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

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.[1–3] Plasma potassium levels are heavly regulated to fall within a narrow range of 3.5 to 5.0 mmol per liter and maintenance at these

concentrations are of extreme importance to the function of many organs in the body.[3] This is underscored by the fact that both hypokalemia or hyperkalemia lead to an increased death rate in certain conditions.[5,6] This places importance on the determination of pathways of regulation and disease that lead to changes in plasma potassium levels. Factors investigated in this study that may lead to changes in plasma potassium levels, but remains understudied, are the effect of O_2 concentration and increased pressure.

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.[7] As of July 2021 the FDA has cleared HBO_2 for 13 different conditions.[8] 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. Concentrated oxygen and hyperbaric treatment were the two treatments administered in this study.

Effects of hyperoxia on plasma potassium levels remain ambiguous.[2] A few studies have demonstrated an increase in plasma potassium as the result of hyperoxic exposure while others have found no similar increase.[2,9] However research has shown that hyperoxia can effect voltage-gated K+ channels in humans[10–12] One group found that long-term exposure to hyperoxia can result in a decrease in activity of voltage-gated K+ channels in lung tissue.[10,11] Where as another study looking at voltage-gated K+ channels of the heart and saw a signifigant reduction of oxygen-sensitive Kv1.5 potassium channel protein expression.[12] Internal potassium homeostasis and the distribution of intracellular and extracellular potassium in the body is primarly the reuslt of ion-exchanges pumps and passive efflux.[1,3] Therefore changes in activity or expression of these channels offers a potential linkage between effects O_2 on plasma poatassium.

References

(1) Aronson, P. S.; Giebisch, G. Effects of pH on Potassium: New Explanations for Old Observations. *Journal of the American Society of Nephrology* **2011**, *22*, 1981–1989.

(2) Adrogué, H. J.; Madias, N. E. Changes in Plasma Potassium Concentration During Acute Acid-Base Disturbances. *The American Journal of Medicine* **1981**, *71* (3), 456–467. https://doi.org/10.1016/0002-9343(81)90182-0.

(3) Gumz, M. L.; Rabinowitz, L.; Wingo, C. S. An Integrated View of Potassium Homeostasis. *New England Journal of Medicine* **2015**, *373* (1), 60–72. https://doi.org/10.1056/NEJMra1313341.

(4) Youn, J. H.; McDonough, A. A. Recent Advances in Understanding Integrative Control of Potassium Homeostasis. *Annual Review of Physiology* **2009**, *71* (1), 381–401. https://doi.org/10.1146/annurev.physiol.010908.163241.

(5) Torlén, K.; Kalantar-Zadeh, K.; Molnar, M. Z.; Vashistha, T.; Mehrotra, R. Serum Potassium and Cause-Specific Mortality in a Large Peritoneal Dialysis Cohort. *Clinical Journal of the American Society of Nephrology* **2012**, *7* (8), 1272–1284. https://doi.org/10.2215/CJN.00960112.

(6) Goyal, A.; Spertus, J. A.; Gosch, K.; Venkitachalam, L.; Jones, P. G.; Van den Berghe, G.; Kosiborod, M. Serum Potassium Levels and Mortality in Acute Myocardial Infarction. *JAMA* **2012**, *307* (2), 157–164. https://doi.org/10.1001/jama.2011.1967.

(7) *Hyperbaric Oxygen Therapy Indications*; Moon, R. E., Ed.; Undersea; Hyperbaric Medical Society, 2019; Vol. 14th.

(8) Hyperbaric Oxygen Therapy: Get the Facts. *Consumer Updates*, 2021.

(9) Fraley, D. S.; Adler, S. Isohydric Regulation of Plasma Potassium by Bicarbonate in the Rat. *Kidney International* **1976**, *9* (4), 333–343. https://doi.org/10.1038/ki.1976.39.

(10) Zyrianova, T.; Lopez, B.; Olcese, R.; Belperio, J.; Waters, C. M.; Wong, L.; Nguyen, V.; Talapaneni, S.; Schwingshackl, A. K2p2.1 (TREK-1) Potassium Channel Activation Protects Against Hyperoxia-Induced Lung Injury. *Scientific Reports* **2020**, *10* (1), 22011. https://doi.org/10.1038/s41598-020-78886-y.

(11) Schwingshackl, A.; Teng, B.; Ghosh, M.; West, A. N.; Makena, P.; Gorantla, V.; Sinclair, S. E.; Waters, C. M. Regulation and Function of the Two-Pore-Domain (K2p) Potassium Channel Trek-1 in Alveolar Epithelial Cells. *American Journal of Physiology-Lung Cellular and Molecular Physiology* **2012**, *302* (1), L93–L102. https://doi.org/10.1152/ajplung.00078.2011.

(12) Chapalamadugu, K. C.; Panguluri, S. K.; Bennett, E. S.; Kolliputi, N.; Tipparaju, S. M. High Level of Oxygen Treatment Causes Cardiotoxicity with Arrhythmias and Redox Modulation. *Toxicology and Applied Pharmacology* **2015**, *282* (1), 100–107. https://doi.org/10.1016/j.taap.2014.10.019.