ORIGINAL RESEARCH

Inability of healthy subjects to deposit potassium during hypokinesia and potassium supplementation

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Abstract

Objective: To determine the effect of potassium (K⁺) supplementation and hypokinesia (HK; diminished movement) on muscle K⁺ content and K⁺ loss.

Methods: Studies were conducted on 40 healthy male volunteers during a pre-experimental period of 30 days and an experimental-period of 364 days. Volunteers were equally divided into four groups: unsupplemented control subjects (UCS), unsupplemented experimental subjects (UES), supplemented control subjects (SCS), and supplemented experimental subjects (SES). A daily supplement of 1.17 mmol potassium-chloride (KCl) per kg body weight was given to the subjects in the SCS and SES groups.

Results: Muscle K⁺ content decreased ($P<0.05$), and plasma K⁺ concentration, and K⁺ loss in urine and feces increased ($P<0.05$) in the SES and UES groups compared with their pre-experimental levels and the values in their respective control groups (SCS and UCS). Muscle K⁺ content decreased more ($P<0.05$), and plasma K⁺ concentration and K⁺ loss in urine and feces increased more ($P<0.05$) in the SES group than in the UES group.

Conclusion: Muscle K⁺ content is not decreased by the K⁺ deficient diet and K⁺ loss is not increased by the higher muscle K⁺ content in the body. Rather it is caused by the inability of the body to use K⁺ during HK and K⁺ supplementation.

List of Abbreviations

Hypokinesia (diminished movement)
Hypokinesia (HK)
Unsupplemented control subjects (UCS)
Unsupplemented experimental subjects (UES)
Supplemented control subjects (SCS)
Supplemented experimental subjects (SES)
Potassium (K⁺)
Sodium (Na⁺)
Adenosine triphosphate (ATP)
Adenosine diphosphate (ADP)

Muscular activity is an important factor in the normal regulation of electrolyte homeostasis. The mechanisms by which muscular activity affects electrolyte homeostasis are not known but, in its absence, such as during hypokinesia (HK; diminished movement) the result is prevalence of catabolism¹, cell mass reduction^{2,3}, hypovolemia²⁻⁵ and decreased electrolyte deposition.²⁻⁵

Any condition which diminishes muscular activity will affect energy production, cell mass^{2,3}, blood volume²⁻⁵ and electrolyte deposition.²⁻⁵ During HK, the plasma electrolyte level and electrolyte loss increases⁶⁻⁹ and tissue electrolyte content decreases.²⁻⁵

There is also a correlation between plasma electrolyte level and electrolyte loss and tissue electrolyte level.²⁻⁹ The higher plasma electrolyte level and electrolyte loss and the lower tissue electrolyte content are attributable to many factors and primarily to the decreased electrolyte deposition.²⁻⁵ The elevated plasma electrolyte level and electrolyte loss in electrolyte deficient tissue shows decreased electrolyte deposition.²⁻⁵ This is most likely to result in higher plasma electrolyte level and electrolyte loss in electrolyte deficient tissue.²⁻⁵ The higher electrolyte loss in electrolyte deficient tissue during HK indicates different mechanisms from those in the decreased electrolyte loss in electrolyte deficient tissues during normal muscular activity.²⁻⁵

Potassium (K^+) is the major intracellular cation of the body. The higher intracellular K^+ levels are maintained because K^+ diffuses only slowly outward through the cell membrane, whereas the Na^+ , K^+ -ATPase pump, which is fueled by oxidative energy, continually transports K^+ into the cell against the concentration gradient. The sodium pump is a critical factor in maintaining and adjusting the ionic gradients upon which nerve impulse transmission and contractility of cardiac and skeletal muscle depend. When the efficiency of the sodium pump decreases because of deficiency of metabolic substrates for adenosine triphosphate (ATP) production or because of competition for ATP between the sodium pump and other energy-consuming activities of the cell, diffusion of K^+ decreases the concentration gradient, out of the cell into the plasma, exceeds sodium pump-mediated K^+ uptake. The skeletal muscle activity, because it draws its energy from anaerobic glycolysis causes K^+ efflux from muscle cells into the plasma.

There has been limited information on the effect of K^+ supplementation on muscle K^+ level, intracellular K^+ level, K^+ flux across the cell membrane, Na^+ , K^+ -ATPase pump, K^+ transport, energy production, ATP synthesis, K^+ deficiency and K^+ loss during HK. It is not known how muscle K^+ deficiency and K^+ loss occur or if muscle K^+ deficiency comes from K^+

shortage in the food consumed and K^+ loss comes from the impossibility of the body to utilize K^+ . Each electrolyte has a well-defined and separate homeostatic mechanism to control mineral content in a tissue at both cell membrane level and higher organ level. As K^+ is a major electrolyte which works with Na^+ to maintain mineral composition, fluid volume and osmotic pressure it is vital to determine if K^+ supplements and HK affects muscle K^+ deposition and muscle K^+ content and K^+ loss. To establish a potential of a lower K^+ deposition and K^+ loss in deficient K^+ muscle, it is important to study the effect of K^+ supplements and HK on muscle K^+ loss.

The objective of this study was to determine the effect of K^+ supplementation and HK on muscle K^+ content and K^+ loss which aimed at establishing the ability of the body to use K^+ . Measurements of muscle K^+ content, plasma K^+ level and K^+ loss with and without K^+ supplementation were carried out in physically healthy subjects during prolonged HK.

Materials and methods

Forty physically healthy male volunteers 21.0 ± 2.1 years of age were chosen as subjects. There were no medical problems among the subjects and none was under any drug therapy that could have interfered with potassium metabolism. They gave informed consent to take part in the study after a verbal and written explanation of risks and methods involved were given. Procedures were reviewed and approved by the Committee for the Protection of Human Subjects. Financial incentives were used to encourage compliance with the study protocol. Subjects were students and had been trained for the last 2 to 3 yr, at an average rate of 5.0 times per week at $45.3 \pm 2.2 \text{ km} \cdot \text{wk}^{-1}$. Subjects ran average distances of $9.0 \pm 1.2 \text{ km} \cdot \text{day}^{-1}$ at a speed of $9.9 \pm 1.2 \text{ km} \cdot \text{h}^{-1}$. They had a body weight of $70.1 \pm 4.4 \text{ kg}$ and a peak oxygen uptake of $58.4 \pm 6.0 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. During the pre-experimental period subjects ran average distances of $9.0 \pm 1.2 \text{ km} \cdot \text{day}^{-1}$ at a speed of $9.9 \pm 1.2 \text{ km} \cdot \text{h}^{-1}$.

Assignment of subjects into four groups was conducted randomly and their conditions were as follows: Group 1: Ten healthy subjects ran an average distance of $9.0 \pm 1.2 \text{ km} \cdot \text{day}^{-1}$ for 364-days. They were assigned to the unsupplemented control subjects (UCS) group. Group 2: Ten healthy subjects walked an average distance of $1.3 \pm 0.1 \text{ km} \cdot \text{day}^{-1}$ for 364-days. They were assigned to the unsupplemented experimental subjects (UES) group. Group 3: Ten healthy subjects ran an average distance of $9.0 \pm 1.2 \text{ km} \cdot \text{day}^{-1}$ for 364-days and were supplemented with 1.17 mmol potassium chloride (KCl) per kg body weight per day. They were assigned to the supplemented control subjects (SCS) group. Group 4: Ten healthy subjects walked an average distance of $1.3 \pm 0.1 \text{ km} \cdot \text{day}^{-1}$ for 364 days and were supplemented with 1.17 mmol KCl per kg body weight per day. They were assigned to the supplemented experimental subjects (SES) group.

Protocol

The study consisted of a 30-day pre-experimental phase and a 364-day experimental phase. Diets were served on a 7-day menu rotation. Meals were prepared under standard conditions in a research kitchen. The mean daily energy value of the metabolic diet was 3530 ± 557 , 3050 ± 410 , 3587 ± 588 and 3055 ± 424 Kcal and mean daily dietary potassium consumption was 81 ± 7 , 82 ± 6 , 83 ± 7 and 83 ± 7 mmol for the UCS, UES, SCS and SES groups, respectively. The SCS and SES groups were supplemented with 1.17 mmol of potassium-chloride per kg body weight per day.

Simulation of hypokinesia

To simulate hypokinesia the number of km walking per day was restricted to an average of $1.3 \pm 0.1 \text{ km} \cdot \text{day}^{-1}$ and was monitored by an accelerometer. The activities allowed were those that approximated the normal routines of sedentary individuals. Subjects were allowed to walk to the dining tables, lavatories and different laboratories where the tests were administered. Climbing stairs and other activities which re-

quired greater efforts were not allowed. These subjects were mobile and were not allowed outside the hospital grounds.

Blood, urine and fecal sample collection

To accommodate inter-individual differences in bowel habits, urine and feces were collected daily and pooled to form 6-day composites, while plasma samples were collected every 6-days during the pre-experimental of 30 days and experimental period of 364 days. Six--day (consecutive day) pooled samples were collected and mean $\pm$ SDs of the measurements were presented. Blood samples were taken from a superficial (antecubital) arm vein at rest and before the consumption of any meals. Subjects were fasted overnight for about 6-7 h. Blood samples were drawn under identical condition and between 8.00-9.00 a.m., without a venous stasis and after subjects had been sitting for 30 min. The volume of blood sample was 7 to 9 mL. The blood samples collected with polypropylene tubes. To obtain plasma, blood samples were collected in heparinized ice-chilled tubes and were centrifuged immediately at $10.000 \times g$ for 3 min at room temperature and separated using glass capillary pipettes which were washed in hydrochloric acid and deionized distilled water. Plasma samples were frozen on dry ice immediately after centrifugation and were kept at -20°C until analyses were made for plasma K^{+} . Twenty-four hour urine samples were stored at -4°C until needed for K^{+} analyses. Creatinine excretion was measured by colorimetric method to ensure twenty-four hour urine sample collection. Feces were collected in plastic bags, dried, weighed and stored at -20°C for K^{+} analyses. Fecal samples wet ashed with acid, were diluted and analyzed for K^{+} . To ensure complete recovery of feces polyethylene glycol was used as a marker.

Muscle, plasma, urine and fecal potassium measurements

Samples were analyzed in duplicate, and appropriate standards were used for measurements: The K^+ levels in muscle, plasma, feces and urine were measured by an atomic absorption spectrophotometer on a Perkin-Elmer 420 Model, Perkin-Elmer Corp., Norwalk, CT.

Muscle preparations, potassium extraction and analysis

Muscle biopsies were performed by a percutaneous needle technique¹⁰ under local anesthesia. Specimens were taken from the lateral portion of the quadriceps femoris muscle, 15–20 cm proximal to the knee. The muscle (mean weight 15.1 mg) was placed on a piece of quartz glass and with nonmetal tweezers carefully dissected free from all visible fat and connective tissue. All traces of blood were wiped off by rolling the specimens on the piece of quartz glass. The muscle was then placed on a platinum hook and dried in an oven at 110°C to constant weight, extracted in 1 mL of petroleum ether for 2 h and dried to constant weight again, and the fat-free dry solids (FFDS) weight was calculated. The K^+ was extracted from the muscle by treatment with 250 μ L 2.5 M HNO_3 for 24 h. From each sample, 100 μ L of supernatant was diluted to 10 mL with 0.25% $SrCl_2$ and analysis for K^+ content in muscle was performed by atomic absorption spectrophotometry on a Perkin-Elmer 420 Model, Perkin-Elmer Corp., Norwalk, CT. The results obtained were calculated in mmol/100 g FFDS.

Data analyses

The K^+ values in muscle, plasma, urine, and feces were subjected to 3-way analysis of variance (ANOVA) to answer the question would HK produce decrease in the muscle K^+ content and increase in K^+ loss and would muscle K^+ deficiency be attenuated with K^+ supplements and K^+ loss be exacerbated in K^+ deficient muscle; the three-way interaction (duration

of the experimental period, pre-experimental/experimental values, supplemented/unsupplemented groups of subjects, control/experimental groups of subjects) was used. ANOVAS for each time point measurements were used. A Tukey-Kramer post-hoc test was used to establish which means were significantly different from each other. The level of significance was set at $P < 0.05$. The results are reported as mean $\pm$ SD.

Results

During the pre-experimental period, muscle K^+ content, plasma K^+ level, and urine and fecal K^+ loss did not change in the active control and the experimental groups of subjects. With K^+ supplementation the active control and experimental groups of subjects did not show any changes in muscle K^+ content, plasma K^+ level, and urine and fecal K^+ loss (Table 1).

During the experimental period, muscle K^+ content and plasma K^+ level and urine and fecal K^+ loss did not show any changes in the SCS and UCS groups compared with baseline values (Table 1). Muscle K^+ content decreased ($P < 0.05$), and plasma K^+ level, and urine and fecal K^+ loss increased ($P < 0.05$) in the SES and UES groups compared with their pre-experimental levels and the values in their respective control groups (SCS and UCS) (Table 1). The muscle K^+ content decreased more ($P < 0.05$), while plasma K^+ level, urine and fecal K^+ loss increased more ($P < 0.05$) in the SES group than in the UES group (Table 1).

Discussion

During the pre-experimental period muscle K^+ content, plasma K^+ level, and urine and fecal K^+ loss did not change in the supplemented and unsupplemented experimental and the control groups of subjects. It is consistent with prior studies^{11–14} where during the pre-experimental period, K^+ homeostasis, plasma K^+ level, and urine and fecal K^+ loss were relatively stable regardless of the amount of K^+ consumed. This shows that in the pre-experimental period, the K^+ consumed

TABLE 1. Potassium levels in Urine, Feces, Plasma and Muscle Measurements in Physically Healthy Subjects with and without potassium supplementation at the Pre-experimental period, and During the Ambulation Period, and the Experimental Period.

Days	Urinary K ⁺ mmol/days	Fecal K ⁺ mmol/days	Plasma K ⁺ mmol/l	Muscle K ⁺ mmol/100/g ¹ FFDS
<i>Unsupplemented Control Subjects (UCS), n=10</i>				
Pre-experimental	75.0 ± 10.5	20.7 ± 1.7	4.78 ± 0.05	34.15 ± 5.52
60th	73.1 ± 10.6	18.7 ± 2.5	4.77 ± 0.04	34.16 ± 5.43
120th	74.0 ± 11.4	20.4 ± 2.5	4.76 ± 0.04	34.15 ± 5.62
180th	73.8 ± 10.6	21.8 ± 1.6	4.77 ± 0.05	34.16 ± 5.50
240th	74.1 ± 11.5	21.3 ± 2.4	4.76 ± 0.04	34.17 ± 5.42
300th	73.9 ± 10.7	19.7 ± 2.5	4.77 ± 0.05	34.15 ± 5.60
364th	74.1 ± 10.5	20.5 ± 1.7	4.76 ± 0.04	34.16 ± 5.50
<i>Unsupplemented Experimental Subjects (UES), n=10</i>				
Pre-experimental	74.5 ± 11.5	20.8 ± 1.4	4.77 ± 0.04	34.16 ± 5.63
60th	103.5 ± 12.6*	29.6 ± 2.7*	5.30 ± 0.05*	29.67 ± 4.62*
120th	96.2 ± 11.7*	26.5 ± 3.5*	5.24 ± 0.05*	30.41 ± 5.50*
180th	121.7 ± 12.5*	35.1 ± 2.6*	5.41 ± 0.06*	27.94 ± 6.47*
240th	110.3 ± 10.7*	30.4 ± 3.5*	5.35 ± 0.05*	28.72 ± 5.55*
300th	137.5 ± 13.5*	43.7 ± 2.7*	5.48 ± 0.06*	26.86 ± 4.66*
364th	125.0 ± 12.6*	35.3 ± 3.4*	5.42 ± 0.04*	27.57 ± 4.73*
<i>Supplemented Control Subjects (SCS), n=10</i>				
Pre-experimental	81.7 ± 11.5	23.3 ± 1.5	4.88 ± 0.04	34.80 ± 5.73
60th	83.6 ± 10.6	24.7 ± 1.6	4.87 ± 0.05	34.81 ± 5.72
120th	84.3 ± 11.5	23.8 ± 1.5	4.86 ± 0.07	34.85 ± 4.60
180th	83.6 ± 10.7	24.4 ± 1.4	4.88 ± 0.06	34.83 ± 5.54
240th	84.5 ± 12.4	23.7 ± 1.5	4.87 ± 0.04	34.87 ± 4.60
300th	83.2 ± 11.6	24.5 ± 1.6	4.85 ± 0.05	34.84 ± 5.53
364th	84.5 ± 11.5	23.0 ± 1.4	4.87 ± 0.06	34.88 ± 4.62
<i>Supplemented Experimental Subjects (SES), n=10</i>				
Pre-experimental	81.6 ± 10.7	23.3 ± 1.7	4.88 ± 0.05	34.81 ± 5.62
60th	138.0 ± 13.6**	38.7 ± 3.5**	5.89 ± 0.07**	26.15 ± 5.54**
120th	124.7 ± 12.7**	34.6 ± 1.8**	5.77 ± 0.05**	27.40 ± 4.61**
180th	158.8 ± 14.5**	47.2 ± 2.7**	5.97 ± 0.06**	24.52 ± 5.57**
240th	145.1 ± 12.6**	40.1 ± 3.6**	5.86 ± 0.05**	25.86 ± 6.48**
300th	178.2 ± 13.7**	57.6 ± 3.5**	6.10 ± 0.08**	24.17 ± 5.65**
364th	166.5 ± 12.6**	47.7 ± 2.6**	5.99 ± 0.05**	25.23 ± 4.75**
<i>Supplemented Experimental Subjects (SES), n=10</i>				
Pre-experimental	81.6 ± 10.7	23.3 ± 1.7	4.88 ± 0.05	34.81 ± 5.62
60th	138.0 ± 13.6**	38.7 ± 3.5**	5.89 ± 0.07**	26.15 ± 5.54**
120th	124.7 ± 12.7**	34.6 ± 1.8**	5.77 ± 0.05**	27.40 ± 4.61**
180th	158.8 ± 14.5**	47.2 ± 2.7**	5.97 ± 0.06**	24.52 ± 5.57**
240th	145.1 ± 12.6**	40.1 ± 3.6**	5.86 ± 0.05**	25.86 ± 6.48**
300th	178.2 ± 13.7**	57.6 ± 3.5**	6.10 ± 0.08**	24.17 ± 5.65**
364th	166.5 ± 12.6**	47.7 ± 2.6**	5.99 ± 0.05**	25.23 ± 4.75**

FFDS, fat free dry solids. All values were expressed as mean ± SD.

*P<0.05 significant differences between the control and the experimental groups of subjects. Each of the experimental groups was compared with their respective control groups (UCS vs UES and SCS vs SES).

**P<0.05 significant differences between the supplemented and unsupplemented experimental groups.

during supplementation has been used up for deposition and was taken by the body which protected the net muscle K^+ content, plasma K^+ level, and urine and fecal K^+ loss without showing any gross differences in the experimental and control groups of subjects.

The lower muscle K^+ content in the SES group than in the UES group is attributable to the lower K^+ deposition because the muscle electrolyte content cannot decrease more with than without electrolyte supplementation unless the electrolyte deposition decreases more²⁻⁵. This shows that the higher muscle K^+ deficiency in the SES group than in the UES group may have been induced by the lower K^+ deposition in the SES group than in the UES group. There was lower electrolyte deposition, higher electrolyte loss and greater tissue electrolyte deficiency with than without electrolyte supplementation.²⁻⁵ Some studies have shown that tissue electrolyte content reduces more with than without electrolyte supplementation²⁻⁵ and the electrolyte content decreases more in tissues with less weight-bearing supporting function and morphology.¹⁵⁻¹⁷ The greater muscle K^+ deficiency with than without K^+ supplementation during HK is ensured by different mechanisms than those involved in the greater muscle K^+ deficiency without than with K^+ supplementation during normal muscular activity.²⁻⁵

The higher plasma K^+ level and K^+ loss in the SES group than in the UES group also induced by the lower K^+ deposition in the SES group than in the UES group because plasma electrolyte level and electrolyte loss cannot increase more in electrolyte deficient muscle unless the electrolyte deposition decreases more.²⁻⁵ Because the plasma K^+ level and K^+ loss increased more in the SES group than in the UES group, the SES group may have experienced a lower K^+ deposition than the UES group.²⁻⁵ The decreased K^+ deposition promotes K^+ shifting in plasma leading to higher plasma K^+ level and K^+ loss in K^+ deficient muscle.¹¹⁻¹⁴ The higher plasma K^+ level and K^+ loss in K^+ deficient tissue during HK shows different mechanisms from those involved in the lowered plasma K^+

level and K^+ loss in K^+ deficient muscle during normal muscular activity. Studies have shown that the plasma electrolyte level and electrolyte loss increases more with higher than lower tissue electrolyte deficiency²⁻⁵ and that the tissue electrolyte deficiency increases more with than without electrolyte supplementation.

Because the mechanisms of the muscle K^+ deficiency with K^+ supplementation and higher plasma K^+ level and K^+ loss in K^+ deficient muscle have not been yet identified it is difficult to discuss the mechanisms for this reaction. However, because muscle cell injury as a result of intracellular hyperelectroemia, hypovolemia, and energy and glycine deficiency are considered as the main cause of muscle K^+ deficiency with K^+ supplementation and higher plasma K^+ level and K^+ loss in K^+ deficient muscle some information which indicates muscle cell injury is presented to support this contention.

During muscle K^+ deficiency, glycogen synthesis is impaired while the synthesis of new glycogen is inhibited¹⁸ leading to the reduction in energy production.^{19,20} The muscle K^+ deficiency can have an adverse effect on protein synthesis and energy production.^{19,20} The production of energy is also affected because K^+ which is one of the elements necessary for protein synthesis decreases.²¹ The reduction of intracellular muscle K^+ content and energy deficiency have been implicated in muscle cell injury. Tissue K^+ deficiency had been shown to decrease muscle cell transmembrane voltage and to cause muscle damage.²² Prolonged HK also leads to release of K^+ into intracellular space.^{2,3} That there is a form of K^+ independent cell injury because of deficiency of cellular glycine has also been recognized. A distinctive mechanism of cell injury during HK and adenosine triphosphate (ATP) deficiency involves the loss of cellular glycine. During HK and ATP deficiency the higher intracellular gradients of glycine are dissipated. During HK and ATP deficiency occur a glycine deficiency.²³ The daily provision of glycine during HK and ATP deficiency cannot prevent cell injury.²³

Studies on the effect of HK on energy metabolism revealed a reduction in ATP production²⁴ and adenosine diphosphate (ADP) formation.²⁵ The total amount of creatine phosphate which is the first source of energy use for the reconstitution of ATP also reduces^{1,19,20} and because there is little creatine phosphate there is limited energy to cause bonding of a new phosphate ion to the ADP to reconstitute ATP. The ADP which is a stimulator of oxygen uptake and formation of new ATP molecules reduces due to reduction of oxidative phosphorylation.²⁶ Reduction of mitochondrial number and/or function is indicated as most likely culprit to explain the oxidative phosphorylation reduction.²⁶ There is limitation of reserves of ATP because of inhibition of ADP formation and ATP synthesis. Moreover, the ATP becomes energetically less efficient^{1,19,20} and for the production of ATP more substrates are used, which causes even greater shortage of the already sparse reserves of ATP. Any condition that directly or indirectly decreases the production or use of ATP by muscle, or leads to ATP deficiency can result to muscle cell injury thereby interfering with K⁺ deposition.

The decrease of ATP production and the increase of catabolism^{1,19,20} may be indicative of a higher rate of ATP-consuming processes, especially increase of ATPase transport due to the possible changes in the membrane structure.²⁷ Because of the general catabolism of the body there occurs a reduction of nucleotide pool.^{1,19,20} The decrease of energy metabolism, i.e., decrease of ATP production and increase of glycolysis, is attributable to the triggering of compensatory mechanisms in response to the hypokinetic effect, and they are directed toward preserving the structural integrity of cell which is eventually affected due to ATP deficiency and increase of glycolysis. The decrease of energy production and the increase of glycolysis affect the production of ATP resulting to muscle cell injury. A uniform muscle necrosis, leukocyte and macrophage invasion of degenerated muscle fibers found and ultrastructural changes include the separation of

myofibrils and other cellular elements by clear spaces.²⁸

The potential mechanisms of K⁺ loss in K⁺ deficient muscle may also be attributable to cell injury owing to inadequate supplies of blood and oxygen delivery to muscle. Deconditioning of vessels of the lower part of the body due to absence of muscular activity results in shifting of fluid to the lower extremities and the retention in them of large fluid volume than what is the norm for the lower part of the body and fluid volume decreases²⁹. Because the plasma electrolyte level and electrolyte loss increases in hypovolemia, it is in the nature of a reverse fluid volume regulating reflex.³⁰ Depending on the level of hypovolemia and compensatory ability of cell, the response at the cellular level may be one of compensation, dysfunction, or injury. The aerobic respiration apparatus of cell, i.e., oxidative phosphorylation by mitochondria, is the most susceptible to hypovolemia and oxygen delivery to the tissue. As the blood flow and oxygen tension within the cell reduces, there is a reduction in oxidative phosphorylation²⁶ and production of ATP slows. The loss of ATP has widespread effects on the cellular morphology and function. As oxidative phosphorylation slows, the cell shifts to anaerobic glycolysis that allows ATP synthesis from breakdown of cellular glycogen. There the glycogen stores are depleted¹⁸, and anaerobic glycolysis is much less efficient than the oxygen-dependent mitochondrial pathways and the cell is eventually injured. Hypovolemia can indirectly result in cell injury^{31,32} which change the integrity of cell and lead to release of intracellular contents into the plasma which can result to K⁺ loss in K⁺ deficient muscle.

Conclusion

The lower muscle K⁺ content in the SES group than in the UES group shows that muscle K⁺ content decreases more with than without K⁺ supplementation. The higher K⁺ loss with higher muscle K⁺ deficiency, in turn, shows that K⁺ loss increases more in the SES

group than the UES group. Dissociation between muscle K^+ content and K^+ supplementation, and K^+ loss and muscle K^+ deficiency shows that decreased K^+ deposition is the main cause of decreased muscle K^+ content with K^+ supplementation and K^+ loss in K^+ deficient muscle; because muscle K^+ content cannot decrease with K^+ supplementation and K^+ loss cannot increase in K^+ deficient muscle unless K^+ deposition decreases. It is concluded that muscle K^+ deficiency during HK is more evident with than without K^+ supplementation and K^+ loss exacerbated more with higher than lower muscle K^+ deficiency. In all, the decreased muscle K^+ content is not resulted by the K^+ deficient diet and K^+ loss is not induced by the higher muscle K^+ level. Rather, it is caused by the inability of muscle to use K^+ during HK and K^+ supplements.

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