JEPonline
Journal of Exercise Physiologyonline

Official Journal of The American
Society of Exercise Physiologists (ASEP)

ISSN 1097-9751

An International Electronic Journal
Volume 7 Number 1 February 2004

Nutrition and Exercise

EFFECT OF ONE WEEK VERSUS TWO WEEKS OF DIETARY NaCl RESTRICTION ON SEVERITY OF EXERCISE-INDUCED BRONCHOCONSTRICTION

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ABSTRACT

EFFECT OF ONE WEEK VERSUS TWO WEEKS OF DIETARY NaCl RESTRICTION ON SEVERITY OF EXERCISE-INDUCED BRONCHOCONSTRICTION. **R. W. Gotshall, J.J. Rasmussen, and L.J. Fedorczak**. **JEP**online. 2004;7(1):1-7. Two weeks of a low NaCl diet has markedly improved pulmonary function in those with exercise-induced bronchoconstriction (EIB). The purpose of this study was to determine if one week of NaCl restriction would also prove effective. Ten subjects with EIB (EIB) and 10 subjects without EIB (Control) entered into the study while on their usual diet (normal salt diet, NSD). NaCl intake was restricted (~ 1,500 mg sodium) for two weeks, with repeat testing at one (LSD1) and two (LSD2) weeks. Forced vital capacity was performed before and after 9 min of treadmill exercise at 85-90% of age-predicted maximal heart rate. Post-exercise forced expiratory volume in 1 sec (FEV_1) was measured at 1, 5, and 15 min. There was no effect of exercise or diet in Controls. EIB subjects demonstrated significant reductions in post-exercise FEV_1 while on the NSD (-27 ± 11%, -24 ± 5%, -20 ± 8% [mean ? SD] at 1, 5, and 15 minutes, respectively). At LSD1, post exercise FEV_1 was significantly improved to -4.5 ± 4%, -8.9 ± 4%, and -7.6 ± 3%; and this was the same at LSD2, -3.2 ± 7%, -8.9 ± 10%, and -7.7 ± 5%. A LSD effectively reduced EIB to sub-clinical (<10% decrease) levels, and had a similar effect at one and two weeks.

Keywords: Sodium restriction; exercise-induced asthma; pulmonary function; asthma

INTRODUCTION

In three previous studies, this laboratory demonstrated that two weeks of a NaCl-restricted diet improved post-exercise pulmonary function in subjects suffering from exercise-induced bronchoconstriction (EIB) (1-3). Additionally, in these studies two weeks of an elevated dietary NaCl intake worsened post-exercise pulmonary function in these same subjects. The question arose as to whether a shorter period of reduced dietary NaCl would have a similar positive effect on EIB. Athletes often find a low-NaCl diet restrictive and compliance is difficult. Thus, reducing the time required to achieve the positive benefits of a low-NaCl diet on pulmonary function has practical implications for competition and training.

Therefore, it was hypothesized that a one-week period of dietary NaCl restriction would provide the same post-exercise pulmonary benefits as a two-week protocol in subjects with EIB, and would have no measurable effect on pulmonary function in subjects without EIB. Because the standard pulmonary function testing protocol for diagnosing EIB typically focuses on forced expiratory volume in one second (FEV_1) as an indicator of airway caliber (4), FEV_1 was used as the primary variable examined.

METHODS

Subjects

Ten subjects with clinically-diagnosed EIB (EIB group) and ten subjects with no history, signs, or symptoms of EIB (Control group) volunteered for the study (Table 1). Subjects were recruited from the university and community population and were recreationally active. Each subject completed a health questionnaire and gave written informed consent to participate prior to enrollment in the study, which was pre-approved by the Colorado State University Institution Review Board. All EIB subjects had a history of post-exercise shortness of breath, and intermittent wheezing, relieved by bronchodilator therapy; otherwise they were free of atopic asthma, as diagnosed by their personal physician. This medical history was confirmed by the researchers using a medical history questionnaire. All EIB subjects had been using physician-prescribed medication (short-acting or long-acting beta-2 agonist by inhalation prior to exercise) for EIB prior to participation in the study for a minimum of one year and for a maximum of 4 years. All EIB subjects demonstrated the presence of EIB during screening as indicated by a reduction in post-exercise FEV_1 of greater than 10% (5). Table 1 indicates that the two groups, EIB and Control were well matched according to age and physical characteristics.

Table 1. Subject characteristics.

Group	*Age (y)*	*Gender (#)* Male,Female	*Ht (m)*	*Wt (kg)*	*BMI (kg/m^{2+})*
Control	23.6 ? 1.0	6,4	1.76 ? 0.13	75.6 ? 18.3	24.2 ? 3.4
EIB	24.4 ? 6.6	4,6	1.68 ? 0.07	72.2 ? 13.3	24.8 ? 3.4

Values are Mean ? SD. Ht=height; Wt=weight; BMI=body mass index; EIB=exercise-induced bronchoconstriction.

Study protocol

All subjects entered the study on their normal NaCl (salt) diet (NSD), after which they were placed on a low NaCl (salt) diet (LSD) for two weeks. The LSD was achieved by adherence to a menu plan, permitting choice. The target NaCl intake for the LSD was 1500 mg/d of sodium (~2250 mg/d of chloride). To monitor dietary compliance, 24-hour urine collections for the determination of 24-hour sodium excretion were made at the beginning of the study while on the NSD and at the end of week one and two of LSD.

Measurements

For the period of 24 hours prior to the exercise test, each subject was instructed to avoid any strenuous physical activity and to refrain from using therapeutic drugs, alcohol or caffeine. Initially, and at the end of each treatment period, the subjects underwent a standardized exercise challenge routinely used for the diagnosis of EIB (5). The exercise test protocol lasted approximately 9 min and required the subject to run on a treadmill (Quinton Instrument Company, Model Q65, Seattle, WA) at 85-90% of age-predicted maximum heart rate (PMHR) for at least 5 min of the exercise (6) using a standard graded protocol of incremental increasing workloads. The exercise protocol was tailored to each subject to achieve heart rate criteria. Heart rate was determined from the ECG and monitored continuously (Quinton 4500 Stress Test Monitor, Quinton Instruments, Seattle, WA). Subjects wore a nose clip to force oral breathing. Environmental conditions were 23 ? 2^{o} C and 50 ? 7% relative humidity.

Pulmonary function was determined pre exercise and at 1, 5 and 15 min post-exercise, during NSD and at 1 and 2 weeks of LSD. Pulmonary function tests were performed using the Sensormedics Vmax 22 computerized spirometry (Sensormedics Corporation, Yorba Linda, CA). Subjects were required to perform three acceptable spirograms (forced vital capacity) according to the American Thoracic Society Standardization of Spirometry (7).

Urine samples were analyzed for sodium and potassium concentrations using ion-specific electrodes (Beckman Astra analyzer, Beckman Instruments, Inc., LaBrea, CA). Urinary creatinine concentration was determined by a modified Jaffe rate reaction, using the same instrument, in order to verify complete collection of the 24-hour urine samples.

Statistical analyses

Data were analyzed using the NCSS 2000 statistical software (NCSS, Kaysville, UT). Alpha was set aprori at p<0.05. Subject characteristics between the two groups were compared with independent *t*-tests. Urine values and baseline pulmonary function were analyzed with a two-factor (group, diet), repeated-measures (diet) ANOVA, with Fisher's post hoc LSD test applied when the *F*-ratio was significant. Post exercise FEV_1 was expressed as the percent change from pre-exercise, baseline value. The percent change in FEV_1 for the three post exercise times was analyzed for each group with a two-factor (diet, time), repeated-measures (diet, time) ANOVA. A Fisher's post hoc LSD test applied when the *F*-ratio was significant. Data are expressed as mean ? standard deviation (SD).

RESULTS

Tables 2 and 3 present the 24-hour urine data for Control and EIB, respectively. Both groups met and maintained the target daily intake of NaCl.

Table 2. Control subjects' twenty-four hour urine volume, creatinine, and electrolyte excretion.

	NSD	*LSD1*	*LSD2*
Volume (ml)	1291 ? ?611	1622 ? ?618	1738 ? ?484
Creatinine (gm)	1.4 ? ?0.5	1.5 ? ?0.6	1.6 ? ?0.6
Sodium (mg)	4322 ? ?2253[a]	1035 ? ?667[b]	1035 ? ?? ? ?[b]
Chloride (mg)	4857 ? ?1773[a]	? ? ? ?? ?? ? ?[b]	957 ? ?? ? ?[b]
Potassium (mg)	2307 ? ?704	2698 ? ?1134	2737 ? ?? ? ? ?
Sodium/Creatinine (mg/gm)	2897 ? ?943[a]	? ? ? ?? ?? ? ?[b]	690 ? ?? ? ?[b]
Chloride/Creatinine (mg/gm)	3545 ? ?1276[a]	638 ? ?319[b]	638 ? ?? ?9[b]
Potassium/Creatinine (mg/gm)	1603 ? ?? ? ?	1916 ? ?743	1877 ? ?743

Values are Mean ? SD. Control=non-asthmatic; NSD=normal salt diet; LSD1=1 week of low salt diet; LSD2=2 weeks of low salt diet. Significance (p<0.05) across diets shown by differing letters, [a,b]. Similar letters are not significant; no letters indicate lack of significance across diets.

Table 4 presents baseline pulmonary function values for both groups preceding each exercise test. Resting pulmonary function was normal for both groups, and was unaffected by diet or number of weeks on the diet.

Figure 1 shows post-exercise FEV_1 for Control and EIB subjects, expressed as a percent change from pre-exercise values. For the control subjects (blue line) there were no significant changes in FEV_1 after any exercise test, and no effect of diet or week. In contrast, EIB subjects (red line) had marked decreases in post-exercise FEV_1 values when on their NSD, confirming the diagnosis of EIB. After one and two weeks of LSD, EIB subjects demonstrated significantly improved post-exercise FEV_1 values. One week and two weeks of LSD had the same positive effect on post-exercise FEV_1 in those with EIB.

Table 3. EIB subjects' twenty-four hour urine volume, creatinine, and electrolyte excretion.

	NSD	***LSD1***	***LSD2***
Volume (mL)	1825 ? ?771	1750 ? ?571	1315 ? ?342
Creatinine (gm)	1.4 ? ?0.4	1.0 ? ?0.4	1.1 ? ?0.6
Sodium (mEq/L)	5127 ? ?2460[a]	989 ? ?1081[b]	966 ? ?621[b]
Chloride (mEq/L)	4467 ? ?2730[a]	1630 ? ?2269[b]	1134 ? ?1134[b]
Potassium (mEq/L)	1955 ? ?665	2502 ? ?1173	1955 ? ?1290
Sodium/Creatinine (mEq/gm)	3449 ? ?1035[a]	828 ? ?667[b]	828 ? ?299[b]
Chloride/Creatinine (mEq/gm)	2836 ? ?1347[a]	1241 ? ?1418[b]	957 ? ?780[b]
Potassium/Creatinine (mEq/gm)	1446 ? ?508	2229 ? ?743	1759 ? ?547

Values are Mean ? SD. EIB=exercise-induced bronchoconstriction; NSD=normal salt diet; LSD1=1 week of low salt diet; LSD2=2 weeks of low salt diet. Significance ($p<0.05$) across diets shown by differing letters, [a,b]. Similar letters are not significant; no letters indicate lack of significance across diets.

Table 4. Baseline, pre-exercise, pulmonary function in Control and EIB subjects.

	NSD		***LSD1***		***LSD2***	
	Control	EIB	Control	EIB	Control	EIB
Forced Vital Capacity (L)	5.4 ± 1.6	5.3 ± 0.6	5.5 ± 1.7	5.4 ± 0.8	5.2 ± 1.6	5.4 ± 0.6
Forced Expiratory Flow-1 sec. (L)	4.55 ± 1.32	4.46 ± 0.56	4.6 ± 1.2	4.4 ± 0.6	4.4 ± 1.3	4.3 ± 0.7
FEV%	84.3 ± 8.1	84.2 ± 9.5	83.6 ± 8.1	81.5 ± 9	84.6 ± 9.2	79.6 ± 9.3
FEV1 as % predicted	98.6 ± 10.1	97.3 ± 11.0	99.7 ± 11	96.1 ± 11.4	96.1 ± 11.2	93.9 ± 10.9

Values are Mean ? SD.

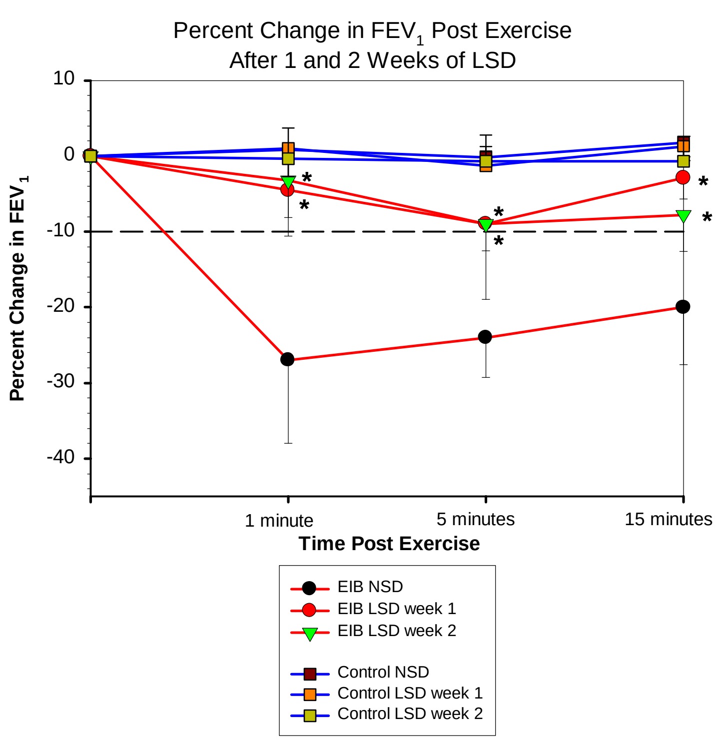

Figure 1. Post-exercise forced expiratory volume in 1 sec (FEV_1), expressed as percent of pre-exercise value for Control (blue lines) and EIB (red lines) subjects. *$p<0.05$, NSD vs. LSD1 and LSD2.

DISCUSSION

This study proved two new results. First, this study indicated that one week of dietary NaCl restriction was effective in significantly improving EIB, as indicated by improved post-exercise pulmonary function. Secondly, this study also demonstrated that one week was equally as effective as two weeks of dietary NaCl restriction in improving post-exercise pulmonary function in those with EIB. Additionally, in support of our previous studies (1-3), this study confirmed that two weeks of dietary NaCl restriction significantly improves pulmonary function, as indicated by post-exercise FEV_1, in those with EIB. Notably, in the current study, the improvement in post-exercise FEV_1 at both one and two weeks was to sub clinical levels (less than a 10% reduction in FEV_1 post exercise).

The dietary target for NaCl restriction in this and previous (1-3,8) studies was 1,500 mg of sodium/day. This value is three times the RDA (9), below the 2,400 mg/day limit for reducing hypertension (10), but well below the average daily sodium intake of Americans (in excess of 3,900 mg of sodium/day) (9). Based on the present study and our previous studies (1,3,8), we conclude that the EIB response to dietary sodium chloride is dose dependent, as post-exercise pulmonary function declines progressively from a LSD, through a NSD, to a HSD. However, the minimal NaCl restriction level and duration required for improvement of post-exercise pulmonary function to sub clinical levels is not known.

The mechanism by which dietary NaCl influences pulmonary function in EIB is unknown. Both sodium and chloride, however, have been implicated. Supplementation of diet for two weeks with sodium chloride to above normal (NSD) levels significantly worsened post-exercise pulmonary function in EIB (1,2). When the diet (NSD) was supplemented with the same amount of sodium, but bicarbonate was substituted for chloride (i.e. sodium bicarbonate instead of sodium chloride), pulmonary function was significantly improved again (8). However, in this case, pulmonary function did not improve as much as when both sodium and chloride were restricted (LSD), implicating both sodium and chloride as having negative influence on pulmonary function in EIB (8).

Clearly, inflammatory mediators are involved in the post-exercise airway response in those with EIB. The inflammatory response to EIB has not been fully examined, but it is certain that a variety of inflammatory mediators from mast cells, neutrophils, lymphocytes, and macrophages are required for full expression of EIB (11-14,18). With regard to dietary NaCl, Mickleborough et al. (16) demonstrated that an intact leukotriene system was required for expression of hyperpnea-induced airways obstruction (HIAO) in guinea pigs. In this animal model of EIB (16), a high NaCl intake worsened the HIAO, and this response was also blocked by a non-specific leukotriene inhibitor. Thus, it may be that dietary sodium chloride moderates EIB by altering the levels of inflammatory mediators, though this remains to be determined.

Regardless of the mechanism underlying the effect of reducing dietary NaCl on improving EIB, the time required for reduced dietary NaCl to alter the mechanism of EIB is less than one week. The current data indicate that the full effect of reduced NaCl on EIB apparently occurs within the one week period, and beyond this time (up to two weeks at least) there is no further benefit. These data imply, but do not confirm, that extending the dietary restriction past two weeks will not likely result in further improvement in EIB. However, this has not been tested experimentally.

In conclusion, this study has reinforced the role of dietary sodium in severity of EIB. Furthermore, a LSD of one week was as effective as two weeks in improving EIB in reducing symptoms to sub clinical levels. The mechanism by which dietary NaCl modifies the pulmonary response to exercise in those with EIB is undetermined, though one suggestion is modification of the inflammatory response, and this must occur within one week of dietary modification. Whether a LSD will reduce the dependence of an individual with EIB on medications has not been determined, but is implied from these results.

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