Eur Respir J, 1993, 6; 517–522
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European Respiratory Journal
ISSN 0903 - 1936

Respiratory symptoms and bronchial responsiveness are related to dietary salt intake and urinary potassium excretion in male children

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ABSTRACT: To investigate whether dietary salt intake and urinary sodium and potassium levels are related to respiratory symptoms and bronchial responsiveness, a cross-sectional study among 2593 subjects aged 9 to 16 was conducted in four communities of the Latium region (Italy).

Questionnaires were administered to the parents, urine samples were collected, lung function, methacholine challenge tests and prick tests were performed. Information about familial and personal dietary salt use and respiratory health was collected from the parents of 2439 (94%) subjects. A total of 2020 methacholine challenge tests and 916 urinary sodium and potassium levels were available for analysis. Personal table salt use was strongly related to cough and phlegm apart from colds (adjusted odds ratios, OR, 1.87, 95% confidence intervals, CI, 1.20–2.90), wheezing apart from colds (OR, 2.19, 95% CI, 1.27–3.77), wheezing with dyspnoea (OR, 1.45, 95% CI, 0.98–2.12) and wheezing after exercise (OR, 2.16, 95% CI, 1.35–3.44). These associations were mainly found in boys. Use of familial table salt and canned food showed no relation to respiratory symptoms. Increased bronchial responsiveness was associated with a higher urinary potassium excretion in boys, but not with urinary sodium.

In conclusion, personal table salt use is related to an increased prevalence of bronchial symptoms; an increase in bronchial responsiveness among those with higher potassium excretion also seems to be implied. Although it is difficult to interpret the results of this study in causal terms, the findings might be relevant to the distribution of bronchial symptoms and diseases in the population.
Eur Respir J, 1993, 6, 517–522.

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Keywords: Asthma
bronchial responsiveness
children
potassium excretion
salt intake
sodium excretion

Received: June 26 1992
Accepted after revision December 14 1992

A possible relationship between dietary salt intake and asthma morbidity has recently been suggested. Burney *et al* [1] observed that asthma mortality in adults and children in England was closely correlated with sales of table salt. Schwartz and Weiss [2] found a positive association of reported bronchitis and wheezing with dietary potassium intake and with the sodium/potassium ratio in foods among adults in the Second National Health and Nutrition Examination Survey (NHANES II). Two cross-sectional studies of male adults in the U.K. and the U.S.A. analyzed the relationship between levels of sodium and potassium in the urine, and bronchial reactivity. Airway hyperresponsiveness to histamine was found to be positively associated with 24-hour urine sodium excretion [3]; methacholine hyperresponsiveness, on the other hand, was associated with 24-hour urine potassium excretion but not with sodium excretion [4]. A link between the level of bronchial responsiveness and recent sodium intake was further suggested by two experimental studies on subjects suffering from bronchial asthma [5, 6]; in one study [5], however, the association between increase in bronchial reactivity and high salt intake was found in asthmatic men but not women. Moreover, an experimental increase of sodium intake was associated with a worsening of symptoms and lung function in asthmatics [7].

The evidence supporting an etiological role for dietary salt use in the occurrence of respiratory disease can be regarded as incomplete. No population study has directly investigated the use of salt in foods in relation to respiratory symptoms and bronchial reactivity; moreover, the association between urinary electrolyte excretion and bronchial responsiveness has only been reported in male adults. The aim of the present investigation was therefore to evaluate further the association of some dietary habits and urinary sodium and potassium levels with various respiratory conditions, in a population of children and adolescents.

Materials and methods

The second survey on respiratory health in the Latium region of Italy was specifically designed to evaluate the role of environmental factors in the occurrence of asthma and in changes in lung function and bronchial reactivity. A population of school children and adolescents, who had participated in the first survey in 1987 [8–10], were the target of a second cross-sectional study conducted in 1990–1991. Children attending the fifth grade of primary school in Civitavecchia (four schools) and in small rural communities of the Viterbo province (Canino, Tuscania, Montalto di Castro) (three schools) were selected for the study; in addition, all adolescents attending the nearby secondary schools (three in Civitavecchia and three in the Viterbo province) were also invited to participate. In all, the target sample was 2593 subjects.

The methods used to assess respiratory symptoms [8], lung function [9], bronchial reactivity and atopy [10] in the first survey have already been reported, and were applied in this study as well. Briefly, the parents were asked to complete a self-administered questionnaire adapted from the American Thoracic Society children's questionnaire [11], as well as to give written consent for a clinical examination. A physical examination was performed in order to exclude children in whom spirometry was contraindicated or not feasible; a baseline pulmonary function test (water-filled spirometer manufactured by Biomedin, Padua, Italy) was performed by all others. Only children with forced expiratory volume in one second (FEV_1) >80% of the predicted value or with an FEV_1/forced vital capacity (FVC) ratio >70% performed the methacholine challenge test. This test consisted of two-minute tidal volume breathing of aerosols delivered by a 646 DeVilbiss nebulizer. Phosphate-buffered saline solution was inhaled first, followed by concentrations of methacholine increasing by a multiple of four (from 0.06 to 64 $mg \cdot ml^{-1}$), corresponding to an estimated final dose of 97.9 μmol. The change in FEV_1 from the post-saline value was measured at 30 and 90 s after each inhalation. Inhalations were continued until the FEV_1 had fallen ≥20%, or the last concentration of methacholine had been administered. Subjects with a >10% fall in FEV_1 after the saline solution were not challenged with methacholine.

The drug concentration causing a 20% decline in FEV_1 ($PC_{20}FEV_1$) was calculated by interpolation from the log concentration-response curve. The children were then divided into "non-responders" ($PC_{20}FEV_1$ >64 $mg \cdot ml^{-1}$) and "responders" ($PC_{20}FEV_1$ ≤64 $mg \cdot ml^{-1}$), the latter including a subgroup of "strong responders" ($PC_{20}FEV_1$ ≤4.0 $mg \cdot ml^{-1}$), whose results were also analyzed separately.

Atopic status was evaluated by prick testing with eight allergen extracts, and also by using histamine and diluent as positive and negative controls [12]. A wheal size greater than 4 mm^2 was considered a positive result and such subjects were considered atopic.

A short questionnaire was administered to the subject's parents asking about discretionary salt use: familial table salt use ("In your family, besides adding salt to foods during their preparation, do you usually salt foods also at the table?"), as well as use of table salt by the subject under study ("Does he/she usually salt food at the table before and/or after tasting the food?") were investigated. Two questions regarding familial use of canned foods and stock cubes (sodium glutamate) ("How often do you use canned food?", " How often do you use stock cubes?") were also added, since they could indicate a preference for sodium-rich foods [13, 14]. For the present analysis, familial and personal table salt use were yes or no variables, while canned food and stock cube use were dichotomized (twice per week or more *vs* less than twice per week).

The subjects were invited to collect an untimed sample of early morning urine before the clinical examination. Urinary concentrations of sodium, potassium and creatinine were measured with a Beckman Astra analyzer (diagnostic kits, Beckman Instruments, Brea, CA). Sodium and potassium levels were determined with ion-selective electrodes; urinary creatinine level was determined colorimetrically, based on the reaction between creatinine and sodium picrate.

The association of selected dietary practices with cough or phlegm apart from colds and with wheezing symptoms was studied, using logistic regression. Adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) were computed, controlling for several potential predictors of respiratory health: sex, age, father's education (as indicator of socioeconomic status), parental smoking, familial asthma (asthma in parents or in siblings) and atopy.

Bronchial responsiveness was considered as a categorical variable, and the relation to dietary practices and to urinary sodium and potassium (quartiles of the sodium creatinine and of the potassium creatinine ratios) was evaluated comparing "all responders" as well as "strong responders" with "non-responders", controlling for sex, age, father's education, parental smoking, familial asthma, atopic status, and, alternately, sodium/creatinine or potassium/creatinine. An indicator of the baseline airways calibre (FEV_1/FVC) was also considered in the logistic regression. Previous observations have suggested that the association between sodium intake and respiratory health might be different in males and females [5]; furthermore, it could be speculated that symptomatic subjects (*e.g.* atopic subjects) might experience worsening of bronchial responsiveness as a result of increased salt intake. Therefore, possible modifying effects of sex and atopic status on the relationship between dietary habits and respiratory symptoms as well as between bronchial responsiveness and urinary electrolytes were evaluated by introducing interaction terms into the logistic models.

Results

Table 1 shows the response rates obtained during the survey together with the prevalence rates of selected variables. Data from a total of 2439 (94% of the target) questionnaires and 2020 methacholine challenges, were available for the analysis. A total of 2126 urine samples was collected; however, for the present study, urinary sodium and potassium were analyzed in 916 urine samples collected from children attending elementary school and the third year of secondary school (86.8% response rate). Table 2 shows the prevalence of respiratory symptoms, atopy and bronchial reactivity in the whole sample. Subjects whose urine was analyzed were comparable to those whose urine was not for all investigated factors except age: sex (males: 51.7% *vs* 52.0%), father's education (<6 years: 35.7% *vs* 32.3%), familial asthma (9.4% *vs* 9.6%), and atopy (30% *vs* 27.0%). The age difference (means: 13 *vs* 12 years) was a result of the sampling design.

Table 1. – Distribution of selected characteristics of children and adolescents surveyed in Latium, Italy, 1990–91

	n	%
Response to questionnaire	2439	100
Prick tests	2210	90.6
Methacholine challenge	2020	82.8
Male sex	1265	51.9
Age years:		
9–10	346	14.2
11–12	1214	49.8
13–14	839	34.4
15–16	40	1.6
Mean 12.5±1.2 (SD) years		
Father's education:		
<6 years	819	33.6
6 to 8 years	844	34.6
>8 years	722	29.6
Parental smoking:		
nonsmokers	847	34.7
mother only	260	10.7
father only	714	29.3
both smokers	538	22.1
Table salt use in the family:		
no	2040	83.6
yes	377	15.5
Stock cubes in cooking:		
<2 a week	2134	87.5
≥2 a week	129	5.3
Canned food use in the family:		
<2 a week	2269	93.0
≥2 a week	121	5.0
Personal table salt use:		
no	2073	85.0
yes	342	14.0
Urinary levels (n=916)		
Sodium, $mEq \cdot l^{-1}$, mean (±SD)	150.6 (62.3)	
Potassium, $mEq \cdot l^{-1}$, mean (±SD)	38.5 (21.4)	
Creatinine, $mg \cdot dl^{-1}$, mean (±SD)	151.6 (58.3)	

Totals may vary because of missing values.

Table 2. – Prevalence of respiratory disorders, atopic status and bronchial reactivity among children and adolescents surveyed in Latium, Italy, 1990–91

	n	%
Familial asthma	231	9.5
Cough or phlegm	140	5.7
Wheezing apart from colds	79	3.2
Wheezing with dyspnoea	207	8.5
Wheezing after exercise	104	4.3
Reactors to prick test	624	28.2
Bronchial responsiveness:		
Non-responders to methacholine	1253	62.0
Responders to methacholine	767	38.0
PC_{20} FEV_1 $mg \cdot ml^{-1}$		
≤1.0	124	6.1
1.01–4.0	127	6.3
4.01–16.0	221	10.9
16.01–64.0	295	14.6

Familial table salt use and canned food use bore no relation to respiratory symptoms (table 3). The frequent use of stock cubes was associated only with cough or phlegm. Personal table salt use was strongly related to cough or phlegm apart from colds (OR, 1.87, 95% CI, 1.20–2.90) and to wheezing symptoms: wheezing apart from colds (OR, 2.19, 95% CI, 1.27–3.77), wheezing with dyspnoea (OR, 1.45, 95% CI, 0.98–2.12) and wheezing after exercise (OR, 2.16, 95% CI, 1.35–3.44). All associations with personal table salt use were, however, stronger among boys, whereas no statistically significant increased odds ratio was found in girls (table 4). No effect modification by atopic status was detected.

None of the variables indicating dietary practices were related to an increased bronchial responsiveness (data not shown). When urinary electrolytes were considered in relation to reactivity to methacholine (table 5), there was no association with the sodium creatinine ratio for either "all-responders" or "strong responders". Apart from random variability, no differences in the risk estimates were found between boys and girls or between atopic and non-atopic subjects.

A statistically significant increase of "all-responders" to methacholine was found with quartiles of the potassium creatinine ratio (table 5); odds ratios equal to 1.89 (95% CI=1.19–3.02) and to 1.79 (95% CI= 1.09–2.96) were estimated for the third and the fourth quartile respectively, compared with the first quartile. No excess was found for "strong responders" with increasing potassium concentration. The results were essentially similar when the potassium creatinine ratio was treated in tertiles or in quintiles (data not shown).

When interaction terms for atopic status were included in the logistic models examining the relationship between bronchial hyperresponsiveness and potassium excretion, no effect modification was observed. When we evaluated differences by sex, we found that the association between potassium concentration and being a "responder" or a "strong responder" to methacholine was present exclusively in boys (table 6).

Table 3. – Association between dietary practices and respiratory symptoms. Latium, Italy, 1990–91

	Familial use				Personal use			
	Table salt		Stock cubes per week		Canned foods per week		Table salt	
	No	Yes	<2	≥2	<2	≥2	No	Yes
Total n	2040	377	2134	129	2269	121	2073	342
Cough or phlegm:								
n	113	25	112	17	128	9	103	30
Adjusted OR	1.0	1.25	1.0	2.75	1.0	1.37	1.0	1.87
95% CI		(0.79–1.96)		(1.58–4.78)		(0.67–2.79)		(1.20–2.90)
Wheezing apart from colds:								
n	63	16	69	6	72	7	59	20
Adjusted OR	1.0	1.44	1.0	1.48	1.0	1.95	1.0	2.19
95% CI		(0.81–2.56)		(0.62–3.56)		(0.86–4.46)		(1.27–3.77)
Wheezing with dyspnoea:								
n	168	37	174	13	183	14	166	40
Adjusted OR	1.0	1.26	1.0	1.23	1.0	1.68	1.0	1.45
95% CI		(0.85–1.85)		(0.67–2.27)		(0.92–3.07)		(0.98–2.12)
Wheezing after exercise:								
n	83	21	86	8	92	8	77	27
Adjusted OR	1.0	1.38	1.0	1.53	1.0	1.68	1.0	2.16
95% CI		(0.84–2.28)		(0.72–3.28)		(0.78–3.62)		(1.35–3.44)

Adjusted Odds Ratios (ORs) and 95% confidence intervals (95% CI) were computed controlling for sex, age, father's education, parental smoking, familial asthma and atopy.

Table 4. – Association between personal table salt use and respiratory symptoms by sex. Latium, Italy, 1990–91

	Males		Females	
	Table salt use		Table salt use	
	No	Yes	No	Yes
Total n	1073	179	1000	163
Cough or phlegm:				
n	57	20	46	10
Adjusted OR	1.0	2.20	1.0	1.47
95% CI		(1.26–3.85)		(0.72–3.0)
Wheezing apart from colds:				
n	40	16	19	4
Adjusted OR	1.0	2.71	1.0	1.26
95% CI		(1.44–5.10)		(0.42–3.82)
Wheezing with dyspnoea:				
n	110	29	56	11
Adjusted OR	1.0	1.60	1.0	1.17
95% CI		(1.0–2.56)		(0.59–2.32)
Wheezing after exercise:				
n	42	18	35	9
Adjusted OR	1.0	2.67	1.0	1.56
95% CI		(1.48–4.84)		(0.73–3.73)

Adjusted Odds Ratios (ORs) and 95% confidence intervals (95% CIs) were computed controlling for age, father's education, parental smoking, familial asthma and atopy.

Table 5. – Association of bronchial responsiveness (all responders and strong responders *versus* non-responders) with urinary concentrations of sodium and potassium. Latium, Italy, 1990–91

Variable	Non-responders	All responders			Strong responders		
	n	n	OR	95% CI	n	OR	95% CI
Sodium/Creatinine n=763							
Quartile:							
I	127	63	Referent category		21	Referent category	
II	125	72	1.21	(0.77–1.91)	23	1.15	(0.58–2.29)
III	110	80	1.23	(0.77–1.95)	28	1.42	(0.72–2.81)
IV	122	64	0.76	(0.46–1.26)	25	0.94	(0.45–1.96)
Potassium/Creatinine n=763							
Quartile:							
I	137	57	Referent category		21	Referent category	
II	120	70	1.55	(0.97–2.47)	25	1.43	(0.72–2.80)
III	112	78	1.89	(1.18–3.02)	25	1.37	(0.68–2.74)
IV	115	74	1.79	(1.09–2.95)	26	1.48	(0.72–3.05)

Adjusted Odds Ratios (ORs) and 95% confidence intervals (95% CIs) from logistic regression including the following variables: sex, age, father's education, parental smoking, familial asthma, atopy, FEV_1/FVC. All responders: PC_{20} ≤64.0 mg·ml^{-1}; Strong responders: PC_{20} ≤4.0 mg·ml^{-1}; Non-responders: PC_{20} >64.0 mg·ml^{-1}. For the referent category the OR is 1.00.

Table 6. – Association of bronchial responsiveness (all responders and strong responders *versus* non-responders) with quartiles of urinary potassium/creatinine by sex. Latium, Italy, 1990–91

Variable		Non-responders	All responders			Strong responders		
		n	n	OR	95% CI	n	OR	95% CI
Males	n=394							
Quartile:								
I		77	28	Referent category		8	Referent category	
II		67	34	1.74	(0.89–3.39)	13	2.28	(0.81–6.37)
III		50	40	2.76	(1.40–5.40)	12	2.65	(0.91–7.69)
IV		58	40	2.60	(1.28–5.28)	15	2.68	(0.90–7.95)
Females	n=369							
Quartile:								
I		60	29	Referent category		13	Referent category	
II		53	36	1.39	(0.73–2.68)	12	0.99	(0.39–2.46)
III		62	38	1.34	(0.70–2.55)	13	0.82	(0.32–2.06)
IV		57	34	1.27	(0.65–2.48)	11	0.93	(0.36–2.39)

Adjusted Odds Ratios (ORs) and 95% confidence intervals (95% CIs) from logistic regression including the following variables: age, father's education, parental smoking, familial asthma, atopy, FEV_1/FVC. For definition of responder groups and of referent category see legend to table 5.

Discussion

This study shows that among males: i) table salt use is associated with an increased prevalence of respiratory symptoms such as cough, phlegm and wheezing; ii) an increased bronchial responsiveness to methacholine seems to be related to a higher urinary potassium excretion.

The assessment of respiratory symptoms, atopy and bronchial responsiveness was made using standardized methods. Dietary habits were assessed by means of four simple questions. The use of table salt at meal time, particularly when salting of food occurs even before tasting it, is a good indicator of a diet rich in sodium, which is independent of more specific preferences in diet composition [14]. We addressed this problem by investigating family and individual habits. The question of canned food consumption had previously been considered in epidemiological studies [13]. We also investigated the use of stock cubes, which are rather popular in our country, because it can be an indicator of a dietary tendency to increase the natural flavour of foods [13].

Discretionary salt use has been assessed by means of a questionnaire in other surveys [13, 14]; however, we have no data about the validity or reproducibility of our questions. Given the known difficulties in the assessment of dietary habits, a random misclassification of the actual salt use is likely to have occurred. Such a misclassification, however, tends to bias the risk estimates towards the null and does not justify positive results. With regard to non-random misclassification, the findings that asthma or bronchitis related symptoms are consistently more prevalent only among those who use table salt, and that no consistent association has been found for the three other dietary variables, suggest that information bias can be excluded as an explanation of our results.

The sodium and potassium levels in an untimed early morning sample of urine are clearly a rough approximation of the recent intake of table salt. The use of these indicators is mainly based on the assumption of a steady-state condition. However, there is a diurnal variation in sodium excretion which is not present for creatinine excretion. A 24 hour urine collection has been used by other authors as a possible solution [3, 4]; however, one 24 hour urine collection does not provide a precise estimate of sodium intake either: multiple 24 hour urine specimens are usually needed for a valid assessment [15]. We used untimed samples for obvious practical reasons; furthermore, we could not be certain of collecting 24-hour urine specimens from a large sample of subjects (with a reasonable response rate) without introducing a large and uncontrolled inaccuracy in collection.

We designed the study to explore more fully the hypothesis of a role for salt intake in respiratory health. However, the cross-sectional design of the investigation, cannot take account of the time sequence or provide clear explanations for the biological mechanisms underlying the associations which we found.

Personal table salt use was associated with respiratory symptoms but not with an increased bronchial responsiveness. The apparent discrepancy can be interpreted as corresponding to the only partial overlap between bronchial responsiveness and respiratory symptoms described in other cross-sectional studies [16].

Potassium excretion seemed to be related to an increased bronchial responsiveness in boys in our study, as well as in male adults in the U.S.A. [4]. The mechanism underlying this association, and also the sex difference, are difficult to explain in etiological terms. Potassium excretion is related to age and body mass and its homeostasis is controlled by the adrenergic system [17]. Potassium homeostasis has been found to be modified in asthmatic subjects [18] probably because of an impaired adrenergic control [19]. Potassium channels also play a key role in smooth muscle contraction in airways [20]. Therefore, a link between potassium control, the adrenergic nervous system and bronchial responsiveness could be suggested, but the relationship of dietary potassium intake, as reflected in urinary potassium excretion, to bronchial reactivity remains uncertain.

Previous positive studies of the relationship between sodium intake and bronchial responsiveness have been conducted on samples artificially weighted with asthmatic subjects [3, 5, 6] and, therefore, are not comparable with our study population. Curiously, the only study that deliberately excluded asthmatic patients [4] found bronchial responsiveness to be related to potassium excretion and not to sodium excretion. In addition, positive findings from the literature are exclusively confined to of males [3–5]; no epidemiological data are available on females. A British experimental study has shown that increased salt intake is related to bronchial reactivity but only among males [6]. Our findings, therefore, seem to suggest that dietary salt intake and electrolyte excretion are related to respiratory health differently according to sex. Indeed, respiratory physiology and several clinical aspects of pulmonary diseases are known to be sex-related [21].

In conclusion, it seems that personal table salt use is related to an increased prevalence of bronchial symptoms in males; also, bronchial responsiveness appears to increase with higher potassium excretion in males. The results, however, are difficult to interpret in causal terms. The relevance of these findings to the distribution of bronchial symptoms and diseases in the population seems to merit further investigation.

Acknowledgements: The second survey of asthma in the Latium region was partly supported by the CNR-ENEL Project - Interactions of energy production with human health and environment, Italy 1990.

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