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Oxygen and Carbon Dioxide: Respiration Stimuli or Biochemical Markers of Changes in Blood pH?

Bula-Bula M[1,2*], Lepira F[3] and Mvuama N[4]

[1]*Department of Anesthesia and Resuscitation, Clinic University of Kinshasa.*

[2]*Anesthesia service, General Reference Hospital of N'Djili.*

[3]*Department of Internal Medicine, Clinic University of Kinshasa.*

[4]*School of Public Health, University of Kinshasa.*

[*]Correspondence:
Bula-Bula M, Department of Anesthesia and Resuscitation, Clinic University of Kinshasa.

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ABSTRACT

CO_2, PO_2 and PH are breath stimuli. This documentary study, carried out in the resuscitation care unit of the Clinic University in Kinshasa, is based on analysis of the standard deviations of these differents stimuli as well as on the Henderson-Hasselbalch equation to evaluate the role of the three stimuli. The results of this study show that blood PH, because it's values are much more centered on the average (CV=1,969), is the true stimulus. As a result, $PaCO_2$ and PaO_2 would only act as biochemical markers of variations in the latter.

Keywords

CO_2, PH, O_2, Stimulus, Respiration.

Introduction

CO_2 is the main stimulus of respiration since the function of the latter depends on his values [1,8,10]. In case of chronic hypercapnia, the level of CO_2 being permanently elevated, hypoxia becomes the stimulus [12]. This study re-reads these statements to elucidate the mechanisms underlying breathing.

Methods

A documentary study was conducted from March 1st to June 31st, 2019, in the resuscitation care unit of Clinic University of Kinshasa. Patient records, for all pathologies combined, that had performed a gasometry with arterial measurement of pH, $PaCO_2$ and PaO_2 were analyzed. The standard deviation of the variables of interest (CO_2, PH and O_2), were compared between them. As in physiology the control of a factor implies the constancy of his values, the stimulus which had presented the weakest dispersion [lowest coeffiscient of variation (CV)] was considered as the regulated element. The Henderson-Hasselbalch equation [16] has also been used as a support in the analysis of these stimuli.

Results

Thirty four patients aged 19 to 85 years (average 48.5 ± 20.23 years) benefited from gasometry. The sex ratio was 1.4 in favor of men. The most prevalent pathologies were strokes (27%), sub- and extra-dural hematomas (13%), peritonitis (13%) and polytrauma (13%). The extreme values of Pa CO_2 were 20.4 and 53.1 mmHg with an average of 33.14 ± 5.29 mmHg. The pH ranged from 7.08 to 7.51 (mean 7.35 ± 0.12 mmHg). Oxygen ranged from 23 to 136 mmHg (mean 101.8 ± 60.58mmHg). Thus, the pH with a low CV (1.97%) is the parameter which has a small variability compared to the other two (27.53% for pCO_2 and 42.13% for pO_2).

Discussion

The results of this study show that PH is the regulated element. However, it is known that the main stimulus of respiration is PaCO2 [1,5]. Moreover, in cases of chronic hypercapnia, even though the Henderson-Hasselbalch equation [16] does not consider O2, it is hypoxia that stimulates respiration.

Therefore, taking into account this equation, ventilation, in a situation of chronic hypercapnia, should rather depend on the stimulation of the respiratory centers by the hydrogen ion ; the bicarbonate-dependent variations, the third element of the Henderson-Hasselbalch equation, are more the result of renal correction. Below, we will discuss the role that each of these three stimuli plays in both artificial and spontaneous ventilation.

In artificial ventilation, hypercapnia is corrected by readjustment of respiratory rate and tidal volume [11]. This is seen in physiology, a polypnea with recruitment of accessory respiratory muscles [8] to improve minute volume and eliminate CO_2.

On the other hand, hypoxia requires an adjustment mainly of FiO_2, and PEP [11]. What the respiratory centers can not achieve. The response to hypoxia is therefore not ventilatory. hypoxia is therefore not a stimulus of breathing. The ventilatory response to hypoxia occurs only when the latter is deep, at least 40% below its normal value [12]. One way of saying that this answer only intervenes when this fall leads to a level of anaerobic tissue metabolism which would explain a production of lactates and thus micro-deregulation of the blood PH. Changes in PH that may represent a life threatening threat [7,17] would, in turn, explain the compensatory polypnea.

Pathophysiologically, hypercapnia results in release of catecholamines with the corollary of tachycardia and polypnea [2,14]. In contrast, hypoxia acts at the mitochondrial level and decreases the production of ATP [13]. This explains a state of cellular hypoactivity, a kind of "Pancytoasthenia" that would induce, not an excitation but rather the absence if not a low level of the response of the respiratory centers.

Because of a significant variability in their values around the mean, hypoxia, like hypercapnia, is probably not a stimulus for breathing. They could be both causes and early biochemical markers of subclinical PH changes. Since the PH is the natural logarithm based on the inverse of the concentration of the hydrogen ion, small oscillations of the pH can cause large variations in $PaCO_2$.

Hypercapnia is a direct marker of changes in PH (cf. the Henderson-Hasselbalch equation), whereas hypoxia is indirect by means of anaerobic metabolism induced by hypoxia, lactic acid production and thereby the consumption of bicarbonate. In case of chronic hypercapnia, the permanently elevated $PaCO_2$ can no longer reflect the subclinical PH variations. It is hypoxia that becomes the biochemical marker.

It's this role of markers that could explain the confusion with that of stimulus: as surprising as one might think, there are no significant receptors monitoring $PaCO_2$ [12]. Carotid corpuscles are not very sensitive to $PaCO_2$ change. The central chemoreceptors do not monitor $PaCO_2$ as such, they are rather sensitive to changes in H+ ion concentrations from CO_2 in the extracellular fluid of the brain [6]. As a result, the question arises whether the excitation of the respiratory centers in case of hypercapnia is a direct fact of $PaCO_2$ or that this is due to a decrease in the values of PH [8,9].

The situation is not so different for PaO2. As seen above, peripheral chemoreceptors are not sensitive to moderate changes in arterial PaO_2 [12]. All this would cast doubt on the role of $PaCO_2$ and PaO_2 as stimuli for breathing.

Another argument against the role of these two stimuli is chronic hypercapnia. Pathologies causing a change in the regulating variable (CO_2), due to an increase in metabolism (fever, sepsis) or a change in acidobasic balance (metabolic acidosis), lead to an increase in ventilatory control in the body aim to restore $PaCO_2$ homeostasis [10]. However, in physiology, the regulating variable is the same as that which is regulated (positive or negative feedback effect). In the case of chronic hypercapnia, the two regulating quantities ($PaCO_2$ and PaO_2) are disturbed. And, contrary to the claims of Raux M (2006) and many other authors [4,5,15], the resulting hyperventilation does not target $PaCO_2$ or PaO_2 homeostasis, but rather maintaining a third magnitude, the blood PH within the limits of homeostasis. As a result, it is clear from this analysis that it is the pH that is the regulated element and therefore the magnitude regulating the respiration. Its ongoing monitoring could improve the fate of fragile resuscitation patients.

Finally, unlike most studies of respiratory physiology that are based on experimental studies, the uniqueness of this study is to be based on clinical data, analysis of the results of gasometry of patients in resuscitation, to confirm or deny the role of PH as the sole stimulant of respiration.

Conclusion

Oxygen, although vital, is not included in the Henderson-Hasselbalch equation. Its abundance in the atmosphere could explain the lack of its role in this equation and also as a direct stimulus of respiration. Conversely, the PH, whose variations may represent a vital threat, seems to be the only regulated element. As for the temperature whose regulation is done via sweating and evaporation; the regulation of the blood PH, on the respiratory level, is done via the elimination of CO_2.

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