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The Effect of Acute High Sodium Intake on Calf Venous Compliance in Women as Measured with Venous Occlusion Plethysmography

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THE EFFECT OF ACUTE HIGH SODIUM INTAKE ON CALF VENOUS
COMPLIANCE IN WOMEN AS MEASURED WITH VENOUS OCCLUSION
PLETHYSMOGRAPHY

By

Kajalben Patel

A Research Paper

Submitted in Partial Fulfillment of the Requirements for the
Master of Science in Education Degree

Department of Kinesiology

Graduate School

Southern Illinois University Carbondale

April 13, 2011

RESEARCH PAPER APPROVAL

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Approved by:

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CHAPTER I

INTRODUCTION

In humans, the venous side of the circulation plays a vital role in regulating blood flow and blood pressure. The ability of the venous system to accommodate changes in the blood volume at a given pressure is known as venous compliance. The compliance of the veins in the legs is a factor which may contribute to changes in arterial blood pressure. Decreases in venous compliance enhance venous return, which may lead to possible increases in cardiac output and arterial blood pressure. Persistently low venous compliance eventually leads to the development of hypertension. Another issue associated with venous compliance is orthostatic tolerance. A few prior studies have shown that orthostatic tolerance is greater in individuals with decreased venous compliance compared with people having high venous compliance (Luft, Myrhe, Leopsky, & Venters, 1976; Tsutsui, Sagawa, Yamauchy, Endo, & Yamazaki, 2002). A more recent study by Hernandez and Franke (2004), reported no difference in orthostatic tolerance during comparisons of participants with high and low venous compliance, so it appears that this relationship is somewhat unclear.

Several factors such as age, gender, endurance exercise and chronic high sodium intake may influence leg venous compliance. Monahan, Dinunno, Seals, and Halliwill (2001), found that venous compliance is reduced as age increases in both sedentary and endurance exercise trained men. Moreover, they found that venous compliance is higher in endurance trained men compared to sedentary men. This finding was consistent with

evidence that venous compliance improves with consistent endurance training (Hernandez, & Franke, 2005).

It has been reported that women have lower venous compliance than men (Monahan, Dinunno, Seals, & Halliwill, 2001). Meendering, Torgrimson, Houghton, Halliwill, and Minson, (2005) provided further evidence to support this sex difference in venous compliance; however, the study could not find significant differences in venous compliance in women across the menstrual cycle phase or during the course of contraceptive use. This finding indicated that the gender difference may not be consistent in all situations.

A chronically high sodium intake increases blood pressure, increases in blood pressure trigger an increase in capillary filtration and this effect is more evident in women than men (Lindenberger & Lanne, 2007). It is possible that the different response to sodium may be contributing to the differences seen in venous compliance between the sexes. A high sodium diet can lead to hypertension and the other cardiovascular problems in salt sensitive individuals (Rich, McCullough, Olmedo, Malarick, & Moore, 1991). Furthermore, Draaijer, Kool, Van Bortel, Nieman, De Leeuw, Van Hooff, et al., (1995), found that chronic high sodium consumption is related to decreased venous compliance. A recent study found that a high sodium diet can lead to structural changes in venous wall causing decreased venous compliance (Sanders, 2009). The results of these studies are important; however none of them assessed the effect of an acute sodium intake on leg venous compliance using venous occlusion plethysmography. Therefore, the primary purpose of this investigation is to determine if acute high sodium intake will affect the

assessment of limb venous compliance using venous occlusion plethysmography in women. We hypothesized that venous compliance would be decreased following acute sodium intake in women.

CHAPTER II

REVIEW OF LITERATURE

In this chapter, assessment of venous compliance is reviewed along with the influences of gender, age, and fitness level. It is hoped that this review of literature would reveal the importance of the current study and also encourage further research into the area of venous compliance.

Venous Compliance Protocol:

Halliwill, Minson, and Joyner (1999) developed a non-invasive method to measure limb-venous compliance in humans. A four-study protocol was implemented in order to address many of the major limitations used in measuring limb venous compliance. The limitations mentioned by the authors included the following: (1) time required for the study of compliance during short sympathoexcitatory maneuvers (2) the insufficiency of methods used to account for hysteresis of the limb during changes of venous pressure and (3) most studies have assumed that resting venous pressure in the limb is equal to zero. The new method was developed in order to help evaluate the extent to which an increase in sympathetic outflow can decrease whole-limb venous compliance. The researchers based their planned method on three observations: (1) resting pressure is not equal to zero but is below 10mmHg in the majority of healthy individuals. Thus only the pressure range from 10 to 60mmHg should be analyzed (2) when the collecting cuff is inflated to 60mmHg, intravenous pressure will rise to that level when given enough time. Based on their results with direct intravenous pressure measurements, young healthy individuals

reach this pressure within 4 min.; however, 4 min. may be insufficient in other populations that have either reduced blood flow or increased venous capacity. (3) Intravenous pressure will imitate collecting cuff pressure when cuff pressure drops at a rate of $\sim 1\text{mmHg/s}$. The shorter duration of data collection minimizes and standardizes the effect of hysteresis on the slope of the pressure-volume curve (Halliwill, Minson, & Joyner 1999). The study also tested the one remaining hypothesis of their new method: the amount of interstitial fluid accumulation, secondary to the increased capillary leak, would not have an impact on the estimation of venous compliance. Using this method, it was found that neither forearm nor calf venous compliance is under functional sympathetic regulation but changes in unstressed volume may be mediated by the sympathetic nervous system.

Risk, Lirofonis, Armentano, and Freeman (2003) used various models of data representation in order to measure limb venous compliance. It was hypothesized that limb venous compliance could be explained by using a biphasic model with two linear phases: a low-pressure phase that represents the steep gradient of the low pressures of the venous compliance curve and a high-pressure phase that represents the shallow gradient and plateau of the mid to high pressures. This particular model is reliable with the two physiological functions of the venous system: to enable large translocations of blood from the venous system in response to small changes in pressure at low venous pressure and to minimize venous pooling at high venous pressures. The results of the study show that although all three models tested (biphasic, linear, & single-exponential) are justifiably able to measure compliance, the biphasic model most consistently maintains

accuracy across the entire range of pressures. The biphasic model yields separate venous compliance vs. pressure slopes for the low and high pressure. The biphasic model allows the purpose of a breakpoint pressure that separates the high and low -pressure phases. The biphasic model was able to address the nonlinear features of venous compliance; mainly that the venous system has high compliance at low pressure and low compliance at high pressures.

Factors affecting venous compliance:

Hernandez and Franke (2004) found that venous compliance is higher in individuals with higher levels of cardiovascular fitness. Research conducted by Meendering and colleagues (2004) compared venous compliance of normally menstruating women (during the early follicular, ovulatory, and midluteal phases of the menstrual cycle), oral contraceptive users, and men. There were three specific findings that were found from this study. (1) Normally menstruating women and oral contraceptive users have lower limb venous compliance than men. (2) The fluctuating levels of estrogen and progesterone that accompany the normal menstrual cycle do not elicit cyclic changes in lower limb venous compliance between the early follicular, ovulatory, and midluteal phases of normally menstruating women. (3) Fluctuations in hormone concentrations delivered through oral contraceptives do not cause cyclic changes in lower limb venous compliance between high and low hormone weeks of oral contraceptive use.

A Monahan and Ray (2003) added three primary findings relating to the difference in venous compliance and venous function in men and women: (1) Calf

venous compliance was 48% lower in women during a baseline-resting trial, (2) Reductions in calf venous compliance during sympathoexcitation due to lower body negative pressure stress (LBNP) stress appear to be specific to baroreceptor unloading and not muscle reflex engagement or cold stress in men, and (3) Calf venous capacitance is lower in women than men at rest, but is equally reduced in men and women during baroreceptor unloading (orthostatic stress due to LBNP). Lindenberger and Lanne (2006) found similar results from the standpoint of baroreceptor deactivation and sympathetic response due to LBNP. The authors found that at lower transmural pressures ($< 22\text{mmHg}$) women tended to show significantly reduced calf venous compliance compared to the men. It was also found that there was a simultaneous reduction in venous capacitance response during the LBNP stress. The lower capacitance could have been due to a lower central hypovolemic sympathetic response in women; however, with increasing transmural pressures ($> 22\text{mmHg}$) no sex differences were seen. The increased capillary fluid filtration shown in women helps to explain why no significant difference was found between men and women in calf volume.

Monahan, Dinunno, Seals, & Halliwill (2001) found that calf-venous compliance was reduced with age in sedentary ($\sim 40\%$) and endurance-trained men ($\sim 20\%$). Also, calf-venous compliance was $\sim 70\text{-}120\%$ greater in endurance-trained compared with age-matched sedentary men and $\sim 30\%$ greater in older endurance-trained compared with young sedentary men. Following are the new findings discerned from the study: (1) Calf venous compliance is reduced with age in both healthy sedentary and endurance exercise-trained men, suggesting that the changes are partially due the effects of human aging. (2)

Calf venous compliance is greater in both young and older endurance exercise-trained compared with age-matched sedentary men. (3) The magnitude of the age-associated decline in calf venous compliance appears to be only half as great in men who exercise regularly compared to their sedentary counterparts. (4) Older endurance-trained men demonstrate high calf venous compliance compared with young sedentary men. This final finding indicated that sedentary lifestyle may have a greater negative influence on venous compliance than aging (Monahan et al., 2001).

In a study by Hernandez and Franke (2005), the authors investigated the extent to which exercise training in a previously sedentary older population could affect venous compliance. The endurance training protocol consisted of a 6-month aerobic training program with the participants exercising 3 days/week, 20-45 min. per session, at 40-85% of their HR reserve. All training was increased accordingly and during the last 3 months of the training and all participants were exercising at 65-85% of their HR reserve for a 40 min. session. It was found that the exercise group improved their fitness level with the 6 month endurance program, but the control group did not. Venous compliance was not different between groups or trials initially or after 3 months of endurance training; however venous compliance was greater in the exercise group after 6 months of training. These data suggest that even at advanced ages, venous compliance can be improved with an aerobic exercise intervention. Hernandez and Franke (2004) added that venous compliance is greater in a fit population than in a sedentary population and that the younger fit have greater compliance than both the older fit and unfit. The authors also found that the young fit group had ~50% greater compliance than the young unfit group

and the difference in compliance between the older fit and the young unfit groups was ~35%. Among all the studies completed on venous compliance with aging found that the young fit have greater compliance and venous function than any other group. The studies on the older populations tend to show that venous function in older fit is better than young unfit.

Some of the studies on hypertension found that high sodium consumption can lead to structural changes in venous walls causing decreased venous compliance which can eventually lead to hypertension (Rich et al., (1991); Draaijer et al., (1995); & Sanders, (2009)).

Draaijer et al. (1995), found that chronically high sodium consumption is associated with decreased venous compliance in sodium sensitive and sodium resistant borderline hypertensive patients. The study by Sanders (2009) provided the indication that high sodium diets can lead to structural changes in venous wall.

CHAPTER III

METHODS

Participants: Ten healthy, normotensive, nonsmoking women between the ages of 21 and 24 years from the SIU campus and community were recruited for participation in this investigation. All participants were healthy based on medical history, resting arterial blood pressure less than 140/90 mmHg, non smoking status, body mass index less than 27 kg/m², not taking medication with known cardiovascular or autonomic nervous system actions and no history or symptoms of venous insufficiency. This study was approved by the Institutional Review Board of Southern Illinois University and each participant signed informed consent prior to participation.

General experimental design: The experiment was a within participants design with two different conditions. One condition was a fasting condition, which required the participants to fast for 12 hours (8pm-8am) prior to venous compliance testing. The other condition involved supplementation of a high sodium diet (>3000mg NaCl) in the twelve hours prior to testing. The high sodium trial included participants consuming a high sodium meal around 8 PM the evening before testing, a snack sometime later that night, and another high sodium meal at 7 AM in the morning of testing. The participants reported to the laboratory on three separate occasions. The first meeting was to assess anthropometric and randomly determined the order of the treatment (high sodium vs. fasting). The second and third visits were conducted to assess calf venous compliance in either the fasted state or following the high sodium meals. All participants were instructed to refrain from caffeine ingestion for 12 hours prior to testing. Data collection

was performed at a stable room temperature between 22-25°C in the cardiovascular laboratory in Davies Hall on the Southern Illinois University Carbondale campus. All the participants received a reminder email or call for their condition (fasting/ high sodium) before their testing day.

Measurement Techniques:

A balance scale and stadiometer were used to assess body mass (kg) and height (cm). Body composition was estimated by a 3-site protocol using Lange skinfold calipers. Blood pressure and heart rate were continuously monitored by Dinamap non-invasive blood pressure monitor. Change in calf volume was measured by non-invasively using strain gauge plethysmography (ECR5 Hokanson, Bellevue, WA) at the maximal calf circumference. A venous collecting cuff was used to control the pressure (AG101 Hokanson, Bellvue, WA). For the limb venous compliance testing, participants were placed in the supine position and instrumented for measurement of calf volume (strain gauge plethysmography) and venous collecting cuff pressure. The right leg was positioned above the level of heart to promote venous drainage. Calf venous compliance in the right leg was determined using a slightly modified version of Halliwill et al. (1999) that has been utilized previously in this lab (Hernandez & Franke, 2004; Hernandez & Franke, 2005). Following instrumentation and a period of rest (20 minutes) venous collecting calf pressure was applied at 60 mm of Hg for 8 minutes. After 8 minutes, collecting cuff pressure was reduced at a rate of 5 mm of Hg/ 5 seconds to 0 mm of Hg. When cuff pressure was first applied, an initial rapid increase of calf volume occurred (capacitance response) followed by a slower, but continuous rise in volume caused by net

transcapillary fluid filtration from blood to tissue. Calf volume declined rapidly during cuff pressure reduction (5mmHg/5 seconds).

Data Analysis:

Data was recorded on a Dell PC (Biopac data acquisition software) and analyzed with SPSS. During assessment of calf venous compliance, the resulting pressure-volume curves during the step down in pressure are non-linear and well described by the quadratic regression equation, $[(\Delta \text{ limb volume}) = \beta_0 + \beta_1 * (\text{calf pressure}) + \beta_2 * (\text{calf pressure})^2]$. Due to the derived non linear pressure-volume curves, a single number is inadequate to characterize the slope of this relation because compliance become a pressure of a specific pressure (i.e. compliance is distinctly different at each pressure level). According to simplify data presentation the first derivative of pressure-volume curve $[\text{Compliance} = \beta_1 + 2 * \beta_2 * (\text{calf pressure})]$ was calculated using the regression equation. The first derivative yields a linear pressure-compliance relation that can be evaluated graphically (7). The slope of the pressure-compliance relation was used to determine group (fasting Vs high sodium) related difference in calf venous compliance. The capacitance response was calculated from the volume increase at the onset of cuff pressure application to the line defined from the filtration slope between 3 and 8 minutes of cuff pressure application. Total capillary filtration during cuff pressure was calculated by multiplying the rate of filtration (ml/min) by the time of the cuff pressure application (8 min). The sum of the capacitance and net capillary filtration volumes equals the total calf volume increase.

A paired t-test was used to determine differences in beta values between the two trials (SPSS version 17).

CHAPTER IV

RESULTS

Participants Characteristics:

Physical characteristics of all participants are summarized in Table 1. There were no significant differences with respect to systolic blood pressure (SBP), and diastolic blood pressure (DBP) between the fasted and acute sodium conditions ($p < 0.05$). Body mass, body mass index (BMI) and body fat% were measured only once during assessment for each participants.

Table 2 displays the regression parameters β_0 , β_1 , and β_2 calculated (means \pm SD) for the fasted and acute sodium condition. No significant differences for any β values existed between the fasted condition and acute sodium condition ($p < 0.05$). The pressure-volume and compliance-pressure slopes demonstrate no differences in fasted and acute sodium conditions ($p < 0.05$, Figures 2 & 3). There were no significant differences in capillary filtration between the fasted condition and acute sodium condition ($p < 0.05$, Figure 1). Interestingly, acute sodium intake showed notable difference in capacitance volumes compared with the fasted condition. The capacitance volume was greater in the acute sodium intake condition than the fasted condition participants.

Table 1. Participants Characteristics

Variable	Fasted Condition	Acute Sodium Condition
Age, yr.	22.4 ± 0.69	
Height, cm	167.3 ± 2.1	
Body Mass, kg.	65.2 ± 3.1	
BMI	23.2 ± 1.0	
Body fat%	24.8 ± 1.4	
Systolic BP, mmHg	122.0 ± 1.6	121.0 ± 1.9
Diastolic BP, mmHg	78.1 ± 1.7	75.0 ± 1.9
VO ₂ max, ml,kg ⁻¹ , min ⁻¹	31.9 ± 6.2	

Values are means ± SEM; n=10 (Female = 10), VO₂max = maximal oxygen consumption, BP = Blood Pressure, BMI = Body Mass Index

Table 2. Pressure-volume regression parameters

	β_0	β_1	β_2
Fasting Condition	-0.1054 ± 0.27799	0.1519 ± 0.033722	-0.0016 ± 0.00063
Acute NaCl Condition	0.5322 ± 0.51602	0.1402 ± 0.03628	-0.0014 ± 0.00060

Values are means ± SEM. Δ Calf Volume = $\beta_0 + \beta_1$ *(cuff pressure) + β_2 *(cuff pressure)²;

^a P < 0.05 Vs Fasting Stage; ^b P < 0.05 Vs Acute High Sodium Stage

Table 2 displays the regression parameters β_0 , β_1 , and β_2 calculated (means \pm SD) for all participants with fasting and acute high sodium intake stage.

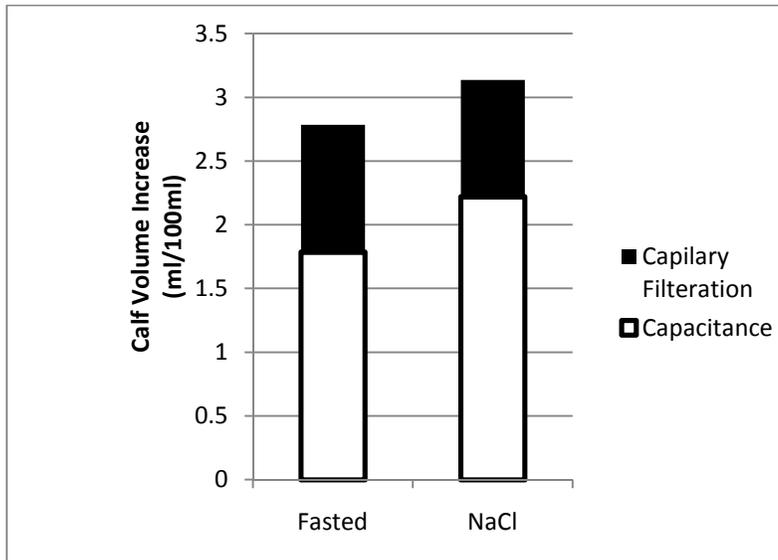


Figure 1 Total Volume Changes. The contribution of venous capacitance and capillary filtration. Values are means \pm SE.

The contribution of venous capacitance (lower part of bars) and capillary filtration (upper part of bars) are also shown. Values are means \pm SE. * The acute sodium trial resulted in significantly greater capacitance volumes.

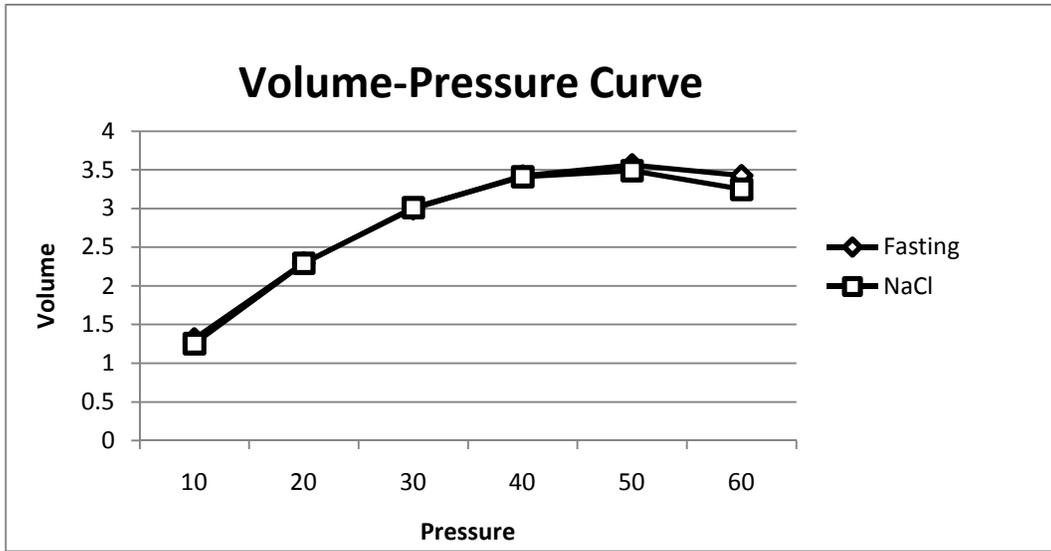


Figure 2- Volume – Pressure slopes. All values are means \pm SE.

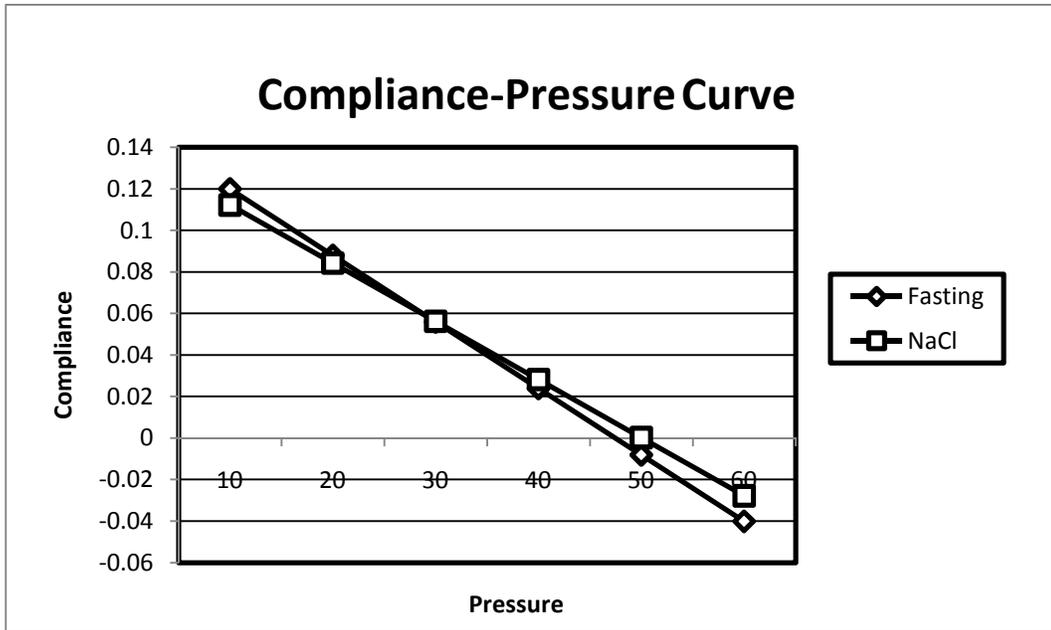


Figure 3- Compliance – Pressure slopes. All values are means \pm SE.

CHAPTER V

DISCUSSION

To the best of our knowledge, this is the first study to investigate the effect of acute high sodium intake on the assessment of limb venous compliance in women (using venous occlusion plethysmography). The purpose of the study was to gain insight into the relationship between the venous compliance and acute high sodium diet. We hypothesized that venous compliance would be decreased following acute sodium intake in women. The main findings of the study do not support this hypothesis showing that an acute high sodium diet has no significant affect on limb venous compliance and net capillary filtration volumes using venous occlusion plethysmography. We did find that capacitance volume is greater in the acute sodium intake condition than the fasted condition in the women studied here; this is likely due to increased fluid volume secondary to the high sodium consumption. The study of Meendering et al, (2005) demonstrated that venous capacitance is greater in females when concentrations of female sex hormones are elevated without a simultaneous increase in vessel wall compliance. Changes in female sex hormones could be the possible reason for greater venous capacitance without showing significant difference in venous compliance in our study; however, this is unlikely given that each condition in the present study was assessed within a within a very short time frame of 24 hours. Future research may want to assess all females at the same point in their menstrual cycle.

Calf Venous Compliance

The results of our study indicated that calf venous compliance did not exhibit any difference in women after an acute high sodium diet compared to fasting; however, research has indicated that chronically high sodium diets can lead to decreased venous compliance (Sanders, 2009) and hypertension. Sanders (2009) found that excess dietary sodium intake impaired production of nitric oxide (NO) and promoted production of transforming growth factor – β (TGF- β). Impaired nitric oxide production reduces venous compliance and promotes hypertension. Draaijer et al. (1995) established the effect of chronic high sodium consumption on venous compliance using strain gauge plethysmography. They found that venous compliance was lower in subjects who had consumed a regular sodium intake of approximately 120 mmol per day as compared to normotensive group. This effect appears to only occur with chronic high sodium consumption. The limited results of this study support this assertion as an acute high dose of NaCl did not affect calf venous compliance.

Limitations:

Several limitations needs to be considered while assessing the result of this study.

- (1) Our study included small sample size. A small sample size has a greater probability that the examination just happened to be unidirectional. Therefore it is harder to find significant relationships from the data, as statistical tests normally require a larger sample size to justify that the effect did not occur by chance alone.
- (2) Our study only researched young and healthy female. This means that we cannot generalize our findings to other populations such as men, children and elderly people.

Specific recommendations regarding recommended daily allowances for sodium do not exist for infants, children, and adolescents.

- (3) We did not assess all females at the same point in their menstrual cycle. The menstrual cycle could be the potential limitation of our study in assessing venous capacitance but not venous compliance. The reason for no significant difference in venous compliance could be that an acute intake of sodium does not alter the venous walls that can attribute to a change in compliance (Takeshita, Ashihara, Yamamoto, Imaizumi, Hoka, Ito, et al. (1984)).

In conclusion, while previous studies have shown that sodium consumption affects venous compliance, this investigation found that acute high sodium intake does not affect limb venous compliance. Therefore, strict control of diet is not required prior to assessment of limb venous compliance using venous occlusion plethysmography. Also, greater control over menstrual status should be exercised in future studies of the female participants in this population.

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