Medical Hypotheses 110 (2018) 101–104

Contents lists available at ScienceDirect

Medical Hypotheses

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

Carbon dioxide therapy in hypocapnic respiratory failure

P.O.O. Julu[a,b], M. Shah[a,b], J.A. Monro[a], B.K. Puri[c,*]

[a] Breakspear Medical Group, Hemel Hempstead, Hertfordshire, UK
[b] Queen Mary University of London and the William Harvey Research Institute, Barts and the London School of Medicine, UK
[c] Department of Medicine, Imperial College London, UK

A B S T R A C T

Oxygen therapy, usually administered by a facemask or nasal cannulae, is the current default treatment of respiratory failure. Since respiration entails intake of oxygen and release of carbon dioxide from tissues as waste product, the notion of administering carbon dioxide in respiratory failure appears counter-intuitive. However, carbon dioxide stimulates the chemosensitive area of the medulla, known as the central respiratory chemoreceptor, which activates the respiratory groups of neurones in the brainstem and stimulates inspiration thereby initiating oxygen intake during normal breathing. This vital initiation of normal breathing is via a reduction in the pH of the cerebrospinal fluid and the medullary interstitial fluid. We hypothesise that in cases of type I respiratory failure in which the P_aCO_2 is low, administration of carbon dioxide by inhalation would stimulate the respiratory groups of brainstem neurones and facilitate breathing, which would be of therapeutic value. Preliminary clinical evidence in favour of this hypothesis is presented and we recommend that a formal randomised study be carried out.

Introduction and background

Human respiration entails intake of oxygen and release of carbon dioxide [1]. We propose here to divide this process into three phases carried out by different sets of effectors organs. Phase 1 is the acquisition of oxygen from the atmosphere by the cooperation of the heart and the lungs. Phase 2 is the transportation and delivery of respiratory gases for consumption or excretion by the cooperation of the heart and the blood vessels. Phase 3 is the consumption of oxygen and production of carbon dioxide by all tissues in the body mainly at organelle level in mitochondria. All three phases are controlled by the central nervous system either directly through nerves or indirectly through various metabolic hormones. In 1962, Fletcher defined respiratory failure as a fall in arterial oxygen saturation or a rise in the arterial partial pressure of carbon dioxide (P_aCO_2) in the absence of the following three factors: (i) blood shunting past the lungs; (ii) compensated metabolic alkalosis; and (iii) lowering of the ambient oxygen tension [2]. Arterial oxygen saturation, rather than the arterial partial pressure of oxygen (P_aO_2), was included in this definition owing to the greater ease with which the former could be measured, as well as the association of the former with the clinical sign of cyanosis [2]. In current practice, the P_aO_2 is preferred and respiratory failure is divided into two types: (i) type I is characterised by a low P_aO_2 and a normal or low P_aCO_2; and (ii) type II is characterised by a low P_aO_2 and a high P_aCO_2 [3]. Since the arterial level of blood gases are the only measures used in this definition of respiration failure, it is clear that phase 1 respiration mentioned above is the major process under consideration in this definition with implication of involvement of the set of the effector organs associated with this phase of respiration. Oxygen therapy, usually administered by a facemask or nasal cannulae, is the current choice of treatment to address the low P_aO_2 of respiratory failure [3], further confirming that phase 1 respiration is the main process being considered in the current definition of respiration failure, particularly since carbon dioxide is also primarily excreted by the lungs, which are also the major effector organs in phase 1 respiration.

Stimulation of the central chemoreceptors of the medulla oblongata activates a large group of respiratory neurones located at the ventrolateral surface of the brainstem starting from the level of the first cervical vertebra up to parabrachial nuclei of the brainstem [4–6]. This also activates the inspiratory group of neurones known as the dorsal respiratory group, which are mostly found adjacent to the nucleus of the tractus solitarius [7,8]. A ramp inspiratory movement is generated through a cascade of integrative synaptic inhibitions involving up to six groups of inspiratory neurones [9]. These neurones control the inspiratory muscles, including the diaphragm, via the spinal cord and the phrenic nerve [7,10–15]. Expiration in normal breathing is passive although there are two groups of expiratory neurones in the brainstem controlling expiratory muscles for active expirations when required [9].

* Corresponding author at: Imaging Directorate, Hammersmith Hospital, Du Cane Road, London W12 0HS, England, UK.
E-mail address: basant.puri@imperial.ac.uk (B.K. Puri).

https://doi.org/10.1016/j.mehy.2017.11.010
Received 17 October 2017; Accepted 30 November 2017

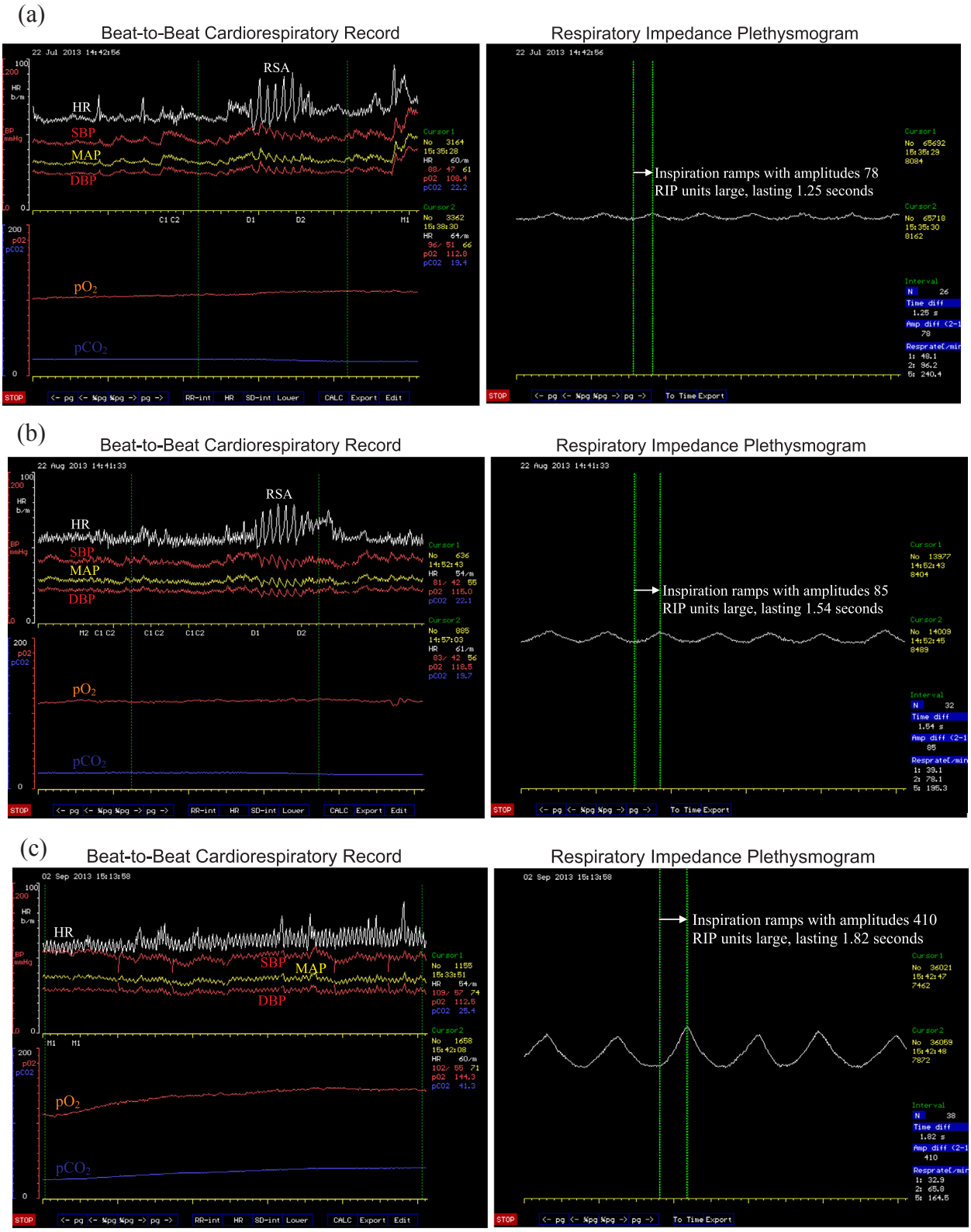

Fig. 1. Screen captures of live and real-time records of cardiorespiratory functions showing beat-to-beat heart rate (HR), systolic (SBP), mean arterial (MAP) and diastolic (DBP) blood pressures. RSA = respiratory sinus arrhythmia of HR during deep breathing at the frequency of 0.1 Hz. pO_2 is the transcutaneous oxygen partial pressure record and pCO_2 is the transcutaneous carbon dioxide partial pressure record. Inspiration ramps are shown in units of the Respiration Impedance Plethysmograph (RIP). Note that the pCO_2 level at rest in the supine position indicated by cursor 1 is 22.2 mmHg during the initial examination carried out on 22nd July 2013 (A) and is similar at 22.1 mmHg during the second examination one month later on 22nd August 2013 (B). The amplitudes of the inspiration ramps were also similar at 78 RIP units during the first (A) and 85 RIP units during the second (B) examinations. Carbon dioxide treatment (see text for details) increased the pCO_2 to 41 mmHg within 8 mins (indicated by cursor 2 in C) and inspiration ramps were also increased by more than fivefold to 410 RIP units (1C).