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Hematological changes in response to a drastic increase in training volume in recreational cyclists

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Hematological Changes in Response to a Drastic Increase in Training Volume in Recreational Cyclists

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by Jessie Axsom

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Accepted by the faculty of the Department of Kinesiology, James Madison University, in partial fulfillment of the requirements for the Honors Program.

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PUBLIC PRESENTATION

This work is accepted for presentation, in part or in full, at the Honors Symposium on April 15, 2016 .

Dedication

This thesis is dedicated to my “4k for Cancer” teammates and the Ulman Cancer Fund for Young Adults for letting pursue this opportunity and follow my passion for research on this trip. It is also dedicated to my research advisor, Dr. Chris Womack for spending his time and energy to mentor me and allow me to grow as a student and individual.

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Acknowledgments

I would like to thank Dr. Chris Womack for serving as my research advisor and dedicating countless hours to making my project a success. His patience and commitment have helped enhance my academic experience at JMU and foster a passion for research. I would also like to thank my readers, Dr. Michael Saunders and Dr. Kent Todd, for also dedicating their time, energy, and expertise to my project. Thank you additionally to the JMU Honors Program for my small grant award that enabled me to complete this research.

Abstract

Changes in blood volume contribute to improvement in VO_{2max} with chronic endurance exercise training. Although hematological changes to chronic endurance training have been well documented, it has not been well established whether an increased volume of training in trained individuals preferentially affects plasma volume vs. red cell volume. To answer this question, we studied 8 female and 3 male recreational cyclists before and after exposure to drastic increases in training volume. Following the 10-week training period, mean Hct of the 10 subjects who completed the study significantly ($p<0.05$) increased from 42.9% to 48.45%. Mean Hb also increased significantly ($p<0.05$) from 14.6g/dL to 16.4 g/dL. The changes in Hct and Hb were not significantly ($p>0.05$) correlated with the change in self-reported weekly mileage ($R = 0.13$ and 0.16 respectively). The major finding of this study is that both Hct and Hb increase substantially following large training volume increases in recreational cyclists. Furthermore, it appears that there are preferential increases in red blood cell volume compared to plasma volume expansion in this population.

Chapter I: Introduction

Changes in blood volume contribute to improvements in VO_{2max} with chronic endurance exercise training. This has been illustrated by the fact that endurance trained athletes have higher blood volumes and VO_{2max} values than sedentary controls. Krip et al found that when comparing six trained male cyclists to six untrained males of similar age, the trained males had, on average, 16% greater total blood volume and a 54.4% higher VO_{2max}.[20] When these untrained subjects were given a 500mL blood volume expansion using 6% Dextran 70 (Marcodex), VO_{2max} increased by 12.7%. Additionally, when the trained subjects underwent a 500mL reduction in blood volume, there was a significant decrease in VO_{2max} (7%). Similar results were found in several other studies; all finding that induced hypovolemic anemia by blood withdrawal decreased VO_{2max}.[4,16] Furthermore, reinfusion of red blood cells following normocythemia results in a subsequent increase in VO_{2max} greater than pre-hypovolemia.[4,16] This indicates a strong link between VO_{2max} and increases in blood volume, and suggests oxygen transport mechanisms could contribute to limitations in maximal aerobic capacity.

These findings are evident for males and females. Stevenson et al found endurance trained females exhibited higher VO_{2max} values, total blood volumes, hematocrit (Hct) and hemoglobin (Hb) concentrations compared to sedentary age-matched controls. VO_{2max} in trained females was strongly associated with total blood volume (r=0.79), plasma volume (r=0.76), and erythrocyte volume (r=0.78), expressed relative to body weight.[28]

Interestingly, when elite cyclists who already possessed high blood volumes and VO_{2max} were given plasma volume expansions, no improvement in VO_{2max} or endurance performance occurred[29]. This could suggest erythrocyte expansion might have a closer association with endurance performance and VO_{2max} than plasma volume expansion in endurance-trained individuals. Additionally it might suggest that increases in plasma volume are only helpful to endurance up to a point, and further improvements are due to alternative mechanisms. Overall, cross-sectional data has found endurance athletes possess 20-25% higher blood volumes than untrained subjects, regardless of age or gender.[5]

Most research has previously shown that initial increases in blood volume are attributed entirely to plasma volume expansion. This is then followed by equal increases in plasma and red cell volumes. A literature review by Convertino observed that most expansions in blood volume plateaued after one week of training and almost all of the blood volume expansion at 10 days of training was attributed to increases in plasma volume. When the training durations increased (four wks- four months), however, increased blood volume was distributed more equally between red blood cell volume and plasma volume. The average increase in blood volume in the longitudinal studies reviewed by Convertino was 7%.[5]

Several longitudinal studies examined the components of the observed blood volume expansions. Nine sedentary untrained females exposed to four weeks of cycle ergometer exercise exhibited a 9% blood volume expansion, a 9.7% plasma volume expansion, and a 7% red cell volume expansion.[10] When 16 sedentary men completed cycling training 4 days/wk, 40 min/day for eight weeks they showed a 8% blood volume expansion, 6% plasma volume expansion, and 11% red cell volume expansion.[25] In a similar study, 14 untrained men completed 10 weeks of controlled cycle exercise for 30 min/day, 4 days/wk at 75-80% of their VO_{2max}. They exhibited an average blood volume increase of 9%, a plasma volume expansion of 9%, and a red blood cell expansion of 8%.[14] Finally, 14 sedentary males completed 47 running sessions over a 16-week period and experienced a 6% blood volume expansion, 6% plasma volume expansion, and 5%

red cell volume expansion.[23] In shorter duration studies (<10 days), as previously mentioned, no significant increases in red blood cell volume expansion have been found.[5,13,15,17,22,24] It does not appear changes in blood volume are influenced by age or gender. Kjellberg et al. found both trained men and women had significantly higher blood volumes than untrained counterparts in both genders. Additionally, both males and females experienced increases in blood volume following a mountain ski training program.[18] It has also been found endurance training causes the same plasma protein system responses regardless of age.[19] While the aforementioned studies all used endurance training interventions, it is not clear whether specific mode of exercise or intensity levels have an effect on blood volume adaptations. However, since two months of endurance training in athletes whose initial blood volume was above 80 ml kg^{-1} failed to produce a blood volume expansion[11,12], it is likely previous training, fitness levels, and genetics will affect blood adaptations to endurance exercise.

Although hematological changes to chronic endurance training have been documented, it has not been well established whether previously trained individuals who significantly increase their training volumes experience preferential changes in plasma volume vs. red cell volume. A group of 27 male and 12 female runners underwent increases in sea level training volumes, but experienced no improvements in VO_{2max}, plasma volume, or red cell volume.[21] By contrast, Benhaddad et al. examined 36 elite male sportsmen and found that subjects who scored high on a standardized overtraining questionnaire had significantly higher Hct values compared to those with low overtraining scores, which may suggest overtraining could be characterized by high red blood cell volumes.[2]

The purpose of this study was to determine the effect of a drastic increase in training volume on Hct and Hb in recreational cyclists. It is hypothesized that subjects will exhibit a preferential expansion of red blood cell volume.

Chapter II: Methods

Potential participants in the study will be identified by their involvement with the program "4k for Cancer." Individuals enrolled in this program will undertake a 4,000 mile bicycle ride across the United States from 06/01/2015 to 08/08/2015 (approximately 70 days total).

Subjects will have a small amount of blood drawn (5-10 mL) from an antecubital vein on two separate occasions; immediately pre-trip and immediately post-trip. Blood draws will be completed on both occasions in the morning and before consumption of food or fluids. Blood will be collected into EDTA tubes at each testing day and a small portion (less than 100 ul) of the whole blood will be immediately analyzed for Hct and Hb using a HemoCue automated analyzer. Samples will be analyzed in duplicate and if there is a greater than 5% difference between the two samples analysis will be repeated a third time. Subjects will also have their age, gender, height, and weight recorded. Subjects will be asked to self-report their cycling mileage prior to and during the 4k for Cancer trip.

Changes in Hct and Hb will be analyzed using paired t-tests. Pearson correlation coefficients will be used to determine the association between the change in weekly mileage over the course of the ride and the change in both Hb and Hct. Statistical significance will be set a priori at $P < 0.05$.

Chapter III: Manuscript

Introduction

Changes in blood volume contribute to improvements in VO_{2max} with chronic endurance exercise training. This has been illustrated by the fact that endurance trained athletes have higher blood volumes and VO_{2max} values than sedentary controls. Krip et al found that when comparing six trained male cyclists to six untrained males of similar age, the trained males had, on average, 16% greater total blood volume and a 54.4% higher VO_{2max}.[16] When these untrained subjects were given a 500mL blood volume expansion using 6% Dextran 70 (Marcodex), VO_{2max} increased by 12.7%. Additionally, when the trained subjects underwent a 500mL reduction in blood volume, there was a significant decrease in VO_{2max} (7%). Similar results were found in several other studies, all finding that induced hypovolemic anemia by blood withdrawal decreased VO_{2max},, and reinfusion of red blood cells following normocythemia results in a subsequent increase in VO_{2max} greater than pre-hypovolemia.[4,14] This indicates a strong link between VO_{2max} and increases in blood volume, and suggests oxygen transport mechanisms could limit maximal aerobic capacity.

Interestingly, when elite cyclists who already possessed high blood volumes and VO_{2max} were given plasma volume expansions, no improvement in VO_{2max} or endurance performance occurred.[22] This could suggest erythrocyte expansion might be more closely associated with endurance performance and VO_{2max} than plasma volume expansion in trained individuals. Additionally it might suggest that increases in plasma volume are only helpful to endurance up to a point, and further improvements are due to alternative mechanisms. Overall, cross-sectional data has found endurance athletes possess 20-25% higher blood volumes than untrained subjects, regardless of age or gender.[5]

Most research has previously shown that initial increases in blood volume are attributed entirely to plasma volume expansion. This is then followed by equal increases in plasma and red cell volumes. A literature review by Convertino observed that most expansions in blood volume plateaued after 1 week of training and almost all of the blood volume expansion at 10 days of training was attributed to increases in plasma volume. When the training durations increased (4 wks- 4 months), however, increased blood volume was distributed more equally between red blood cell volume and plasma volume. The average increase in blood volume in the longitudinal studies reviewed by Convertino was 7%.[5] While these longitudinal studies all used endurance training interventions, it is not clear whether exercise mode or intensity have an effect on blood volume adaptations. However, since two months of endurance training in athletes whose initial blood volume was above 80 ml kg^{-1} failed to produce a blood volume expansion[11,12], it is likely previous training, fitness levels, and genetics will affect blood adaptations to endurance exercise.

Although hematological changes to chronic endurance training have been documented, it has not been well established whether previously trained individuals who significantly increase their training volumes experience preferential changes in plasma volume vs. red cell volume. The purpose of this study was to determine the effect of a drastic increase in training volume on Hct and Hb in recreational cyclists. It is expected that subjects will exhibit an initial plasma volume expansion, followed by equal plasma volume and red blood cell expansions, and finally a further expansion of red blood cell volume.

Methods

Potential participants in the study were identified by their involvement with the program "4k for Cancer." Individuals enrolled in this program undertook a 4,000 mile bicycle ride across the United States from 06/01/2015 to 08/08/2015 (approximately 70 days total). Eleven subjects volunteered for this study (8 females and 3 males). One female subject had to be excluded from the study because she failed to submit information regarding her pre-study training levels. The subjects averaged (mean ± SD) 22.4 ± 1.4 years of age, 175.5 ± 12.2 cm in height, 75.74 ± 27.4 kg pre-weight, and 76.5 ± 34.8 weekly self-reported miles pre-study. All of the subjects were averaging 560 miles/week at the end of study.

Subjects had a small amount of blood (5-10 mL) drawn from an antecubital vein on two separate occasions; immediately pre-trip and on day 55 of the trip. Both blood draws were completed in the morning, prior to consumption of food or fluids. Blood was collected into EDTA tubes and a small portion (less than 100 ul) of whole blood was immediately analyzed for Hct and Hb using a HemoCue automated analyzer. Samples were analyzed in duplicate and if there was a greater than 5% difference between the two samples, analysis was repeated a third time. Subjects also had their age, gender, height, and weight recorded. Subjects self-reported their cycling mileage one month prior to and during the 4k for Cancer trip.

Changes in Hct and Hb were analyzed using paired t-tests. Pearson correlation coefficients were used to determine the association between the change in weekly mileage over the course of the ride and the change in both Hb and Hct. Statistical significance was set a priori at $P < 0.05$.

Results

Following the 55-day training period, mean Hct of the 10 subjects who completed the study significantly ($p<0.05$) increased from 42.9% to 48.45% (Figure 1). Mean Hb also increased significantly ($p<0.05$) from 14.6g/dL to 16.4 g/dL (Figure 2). Subjects exhibited a small non-significant ($p>0.05$) mean weight change from 75.74 kg pre-weight to 74.55 kg post-weight. The changes in Hct and Hb were not significantly ($p>0.05$) correlated with the change in self-reported weekly mileage ($R = 0.13$ and 0.16 respectively).

Discussion

The major finding of this study is that both Hct and Hb increased substantially following large increases in training volume in recreational cyclists. Furthermore, our data suggest that red blood cell volume increased to a greater extent than plasma volume with training.

Previous studies have determined increases in blood volume during the initial two to four weeks of training can be attributed almost entirely to a plasma volume expansion.[5] When the duration of training increases, however, increases in blood volume become equally distributed between red blood cell mass and plasma volume.[1,6,8,18,19] There is evidence that these responses are similar in both men and women.[1,10,13] The average increase in blood volume in prior longitudinal studies that subjected untrained subjects to endurance training protocols was reported to be 7%.[5] In contrast, cross-sectional studies have found endurance athletes have a 20-25% higher blood volume than untrained subjects.[3,7,9,15] This suggests initial fitness levels and previous endurance training can influence hematological adaptations.[5] This discrepancy seems to indicate that hemostatic adaptations continue when individuals are exposed to long-term endurance training regimens. These adaptations may cease to develop, however, when blood volumes reach a certain level. This could explain why young athletes with initial blood volumes above 80 ml kg^{-1} subjected to a 2-month intensive training regimen did not experience hypervolemia.[11,12] This also could explain why athletes subjected to a 4-wk supervised training program did not experience increases in plasma or red blood cell levels.[17]

This study found subjects with previous exposure to endurance exercise and recreational cycling experienced greater red blood cell volume increases than plasma volume increases when exposed to a large increase in training volume. The substantial increase in hematocrit suggests that red blood cells increased either exclusive of PV or to a greater extent than PV. This indicates increases in red blood cell volume may be a more important factor in hemostatic changes in trained individuals than previously thought. While there is a lack of similar studies to help validate results, past findings have indicated overtraining may be associated with increased Hct values.[2] Athletes that scored high on a standardized-questionnaire to identify overtraining parameters also exhibited significantly higher Hct values than low-scoring controls.[2] This indicates increasing the volume of training over a longer time-period in already-trained endurance athletes could preferentially affect red blood cells over plasma. Additionally, the weekly mileage was increased 7-fold, a greater amount than previous studies and thus indicating volume increases of this magnitude will preferentially affect red blood cells.

There were several limitations in this study worth exploring in future research. Total blood volume was not calculated as previous studies suggest that an increase in blood volume would almost certainly occur.[5,14,16] This also means changes in plasma volume could not be calculated. However, due to the increases in Hct, it can be inferred that plasma volume did not increase as much as RBC volume. The effects of altitude-induced increases in Hct during the ride were also not examined. Past studies have identified altitude as having affects on hematological adaptations at altitudes above 2,000m.[6,20,21] Subjects were only exposed to altitudes above this threshold for 2 consecutive days, which is not enough exposure to affect blood volume adaptations.[23] Also, male and female data were combined and menstrual cycles could have influenced variables. However, there was in increase of Hb and Hct in every subject, male and female, which suggests gender differences would not have affected the total mean increases presented.

We did not observe a correlation between the amount of increase in mileage and the degree of hemostatic change. One explanation could be there is a mileage or mileage increase above which Hct and Hb do not increase further. Another explanation could be the homogenous subject group for initial mileage, so the magnitude of increases in training mileage were fairly uniform across subjects; making a high correlation more difficult. Finally, there could be a relationship between increased mileage and changes in Hct and Hb but we did not have enough statistical power to detect it because of the low subject number. In conclusion, results of the present study suggest that a large training volume increase substantively increases hematocrit and hemoglobin in recreational cyclists. Furthermore, these findings may suggest a preferential increase in red blood cell volume over plasma volume in this population.

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Figure Legends

Figure 1. Pre and post-training mean hematocrit (%) values of 10 recreational cyclists following a dramatic increase in training volume over a 10-week period. *-Significantly higher than pre-trip values ($p<0.05$).

Figure 2. Pre and post-training mean hemoglobin (g/dL) values of 10 recreational cyclists following a dramatic increase in training volume over a 10-week period. *-Significantly higher than pre-trip values ($p<0.05$).

Figure 1

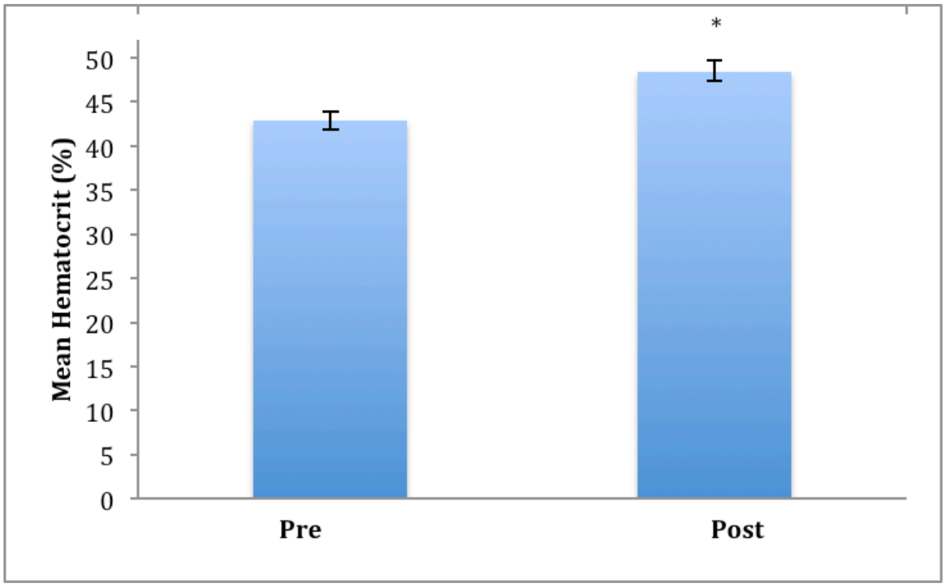
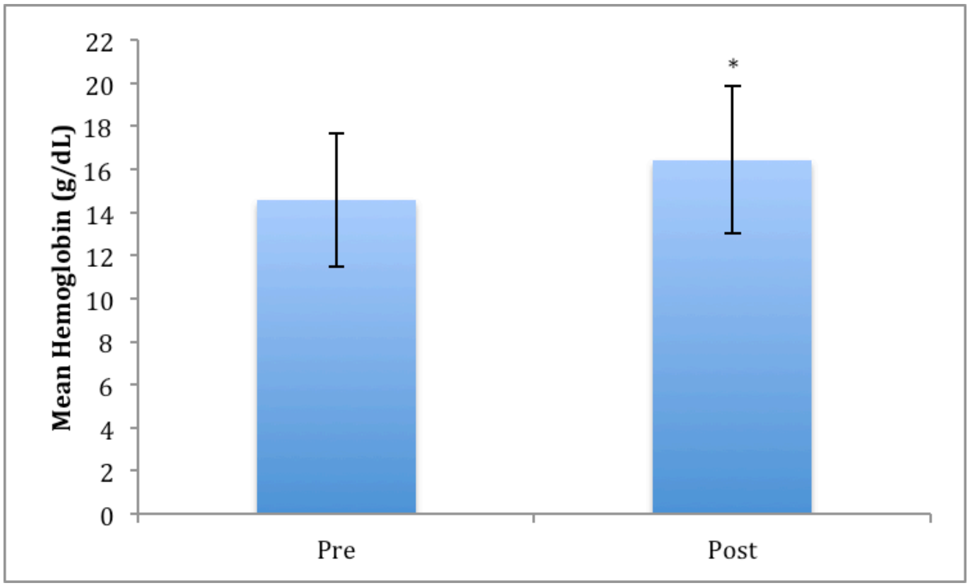


Figure 2



Appendix

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