Dietary salt restriction improves pulmonary function in exercise-induced asthma

ROBERT W. GOTSHALL, TIMOTHY D. MICKLEBOROUGH, and LOREN CORDAIN

Department of Health and Exercise Science and Department of Physiology Colorado State University, Fort Collins, CO 80523-1582

ABSTRACT

GOTSHALL, R. W., T. D. MICKLEBOROUGH, and L. CORDAIN. Dietary salt restriction improves pulmonary function in exercise-induced asthma. *Med. Sci. Sports Exerc.*, Vol. 32, No. 11, pp. 1815–1819, 2000. **Purpose:** Exercise-induced asthma (EIA) occurs in approximately 90% of persons with asthma. The mechanism has not been delineated. Epidemiological studies have suggested that dietary salt may play a role in airway responsiveness. Therefore, the purpose of this study was to determine the influence of both elevated and restricted salt diets on pulmonary function in subjects with EIA. **Methods:** Eight subjects with EIA and eight subjects without EIA (control) participated in a double-blind crossover study. Pulmonary function was determined pre- and post-exercise challenge before and after 2 wk on a normal salt, sodium chloride, diet (NSD), a low salt diet (LSD), and a high salt diet (HSD). A 1-wk washout occurred between diets. **Results:** Diet had no effect on preexercise pulmonary function values in either group and had no effect on postexercise pulmonary function values in control subjects. However, LSD improved and HSD worsened postexercise pulmonary function values in EIA subjects. Forced expiratory volume in 1 s (FEV_1) decreased by at least 10% in EIA subjects with exercise. In EIA subjects, FEV_1 decreased by 14 ± 6% on LSD, 20 ± 7% on NSD, and 24 ± 6% on HSD at 15 min postexercise. Similar patterns were observed for forced vital capacity and peak expiratory flow rates. Although LSD did not normalize pulmonary function in EIA, it did improve it. **Conclusions:** These data suggest that individuals with EIA might benefit from lower salt diets. **Key Words:** EXERCISE-INDUCED BRONCHOCONSTRICTION, DIETARY SODIUM, ASTHMA

Exercise-induced asthma (EIA) occurs in 80–90% of all persons with asthma, 35–40% of those with allergic rhinitis, and 12–15% of the general population (2,15,16,22). Additionally EIA has been reported to be as high as 19.3% of Australian school children (13,14). A study of the 1984 Olympic games indicated that approximately 11% of U.S. Olympic athletes suffered from EIA (22,34). EIA, or exercise-induced bronchoconstriction (EIB), refers to the postexercise decrement in pulmonary function characterized by airway narrowing and increased airway resistance. This is typically diagnosed by a standard exercise protocol of approximately 80% of age-predicted heart rate maximum for 10 min with pulmonary function measured 5 min postexercise (33). A greater than 10% reduction in forced expiratory volume at 1 s (FEV_1) compared with preexercise values supports the diagnosis of EIA (33).

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Dietary sodium has been linked to the prevalence and severity of asthma in several epidemiological studies (4–6,27). In general, the higher the salt intake within a population, the greater prevalence of asthma and the greater the severity of the asthma (4–6,27). Additionally, most (7,8,31), but not all (3,10,21), interventional studies have indicated that increased salt worsens bronchiolar smooth muscle reactivity. Therefore, there is a rationale to hypothesize that alteration in dietary sodium intake will influence pulmonary function in those with EIA. Thus, the experimental hypothesis tested in the current study was that dietary salt restriction would improve, and dietary salt enhancement would worsen, pulmonary function in subjects with EIA, but have no effect on pulmonary function in subjects without EIA.

METHODS

Subjects. Eight subjects with clinically diagnosed EIA volunteered for this study. Eight subjects with no history, signs, or symptoms of EIA also volunteered for the study. Subjects were recruited from the Colorado State University student population and were recreationally active. All EIA

TABLE 1. Subject characteristics.

Group	Gender (M, F)	Age (yr)	Weight (kg)	Height (cm)	??O_{2peak} (mL·min^{-1}·kg^{-1})NSD
Control	4,4	23 ± 1.7	66 ± 3	170 ± 3	43.6 ± 2.8
EIA	1,7	23 ± 1.0	60 ± 4	166 ± 2	44.1 ± 5.8

Values are means ± SEM.

subjects had a history of postexercise shortness of breath and intermittent wheezing, relieved by bronchodilator therapy, but were otherwise free of atopic asthma as diagnosed by their physician. All EIA subjects had been using physician-prescribed medication for EIA before participation in the study for a minimum of 1 yr and a maximum of 10 yr. All EIA subjects demonstrated the presence of EIA during screening as indicated by a reduction in postexercise FEV_1 of greater than 10% (33). Each subject completed a health questionnaire and gave written informed consent to participate before enrollment in the study, which was approved by the Colorado State University Institution Review Board. Table 1 indicates that the two groups, EIA and control were well-matched according to age, physical characteristics and fitness level. Table 2 shows that subjects were using traditional short-acting or "rescue" medications and none were on maintenance medications.

Study design. The study was conducted as a randomized double-blind crossover trial over 5 consecutive weeks. A 1-wk washout period followed each treatment period. All subjects entered the study on their normal salt diet (NSD), after which they were randomly assigned to either the high salt diet (HSD) or low salt diet (LSD) for 2 wk. Thereupon, they followed a 1-wk washout on their NSD, followed by the alternative diet for the remaining 2 wk. All subjects were required to consume a base diet of 1500 mg·d^{-1} of sodium (~2250 mg·d^{-1} of chloride), whether on the LSD or HSD, which was provided by means of a menu plan. The base diet was supplemented during the HSD with ten 1-g salt capsules per day (4000 mg·d^{-1} of sodium, ~6,000 mg·d^{-1} of chloride). For the LSD, the base diet was supplemented in the same manner with placebo (sucrose) capsules. The contents of the capsules were unknown to the subjects and investigators. To monitor dietary compliance, 24-h urine collections for the determination of 24-h sodium excretion were made at the beginning of the study while on the NSD and at the end of each dietary period.

Protocol and measurements. Each subject was instructed to avoid any strenuous physical activity 24 h before the exercise test and to refrain from using therapeutic drugs before the exercise test. Initially, and at the end of each treatment period, the subjects underwent a standardized exercise challenge routinely used for the diagnosis of EIA (33). The exercise test protocol lasted approximately 10 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 (33) 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). Environmental conditions were 23°C and 50% relative humidity. At the end of the 5 min of steady-state exercise, the treadmill was elevated by 1% per minute until volitional fatigue to achieve a measure of peak exercise capacity. During the exercise, metabolic analyses of expired gases were accomplished by indirect open circuit calorimetry (SensorMedics 2900 Metabolic Cart, SensorMedics Corp., Yorba Linda, CA).

Pulmonary function was determined preexercise and at 1, 5, 10, and 15 min postexercise. Pulmonary function tests were performed using the SensorMedics' V_{max} 22 computerized spirometry. Subjects were required to perform three acceptable spirograms (forced vital capacity) according to the American Thoracic Society Standardization of Spirometry (1).

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, to verify complete collection of the 24-h urine samples.

Statistical analysis. Data were analyzed using the NCSS 2000 statistical software (NCSS, Kaysville, UT). The data were analyzed for cross-over effects and none were detected. A two-factor repeated-measures ANOVA was performed on the data with both treatment and time as "within-subject" effects. Where a significant F-ratio was found ($P < 0.05$), Fisher's protected least-significant-difference *post*

TABLE 2. Subject medications for EIA.

Subject	Medication
1	Terbutaline (Bricanyl)
2	Albuterol (Ventolin)
3	Albuterol (Ventolin)
4	Terbutaline (Bricanyl)
5	Albuterol (Ventolin)
6	Albuterol (Ventolin)
7	Terbutaline (Bricanyl)
8	Albuterol (Ventolin)

TABLE 3. Twenty-four–h urinary excretion of sodium, potassium, and creatinine (mg·d^{-1}).

Group	LSD	NSD	HSD
Control			
Sodium	1580 ± 173^a	3478 ± 425^b	10547 ± 1,868^c
Potassium	2561 ± 417	2405 ± 435	2213 ± 252
Creatinine	1174 ± 253	1485 ± 219	1821 ± 204
EIA			
Sodium	1335 ± 227^a	2414 ± 416^b	6750 ± 1159^d
Potassium	1802 ± 325	2362 ± 652	2973 ± 1410
Creatinine	1305 ± 136	1353 ± 102	1311 ± 99

Values are means ± SEM.
Letters $^{(a,b,c,d)}$ designate significance ($P<0.05$). For sodium, values with the same letter are not statistically different, differing letters show significance among values. There are no significant differences among potassium or creatinine values.

TABLE 4. Baseline pulmonary function.

	FVC (L)	FEV_1 (L)	FEV_1/FVC (%)	PEFR ($L \cdot s^{-1}$)
Control				
NSD	4.70 ± 0.26	3.92 ± 0.23	83 ± 2	7.61 ± 0.81
LSD	4.63 ± 0.30	3.87 ± 0.24	84 ± 3	8.37 ± 0.80
HSD	4.62 ± 0.26	3.71 ± 0.27	83 ± 2	8.8 ± 0.70
EIA				
NSD	4.09 ± 0.30	3.33 ± 0.18	82 ± 2	6.14 ± 0.63
LSD	4.13 ± 0.31	3.37 ± 0.21	82 ± 2	6.10 ± 0.66
HSD	3.92 ± 0.36	3.18 ± 0.25	82 ± 3	5.89 ± 0.74

Values are means ± SEM. FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; PEFR, peak expiratory flow rate; NSD, normal salt diet; LSD, low salt diet; HSD, high salt diet. There are no significant differences for any variable among diets or groups.

hoc test was applied to identify differences in group means ($P < 0.05$). Data are expressed as mean ± SEM.

RESULTS

Subject's diets were compliant, demonstrating sodium restriction on the LSD and sodium enhancement on HSD as indicated by the 24-h urinary excretions of sodium (Table 3). Neither potassium nor creatinine excretions were altered by the diets (Table 3).

Preexercise pulmonary function is shown in Table 4. Both control and EIA subjects had similar preexercise pulmonary function values. Preexercise, pulmonary function values were not altered by the diets in either group.

Postexercise pulmonary function values are presented in Tables 5 and 6. For control subjects (Table 5), there was no effect of either the exercise or the diets upon pulmonary function values postexercise. These results differed from EIA subjects (Table 6). EIA subjects experienced significant reductions in FVC, FEV_1, and PEFR postexercise on all diets at all postexercise times. FEV_1/FVC was reduced postexercise on occasion on all diets. Diet altered the postexercise change in pulmonary function in EIA subjects. For FVC, FEV_1, and PEFR, the postexercise values were highest on the LSD, less on the NSD, and less still on HSD. Diet did not alter FEV_1/FVC.

Figures 1 and 2 demonstrate the differential effect of dietary salt in control (Fig. 1) and EIA (Fig. 2) subjects on the percent change in FEV_1 pre- to post-exercise. Control subjects (Fig. 1) demonstrated no difference in the percent change in FEV_1 pre- to post-exercise on any diet. EIA subjects (Fig. 2) had a significant percent change in FEV_1 pre- to post-exercise with all three diets. There was a significant gradation of response from LSD to NSD to HSD. However, the minimum 10% reduction in FEV_1 was observed during all diets.

TABLE 5. Pulmonary function post exercise in control subjects.

	FVC (L)	FEV_1 (L)	FEV_1/FVC (%)	PEFR ($L \cdot s^{-1}$)
NSD				
1 min	4.55 ± 0.28	3.86 ± 0.22	85 ± 3	7.93 ± 0.78
5 min	4.64 ± 0.28	3.90 ± 0.21	85 ± 3	8.01 ± 0.77
10 min	4.65 ± 0.28	3.89 ± 0.23	84 ± 2	8.14 ± 0.78
15 min	4.71 ± 0.30	3.95 ± 0.26	84 ± 2	7.79 ± 0.74
LSD				
1 min	4.56 ± 0.30	3.90 ± 0.25	87 ± 3	8.41 ± 0.71
5 min	4.62 ± 0.33	3.94 ± 0.27	86 ± 3	8.50 ± 0.71
10 min	4.60 ± 0.33	3.97 ± 0.28	85 ± 3	8.46 ± 0.72
15 min	4.73 ± 0.33	3.99 ± 0.28	85 ± 3	8.59 ± 0.74
HSD				
1 min	4.54 ± 0.28	3.80 ± 0.25	84 ± 3	8.58 ± 0.68
5 min	4.52 ± 0.29	3.78 ± 0.25	84 ± 3	8.38 ± 0.74
10 min	4.58 ± 0.29	3.70 ± 0.29	81 ± 4	8.55 ± 0.76
15 min	4.56 ± 0.30	3.68 ± 0.29	81 ± 4	8.44 ± 0.79

Values are means ± SEM. There were no significant differences in control subjects for postexercise values by time or diet.

TABLE 6. Pulmonary function postexercise in EIA subjects.

	FVC (L)	FEV_1 (L)	FEV_1/FVC (%)	PEFR (L/s)
NSD				
1 min	$3.72 \pm 0.37^{*a}$	$2.99 \pm 0.30^{*a,b}$	81 ± 3^{a}	$5.39 \pm 0.78^{*a,b}$
5 min	$3.71 \pm 0.36^{*c}$	$2.76 \pm 0.29^{*c}$	$74 \pm 3^{*a}$	$4.94 \pm 0.81^{*b}$
10 min	$3.72 \pm 0.37^{*c}$	$2.76 \pm 0.29^{*c}$	$74 \pm 3^{*a}$	$4.90 \pm 0.81^{*c}$
15 min	$3.63 \pm 0.38^{*c}$	$2.65 \pm 0.33^{*c}$	$72 \pm 3^{*a}$	$4.68 \pm 0.83^{*b}$
LSD				
1 min	$3.86 \pm 0.35^{*a}$	$3.14 \pm 0.27^{*a}$	82 ± 3^{a}	$5.62 \pm 0.72^{*a}$
5 min	$3.86 \pm 0.38^{*a}$	$3.03 \pm 0.29^{*a}$	80 ± 3^{a}	$5.49 \pm 0.74^{*a}$
10 min	$3.92 \pm 0.38^{*a}$	$2.99 \pm 0.28^{*a}$	76 ± 3^{a}	$5.26 \pm 0.78^{*a}$
15 min	$3.88 \pm 0.38^{*a}$	$2.90 \pm 0.31^{*a}$	$75 \pm 3^{*a}$	$5.17 \pm 0.82^{*a}$
HSD				
1 min	$3.51 \pm 0.39^{*b}$	$2.85 \pm 0.29^{*b}$	82 ± 3^{a}	$5.22 \pm 0.77^{*b}$
5 min	$3.38 \pm 0.42^{*b}$	$2.57 \pm 0.32^{*b}$	77 ± 4^{a}	$4.79 \pm 0.80^{*b}$
10 min	$3.31 \pm 0.43^{*b}$	$2.51 \pm 0.31^{*b}$	77 ± 3^{a}	$4.52 \pm 0.83^{*b}$
15 min	$3.19 \pm 0.41^{*b}$	$2.42 \pm 0.33^{*b}$	$76 \pm 4^{*a}$	$4.40 \pm 0.84^{*b}$

Values are means ± SEM.
* $P < 0.05$ compared with respective pre-exercise value.
Letters^{a,b,c} refer to comparisons by diet for the postexercise time period within specific variable; different letters designate significant difference.

DISCUSSION

This study has shown for the first time that 2 wk of altering dietary intake of salt (sodium chloride) can alter the pulmonary function of those with EIA. Lowering dietary salt intake improved postexercise pulmonary function, and increasing dietary salt intake worsened postexercise pulmonary function in EIA subjects. Restricting salt intake did not, however, normalize postexercise pulmonary function.

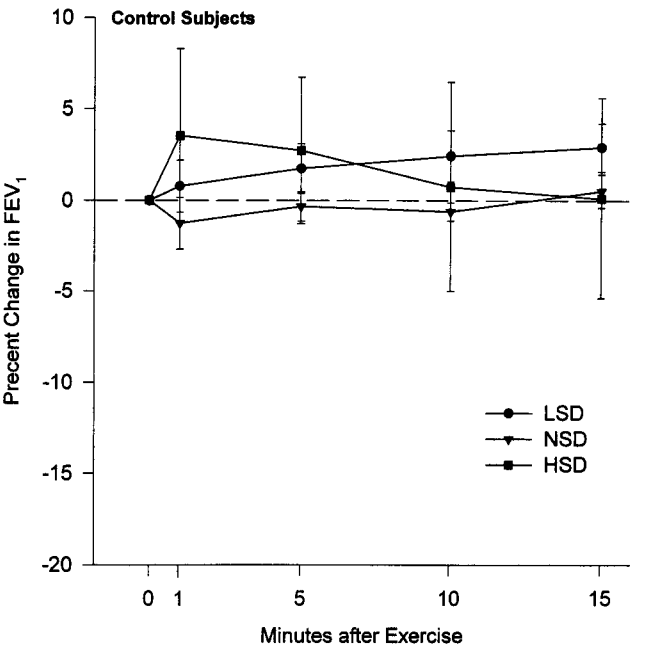

Figure 1—The percent change in FEV_1 from pre- to post-exercise in subjects without asthma (control) across the three diets.

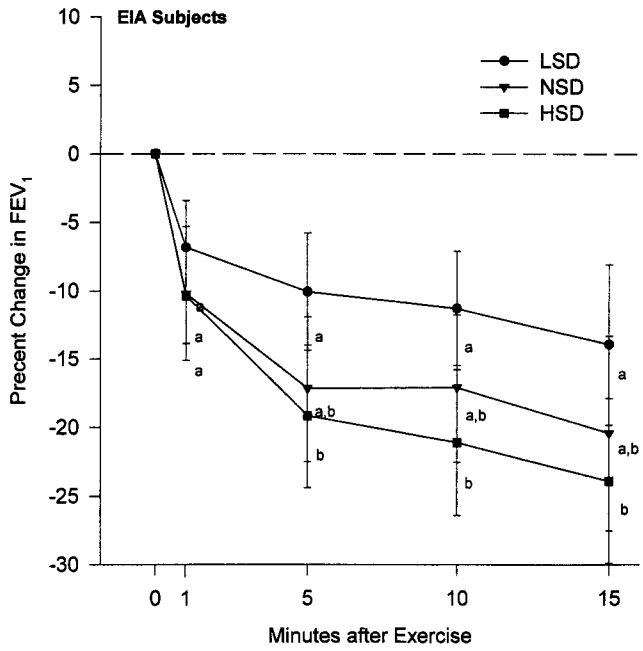

Figure 2—The percent change in FEV_1 from pre- to post-exercise in subjects with exercise-induced asthma (EIA) across the three diets.

Dietary goals were achieved as sodium excretions fell significantly while on the LSD and rose significantly while on the LSD. These changes in sodium excretion occurred without a change in potassium excretion or glomerular filtration rate (creatinine excretion). Thus, a graded dose of dietary sodium was accomplished in this study from approximately 1300–1500 $mg \cdot d^{-1}$ (~2166–2250 $mg \cdot d^{-1}$ chloride) to 6,000–10,000 $mg \cdot d^{-1}$ (~10,000–16,667 $mg \cdot d^{-1}$ of chloride).

Several investigators have demonstrated the possible influence of dietary salt on the severity of asthma (4–8,27,31). However, this report is the first study demonstrating the potential influence of dietary salt on the symptoms of EIA after exercise. The mechanism of EIA itself has not been determined (33), and (12,24) the mechanism by which dietary salt may influence EIA is unknown. However, studies involving subjects with asthma have attempted to uncover a possible mechanism by which dietary salt might alter the severity of asthma. For example, sodium transport across smooth muscle cells has been implicated in the regulation of airway smooth muscle tone (32). Additionally, studies involving dietary salt and bronchial reactivity have suggested that elevated dietary salt may increase bronchial reactivity (7,8,31). However, not all studies have demonstrated this potential relationship between dietary salt and bronchial reactivity (3,10,21).

There are several possibilities to explain the effect of dietary salt on the severity of EIA. Recently, Tribe et al. (32) evaluated dietary salt intake and airway responsiveness to methacholine in subjects with asthma. Their results suggested that a serum-borne factor found in subjects with asthma caused an increase in cell membrane permeability, thereby stimulating sodium influx into cells. Dietary salt would further increase this influx. Possibly, the increased transcellular flux of sodium alters intracellular calcium concentrations, thus, increasing smooth muscle contractility, as well as enhancing release of inflammatory mediators (9,11,28). Dietary salt may alter the release of histamine by altering intracellular calcium, via inhibition of the sodium-calcium exchanger, resulting in histamine release (29). It is also conceivable that elevated dietary salt may mediate the release of eicosanoids from cells in the airways, such as mast cells, eosinophils, granulocytes, basophils, macrophages, and epithelial cells (25,36). However, the role of dietary salt in influencing these potential mediators of the inflammatory response in humans with EIA remains to be established.

In addition to these possible effects of dietary salt, the influence of dietary salt on circulating blood volume and, consequently, on hemodynamics and pulmonary function cannot be ruled out as another possibility. Finally, because EIA may be a vascular phenomenon and the result of mucosal edema (23), dietary salt could act via alterations in the formation of mucosal edema.

Although the focus of most investigations has been on sodium, salt contains both sodium and chloride. It may be that the anion, chloride, plays a significant role in the influence of salt on asthma and EIA. In hypertension research, there have been several reports that implicate the chloride ion as the major contributor to elevated blood pressures during salt loading (17–20,30,35,37). For example, Kurtz et al. (18) substituted sodium citrate for sodium chloride in diets of five hypertensive men. Sodium chloride elevated blood pressure whereas sodium citrate did not. Shore et al. (30) performed a similar study in six hypertensive men but substituted sodium phosphate for sodium chloride. Blood pressures increased on sodium chloride but not on sodium phosphate. Medici et al. (26) did examine the potential role of chloride in asthma. They placed 14 subjects with asthma on high sodium chloride diets or high sodium citrate diets. Salt loading regardless of type worsened symptoms of asthma and increased the use of inhaled steroids. They suggested that sodium is the mediator of the effect of salt on subjects with asthma. Whether sodium or chloride is the main contributor to the alterations in EIA observed within the current study is not known.

In conclusion, elevating dietary salt intake worsened and lowering dietary salt intake improved postexercise pulmonary function in subjects with EIA. Restricting dietary salt intake did not normalize pulmonary function in these subjects. It is likely that dietary salt is not a cause of EIA but is a modifier of underlying mechanisms and enhances the effects of exercise on pulmonary function in those with EIA. Whether sodium or chloride is most important in this effect is not known.

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Address for correspondence: Robert W. Gotshall, Ph.D., Professor, Colorado State University, Health and Exercise Science, 214 Moby Complex, Fort Collins, CO 80523-1582; E-mail: gotshall@cahs.colostate.edu.

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