

Short communication

Eccrine sweat response in children with asthma

Background: Even though there is a general conviction among parents of asthmatic children and pediatricians that asthmatic children sweat more than healthy ones, this has not been formally tested.

Aim: To determine sweating response and factors affecting this response in children with asthma and compare these findings with healthy children.

Method: Eighty-two children with asthma and 51 healthy controls aged 6–18 years were enrolled in the study. Transepidermal water loss (TEWL) was measured on palmar, volar, forehead, and back surfaces before and after exercise and was expressed as the difference between the measurements recorded before and after exercise.

Results: Transepidermal water loss measurements (after exercise – resting) on the palmar surface were higher in children with asthma [22.8 g/m² h (15–34.3)] compared with healthy children [15.2 g/m² h (6–22.2)] ($P < 0.001$). However, a gender stratified analysis showed that the TEWL measurements were higher on all surfaces only in boys but not in girls. Within the group of asthmatic children, TEWL measurements on the volar surface and back were lower in patients using anti-inflammatory therapy compared with those who were on as needed bronchodilator therapy only.

Conclusion: Our results show that asthma is associated with a higher rate of sweating response to exercise in boys, and anti-inflammatory treatment decreases the amount of sweating. The relationship of eccrine sweating with muscarinic receptor response and methacholine hyperresponsiveness remains to be determined.

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Eccrine sweating is the physiologic response to increased body temperature during exercise or thermal stress (1). Eccrine glands are innervated by sympathetic nervous system, but the effector functions are mediated by acetylcholine and muscarinic receptors. This system may be useful in evaluating the cholinergic responsiveness to exercise in asthma.

In our clinic, we have observed that the parents of children with asthma consistently complain of excessive sweating. Supporting this observation, Trochtenberg and BeLue (2) reported sweating as one of the common complaints of asthma among adult African-American asthmatics. In 1976, Kaliner (3) reported increased sensitivity and increased production of sweat by allergic adults in response to acetyl-beta-methylcholine.

These studies and our observations suggest that increased sweating may be associated with allergies and/or asthma. This relationship has not been formally investigated under physiologic conditions and it is largely unknown whether allergies and asthma are associated with increased sweating following exercise. Therefore, we quantitatively measured sweating from various parts of the skin after exercise in asthmatic children and healthy controls and investigated its

determinants including age, gender, atopy, anti-inflammatory medications, IgE, eosinophil counts, and pulmonary functions.

Methods

Study population

Children with asthma aged 6–18 years were recruited from the Pediatric Allergy and Asthma Unit of Hacettepe Children's Hospital, Ankara. Asthma was diagnosed according to the international guidelines as previously described (4). The healthy control group consisted of children without a history of asthma or significant chronic diseases with normal physical examination and lung function tests (4).

Children with asthma exacerbations or infections within the last 4 weeks, and those with dermatological diseases were excluded from the study. Skin testing was carried out according to standard methods (4).

Measurement of transepidermal water loss (TEWL)

All measurements were carried out on normal looking skin in a quite room after 20 min of rest. TEWL was measured with DermaLab[®] probe (Cortex Technology, Hadsund, Denmark) (5)

on palmar, volar, mid-forehead, and back. The reading was made 60 s after the probe had been placed and the measurement stabilized with a SD of 0.3 g/m² h. The median air temperature was 20°C (interquartile range 20–22) and relative humidity was 30% (interquartile range 28–30%). After baseline measurement, children ran on a treadmill for 6 min in a graded fashion until the heart rate reached 80% of the age predicted maximum. After the exercise, TEWL was measured again on the same four surfaces.

The magnitude of sweating was calculated as the difference between the measurements before and after exercise and expressed as g/m² h.

Study measurements

Spirometry (2130Spirometer, Sensor Medics Co., CA, USA) and IgE measurements (Uni-Cap, Pharmacia, Kalamazoo, MI, USA) were carried out with standard procedures.

All study procedures were approved by the Ethics Committee of Hacettepe University. All parents provided written informed consent.

Statistical analyses

Statistical analyses were carried out using spss 15 package program (SPSS, Inc, Chicago, IL, USA). Differences between the groups were compared by Student's *t*- or Mann–Whitney *U*-test as appropriate. Logistic regression analysis was performed to establish the factors that were associated with the TEWL. We treated TEWL as a dichotomous variable using a median split because various transformation techniques failed to normalize the TEWL levels. A *P*-value <0.05 was considered significant.

Results

The characteristics of the subjects are summarized in Table 1. There were four children in the control group with positive skin tests. As these children were already enrolled in another study, they refused to participate in the current one. Therefore, all children in the healthy group were nonatopic.

Table 1. Characteristics of the study population

	Asthma (<i>n</i> = 82)	Controls (<i>n</i> = 51)	<i>P</i>
Age	10.9 ± 2.8	11.8 ± 2.7	>0.05*
Gender			
Male	55 (60.7)	24 (47)	0.022†
Female	27 (39.3)	27 (53)	
Atopy (%)	54 (65.9)	0	<0.001
IgE (kU/l)	117 (40.25–324.5)	34 (18–77)	<0.001‡
Eosinophils (/mm ³)	239 (132.25–397.75)	146 (106.75–225.75)	0.002‡
FEV1, % predicted	97 (88–105)	99 (93–110)	0.094‡
Family history for atopic disease (%)	40 (48.8)	9 (17.6)	<0.001†

*By Student *t*-test.

†By Chi-square.

‡By Mann–Whitney *U*-test.

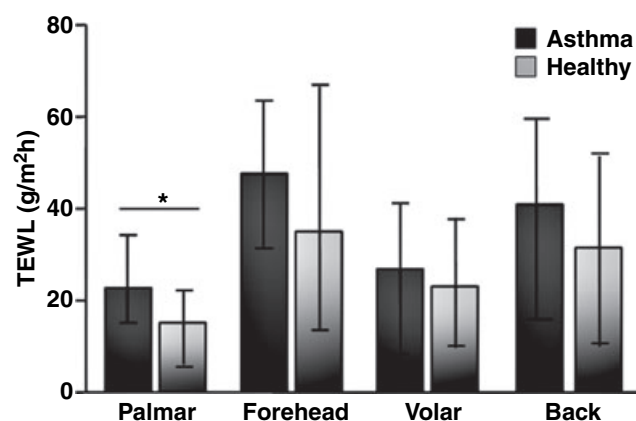


Figure 1. Comparison of transepidermal water loss (TEWL) between asthmatic patients and healthy controls (**P* < 0.05).

TEWL measurements

Transepidermal water loss measurements on the palmar surface were higher in children with asthma [22.8 g/m² h (15–34.3)] compared with healthy children [15.2 g/m² h (6–22.2)] (*P* < 0.001) (Fig. 1). A gender stratified analysis showed that the TEWL measurements were higher on all surfaces only in boys but not in girls (Fig. 2) (Table 2A, B). There was no difference in TEWL measurements between healthy boys and healthy girls or asthmatic boys and asthmatic girls. Logistic regression analysis showed that the presence of asthma was the only factor significantly associated with increased TEWL above the median on the palm (OR: 3.0 CI 95%: 1.4–6.3). The presence of atopy had no influence on the TEWL measurement.

Effect of anti-inflammatory therapy on TEWL

Within the group of asthmatic children, TEWL measurements on the volar surface (boys and girls) and back (boys) were lower in patients using anti-inflammatory therapy (inhaled corticosteroid and/or montelukast) (Fig. 3).

Discussion

Our study shows that exercise induces a higher local TEWL on all surfaces only in asthmatic boys compared with their healthy counterparts. The use of anti-inflammatory drugs significantly decreased the TEWL on the volar surface and back of asthmatic children. We propose two hypotheses to explain the increased sweating in asthmatic children.

(1) *Increased energy expenditure during exercise in asthmatics*: No muscular effort is necessary for expiration to occur at rest. During exercise, active expiration and increase in pulmonary ventilation leads to an increased

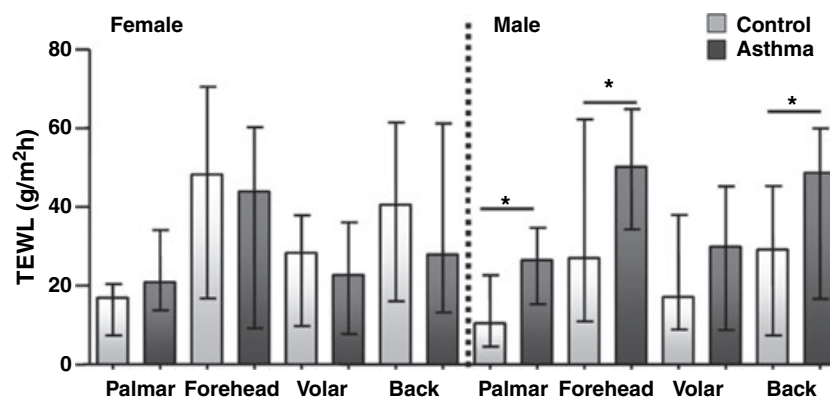


Figure 2. Gender stratified comparison of transepidermal water loss (TEWL) between asthmatic patients and healthy controls (* $P < 0.05$).

Table 2. Transepidermal water loss (TEWL) measurement before and after exercise in boys (A) and girls (B)

	Asthma		Control		<i>P</i> *
	Pre-exercise	Postexercise	Pre-exercise	Postexercise	
A					
Palm	49.9 (39.1–59.2)	75.8 (70.5–83)	57.95 (48.38–69.68)	75 (64.63–81.53)	0.001
Forehead	16.2 (13.5–20.5)	68.2 (50.3–84)	16.3 (11.95–19.55)	44.15 (23.9–74.5)	0.019
Volar	13 (10.9–16.7)	44.4 (24.1–59.5)	15.25 (11.95–19.23)	32.6 (22.1–49.48)	>0.05
Back	9.5 (8.6–12.5)	59.4 (29.4–70.9)	8.85 (8.13–12.08)	42.25 (17.18–55.78)	0.023
B					
Palm	55.2 (45.2–63)	78 (65.1–84)	58.9 (50.7–72.5)	77.8 (77.1–83.4)	>0.05
Forehead	13.3 (10.9–19.7)	60 (20–70.8)	12.4 (10.7–17.4)	59.7 (29.3–81.6)	>0.05
Volar	13 (9.9–17.3)	34 (24.1–50.2)	14.6 (13.5–20.2)	42.6 (28.3–51.5)	>0.05
Back	8.7 (6.8–10.5)	43.8 (20.1–70.4)	10.1 (7.2–13.1)	48.4 (30.4–67.9)	>0.05

*Significance of the difference between postminus pre-exercise values of asthmatic children vs healthy controls.

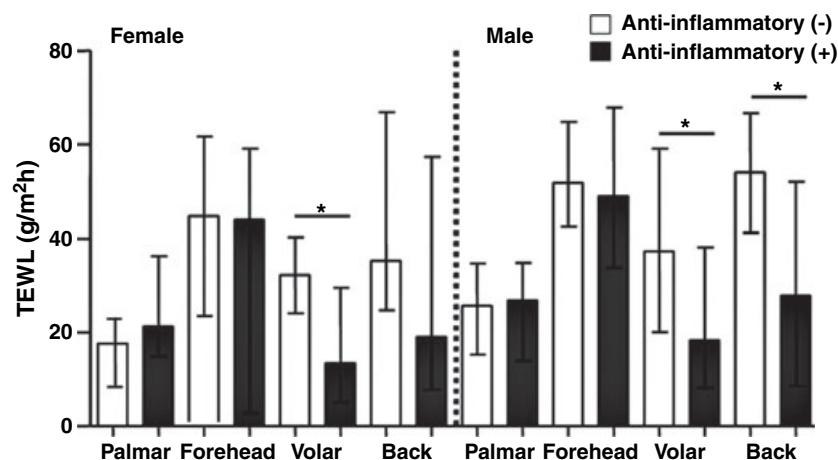


Figure 3. Gender stratified comparison of transepidermal water loss (TEWL) between asthmatic patients using anti-inflammatory drugs and those using as needed bronchodilator therapy (* $P < 0.05$).

workload of breathing, especially in asthma where even a small decrease in airway diameter can result in a large increase in breathing resistance (6). Medelli et al. showed

that in professional cyclists with or without asthma, oxygen consumption was higher in asthmatics than in normal subjects (7). It was also shown that with added

death space, oxygen consumption increased more than with an added resistance, indicating that changes in lung volumes might contribute to oxygen cost of breathing and overall energy expenditure. A greater metabolic heat production results in a relatively greater evaporative heat loss.

Our observation that anti-inflammatory treatment decreases the heat loss on the volar and back surfaces might lend some support to this hypothesis. In children with asthma treatment before exercise resulted in reduced ventilation and energy cost (8). Therefore, the decrease in TEWL might be associated with a reduction in energy expenditure as a result of anti-inflammatory medications. The fact that anti-inflammatory treatment had no effect on the water loss on the palmar surface may be related to higher concentration of eccrine sweat glands on palms (620 glands/cm²) compared with forehead (215), forearm (114), and back (88) (9).

(2) *Hypersensitivity of the muscarinic receptors:* Asthma is characterized by increased sensitivity to cholinergic stimuli (10, 11). Therefore, there is a reason to believe that there is a general overall cholinergic hyperresponsiveness in asthma, which manifests itself as increased sweating on the skin and increased bronchial hyperresponsiveness to cholinergic stimuli. In asthma, cholinergic control of the airways is abnormal and the hyperresponsiveness is regulated partly by the release of acetylcholine onto M₃ muscarinic receptors. Neuronal M₂ receptors are also dysfunctional leading to increased release of acetylcholine from the nerves. The main sympathetic nerve supply of sweat glands is unusual in being cholinergic. A significant correlation between methacholine sensitivity and the size of eccrine sweat glands, sweat rate per gland, sweat rate per unit length of the secretory tubule and sweat rate per unit glandular volume was demonstrated (12).

However, in contrast to our hypothesis, the results of a recent study showed that subjects with excessive methacholine hyperresponsiveness had lower pilocarpine induced sweat secretion (13). There are major differences between the two studies. First of all, our group of

patients consisted of children who have lower sweating rates per gland compared with adults (13), and the other study consisted of young adults. Secondly, the methods of inducing sweat secretions were different between the two studies. Vimieiro-Gomes et al. (14) showed that exercise induced a higher local sweat rate than pilocarpine in healthy volunteers. Finally, the site at which sweating was induced was also different. In the study by Park et al. (13), local sweat rate in response to pilocarpine was only measured on the volar aspect of forearm. Therefore, the results of two studies are not exactly comparable.

One of the major findings of our study is that the TEWL measurement is increased only in asthmatic boys but not in girls. A couple of different observations may help explain this phenomenon. First, Kaliner et al. (3) have reported that the sweating response in males is two-fold higher than females in response to cholinergic stimuli. Secondly, it is generally well appreciated that the boys have higher energy expenditure than girls in response to exercise (15). Therefore, the combination of asthma with male gender may result in increased TEWL measurement in boys both as a result of increased cholinergic sensitivity and increased energy expenditure. Increased energy expenditure and overall hypersensitivity of the muscarinic receptors are not mutually exclusive and both can be operative.

Our study has some weaknesses. We had to leave out four healthy atopic children although this is unlikely to affect the results not only because of the low prevalence of atopy in the healthy population but also because as atopy did not seem to affect sweating in asthmatic children. Additionally, this is an observational study that only documents the presence of increased sweating. It does not provide any information on the mechanisms and whether this can be used a surrogate marker of disease.

To conclude, our results show that asthma is associated with a higher rate of sweating response to exercise in boys. The exact mechanism remains to be investigated.

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