 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 experimental procedures of the study. The study conformed to the Declaration of Helsinki and was approved by the local ethical committee.

2.2. Experimental procedure

All tests were carried out in a room at 22–23 °C. Upon arrival in the laboratory, the subject performed 30 min of breath-hold training. Then, after instrumentation, he took the supine posture. After 5 min had been allowed to achieve steady state conditions, 10 min of measurements were obtained with the subject at rest and spontaneously breathing (quiet rest). Then, the subject was asked to perform two successive maximal apnoeas, separated by a recovery interval of 2 min (Perini et al., 2008). Maximal apnoeas are defined as apnoeas prolonged to volitional exhaustion.

Subjects undertook their pre-dive breathing routine before breath-holding, generally consisting of two-to-three deep respiratory acts. This procedure was ended by a deep inspiration, so that all apnoeas were initiated with a lung volume close to the subject's total lung capacity. As a consequence, the first breathing movement at the end of apnoeas was an expiration, which the subjects were asked to perform as deep as possible.

Two minutes of recovery were allowed after the second apnoea. Then, the system for oxygen administration was connected to the inspiratory side. Oxygen was administered from high-pressure, high-precision cylinders, via a Douglas bag that was used as pressure buffer. Ten minutes were allowed for alveolar gas equilibration, then, after 1 min of quiet breathing for control measurement, a maximal apnoea was performed. This apnoea was carried out with the same procedure as in air. After the end of the apnoea in oxygen, the subject kept breathing pure oxygen for 2 min during recovery. In air, the longest apnoea was retained for further analysis.

2.3. Methods

Arterial blood pressure profiles (PortaPres, TNO-TPD, Amsterdam, The Netherlands) were continuously recorded throughout the experiments. Arterial blood O_2 saturation (SaO_2) was also continuously monitored by infrared spectroscopy (BioPac System Inc., Goleta, CA, USA) at an earlobe. 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. Oxygen uptake ($\dot{V}O_2$) was monitored during air breathing by means of a metabolic cart (Quark b^2, Cosmed, Italy).

2.4. Data treatment

Arterial pressure profiles and respiratory traces were analysed off line. We computed beat-to-beat values of f_H, systolic blood pressure (SBP), diastolic and mean blood pressures (DBP and MBP, respectively). The duration of each apnoea for each subject was calculated as the time over which the flowmeter of the metabolic cart recorded no respiratory air flows.

Beat-by-beat SV was determined by analysing the pulse pressure profiles by means of the Modelflow model implemented in the Beatscope™ software (TNO-TPD, The Netherlands). $\dot{Q}$ was subsequently calculated by multiplying each SV value times the corresponding f_H value. The ratio between MBP and $\dot{Q}$ provided an estimate of total peripheral resistance (TPR). Steady state $\dot{Q}$ was calculated at rest as the mean of the breath-by-breath values over 1 min of regular breathing.

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 (Sivieri et al., 2015). The procedure was based on linear regression analysis, allowing detection of changes in slope between successive phases. Linear regression was also used (i) to analyse the rate of changes of SBP and f_H during ϕ3, (ii) to calculate dynamic baroreflex sensitivity in ϕ1 (Adami et al., 2013; Sivieri et al., 2015), and (iii) to verify steady state of investigated variables in ϕ2 (slope of regression equation significantly equal to zero).

2.5. Statistical analysis

Data are presented as mean and standard deviation (SD). One-way ANOVA for repeated measures was used to evaluate the effect of time of apnoea on various variables, in each of the two experimental conditions. Tukey test was used as post-hoc test to isolate the differences when necessary. A two-tail t-test for paired observations was used to compare the duration of breath-holding and the values attained by the investigated cardiovascular variables between the two investigated conditions. Differences were considered significant when $p < 0.05$. Parameters of linear regression equations were calculated by the least-square method. The Stata 10.0 statistical software (StataCorp, College Station, TX, USA) was used.

3. Results

3.1. Apnoeas in air

In quiet rest in air, $\dot{Q}$ was 358 ± 35 ml min^{-1}. Mean duration of maximal apnoeas in air was 233 ± 43 s. An example of f_H, SBP and DBP recordings obtained on one subject during maximal resting apnoea is shown in Fig. 1 (panel a). All subjects followed similar patterns. Values of all variables obtained in air during quiet rest are reported in Table 1. During the hyperventilation that preceded breath-holding, f_H grew to attain 87 ± 17 b min^{-1} at the beginning of apnoea (NS with respect to control). The corresponding SBP was