Increase in venous [K+] During Hyperbaric Exposure Independent of Changes in pH or O2 Concentration

Increase in venous [K+] During Hyperbaric Exposure

Abstract

Plasma potassium regulation is important for function of numerous cells in the body. Changes in potassium levels during exposure to an increased O2 concentration is thought to be the result of the changes in pH and increasing reactive oxygen species. However, the effects of hyperbaria on plasma potassium concentration are not well understood.

Eight subjects were exposed to 1.3 atmospheres absolute (ATA) of hyperbaric air for 90 minutes, 10-times (M-F) over 12-days. Another eight subjects were exposed to 100% oxygen at 1 ATA over the same interval. Four venous blood draws were taken. On day 1 the first draw was taken immediately preceding treatment and the second was taken immediately following treatment. The third draw was taken prior to the 10th treatment and the 4th draw was taken 72 hours post final treatment. We analyzed samples on a blood gas analyzer and performed statistical analysis using a paired Wilcoxon signed-rank test.

The concentration group saw strong trend towards an increase in the potassium concentration from 4.09 ± 0.12 (mmol/L) to 4.28 ± 0.28 (mmol/L) ($p = 0.065$). In the hyperbaric group we see a significant increase in potassium concentration from 4.19 ± 0.26 (mmol/L) to 4.55 ± 0.27 (mmol/L) ($p = 0.0068$). In the concentration group we also see a significant increase in pH concentration from 7.37 ± 0.03 to 7.39 ± 0.01 ($p= 0.021$). A similar significant increase is not seen in the hyperbaric group.

These finding suggest that changes in potassium concentration in response to hyperbaria are not the result of oxygen concentration nor pH. Possible explanations include increased nitrogen levels due to hyperbaric air, increased CO2 concentration in hyperbaric chamber or changes in the activity of Na+,K+ ATPase pumps at the cellular level which may be a homeostatic response to combat pulmonary edema

Keywords: Potassium, Hyperbarics, Hyperoxia

Introduction

Modulation of inspired O_2 concentration has been used as an effectives treatment for many conditions. The two main methods to administer this concentration increase are by directly varying concentration of inspired gases or

by varying the ambient pressure. By combining these to aspects of concentration, three of the main modes of O_2 administration are obtained. These are hyperbaric O_2, concentrated O_2 and hyperbaric treatment. According the UHMS hyperbaric oxygen therapy (HBO_2) is defined as exposure to near 100% O_2 while inside a pressurized chamber at greater than sea level pressure.[1] As of July 2021 the FDA has cleared HBO_2 for 13 different conditions.[2] In contrast hyperbaric treatment is exposure to an increase in pressure without an increase in administered gas O_2 concentration. Finally concentrated oxygen is the exposure to O_2 gas with a higher concentration of O_2 than normal air.

The effects of long-term hyperoxia (LTH) on blood metabolites is still not entirely understood. A common finding that exists in this area presents the idea that exposure to LTH reduces the activity of voltage-gated K+ channels in lung tissue.[3,4] Specifically, LTH exposure downregulates TREK-1 K+ channels in alveolar tissue, which can cause an increased risk of acute lung injury. LTH exposure also plays a role in the regulation of inflammatory cytokine secretion in alveolar AT2 cells. Such lung injury can potentially cause hypoxic effects and the release of K+ into the blood as seen in such cases. It has been proposed that the mechanism behind this increase in plasma K+ is due to the LTH exposure causing changes in action potentials (APs) on the surface of cell membranes.[5] Rapid depolarization caused by LTH exposure results in a highly positive potential present in the cell.[3] The downregulation of K+ channels such as TREK-1 prolongs APs on the membrane surface due to K+ ions not being able to flow into the cell to repolarize the membrane. Consequently, the repolarization reserve of the action potential appears to be extended by LTH exposure, resulting in a longer repolarization time and a slower return to resting membrane potential.[5] It is widely known that depolarization of cell membranes increases the permeability of membranes to positive ions such as K+, leading to an increase in plasma K+ concentration.

Effects of hyperbaria on blood metabolites

One metabolite of interest in this study was potassium. Plasma potassium levels are dependent on a multitude of factors and result from the interplay of intracellular and extracellular changes and intake and execration rates.[6,7] Regulation of these levels within normal ranges is of extreme importance to the function of various cells in the body.[8] Effects of increased inspired O_2 on plasma potassium remain ambiguous.[7] A few studies have demonstrated an increase in plasma potassium while others have found no similar increase.[7,9] However the fact hypoxia has been shown to cause an increase in arterial potassium levels and cause changes in expression of Voltage gated K+ channel in pulmonary arterial myocytes through $HIF1-\alpha$ indicates some pathway through which potassium levels are modulated via changes in O_2 concentration.[10–13] In contrast the effects of hyperbaria on plasma potassium levels are much less understood.

Methods

Healthy adult subjects were recruited via REDCap using a University of Wisconsin's email list. A questionnaire was administered to determine characteristics of individuals such as pre-existing conditions and age. Individuals who responded to the survey were selected at random contacted via phone. Participants in the study were separated into two groups. The first group received hyperbaric treatment in altitude sickness bags (n=14) while the second group received concentrated oxygen at room pressure (n=12).

Although treatment varied between groups, treatment schedule remained consistent and was the following. Subjects arrived Monday and height and weight were determined. Blood collected via venipuncture before treatment was used for a baseline metabolic panel and analyzed on arterial blood gas (ABG) machine. Following blood draws subjects underwent 1.5 hours of their respective treatments. After treatment blood was collected to determine acute response in blood metabolites. Following this, treatment was given Tuesday through Friday of the following week, taking a break for weekends where no treatment was administered. A blood draw and ABG analysis was preformed before the tenth and final treatment. After a weekend of no treatment following the final treatment a blood draw occurred and subsequent analysis was preformed.

A total of 36 metabolic indicators were reported by the ABG machine. Indicators were compared pairwise between the four draws. Statistical analysis and data visualization was performed using R (The R Foundation) and paired Wilcoxon tests.

Results

Table 1: Metabolite concentrations for concentrated oxygen group from pre, post, day 10 and final blood draws. Signifigance denoted by (* < 0.05), (** < 0.001)

Metabolite	Pre	Post	Day 10	Final
pH	7.374 ± 0.029	$7.393 \pm 0.014^{*}$	7.368 ± 0.033	7.384 ± 0.027
pCO_2	48.46 ± 5.58	47.08 ± 4.28	44.68 ± 6.32	$38.83 \pm 8.69^{**}$
pO_2	26.25 ± 8.22	21.79 ± 5.16	30.51 ± 19.62	26.91 ± 10.2
Na	139.55 ± 0.91	139.23 ± 1.19	139.36 ± 1.66	138.64 ± 3.88
$K+$	4.09 ± 0.12	4.28 ± 0.28	4.28 ± 0.44	4.29 ± 0.27
$Cl-$	106.92 ± 1.5	107.39 ± 1.32	$105.13 \pm 1.76^{*}$	106.36 ± 3.36
$Ca+$	1.19 ± 0.04	$1.21 \pm 0.03^{*}$	1.22 ± 20.02	1.21 ± 0.04

Table 2: Metabolite concentrations for hyperbaric group from pre, post, day 10 and final blood draws. Signifigance denoted by (* $<$ 0.05), (** $<$ 0.001)

Metabolite	Pre	Post	Day 10	Final
pH	7.383 ± 0.033	7.408 ± 0.029	7.387 ± 0.049	7.387 ± 0.037
pCO_2	35.80 ± 6.77	34.46 ± 4.51	36.64 ± 10.20	39.29 ± 10.04
pO_2	42.88 ± 22.94	25.67 ± 6.60	41.64 ± 37.39	43.75 ± 31.82
Na	139.96 ± 1.20	139.65 ± 1.29	139.17 ± 1.18	139.37 ± 1.28
$K+$	4.19 ± 0.26	4.54 ± 0.27	4.15 ± 0.24	4.23 ± 0.25
$Cl-$	106.46 ± 1.58	106.41 ± 1.72	106.23 ± 1.99	106.17 ± 1.99
$Ca+$	1.24 ± 0.03	1.25 ± 0.03	1.22 ± 20.04	1.22 ± 0.05

Discussion

Based on the fact that the classical metabolites implicated in plasma potassium levels experienced no significant fluctuations this hints at a possible novel relationship between plasma potassium and hyperbaric treatment. However, limitations of this study mean that an exact explication for the observed plasma potassium levels in the hyperbaric group was not be determined. In spite of this fact several possible explanations based on findings in the literature and conditions present in this study arose and were as follows: an increase in hyperbaric chamber CO_2 resulting in mild respratory acidosis, increase in N_2 and creation of reactive nitrogen species (RNS) in tissue, potassium mediated fluctuations in vasoconstriction/dilation in resonse to changes in pressure and changes in potassium channel expression via $HIF - 1\alpha$.

Correlations between respratory acidosis and an increase in plasma potassium have been reported with few exceptions.[7] During hyperbaric exprosure subjects exprienced an increase of levels of CO_2 by =FIXME:INSERT CO2 LEVELS IN CHAMBER==. Subject expired gases and a lack of outflow of those respired gases in the altitude sickness bags is most likely responsible for the increase in CO_2 observed in chamber.

Further limitations of this study include lack of dietary restrictions on subjects, single Pre vs Post draw time point and variations between treatment cohorts.

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