RESEARCH PAPER

Slower Rise of Exhaled Breath Temperature in Cystic Fibrosis

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Objective: To measure exhaled breath temperature in patients with cystic fibrosis. **Methods:** 17 patients (6-18 years) with cystic fibrosis and 15 age- and gender-matched healthy controls were recruited in this cross sectional study. Exhaled breath temperature was measured in subjects recruited in both the groups with a device X-halo and analyzed as plateau temperature achieved and rate of temperature rise. **Results:** Patients with cystic fibrosis showed no significant difference in plateau temperature [34.4(32.3-34.6) *versus* 33.9 (33.0-34.4)^{o}C; *P*=0.35] while mean (SEM.) rate of temperature rise was significantly less in patients [0.09 (0.01) *versus* 0.14 (0.02) Δ°C/s ; *P*=0.04] as compared to controls. **Conclusion:** There was a slower rise of exhaled breath temperature in patients with cystic fibrosis whereas plateau temperature was not significantly different from controls.

Keywords: *Cystic fibrosis, Exhaled breath temperature, Inflammation.*

Measurement of exhaled breath temperature (EBT) has been increasingly used as a simple and reproducible marker of airway inflammation [1,2]. Temperature of deep structures of lungs is mainly determined by amount of blood flowing along rich vascular bed of alveoli which transfers its energy to alveolar gas. Inflammation or remodeling of airway walls which could modify blood flow might be reflected in the temperature of outgoing air or EBT [3]. Paredi, *et al*. [2,4] have reported faster rise of EBT in asthma patients and its significant correlation with exhaled nitric oxide and slower rise of EBT in chronic obstructive pulmonary disease patients .

As cystic fibrosis (CF) is characterized by airway inflammation [5] and remodeling [6], we hypothesized that an altered bronchial blood flow will affect EBT in these patients. This study was thus designed and conducted to measure EBT in children with CF and compare it with healthy controls.

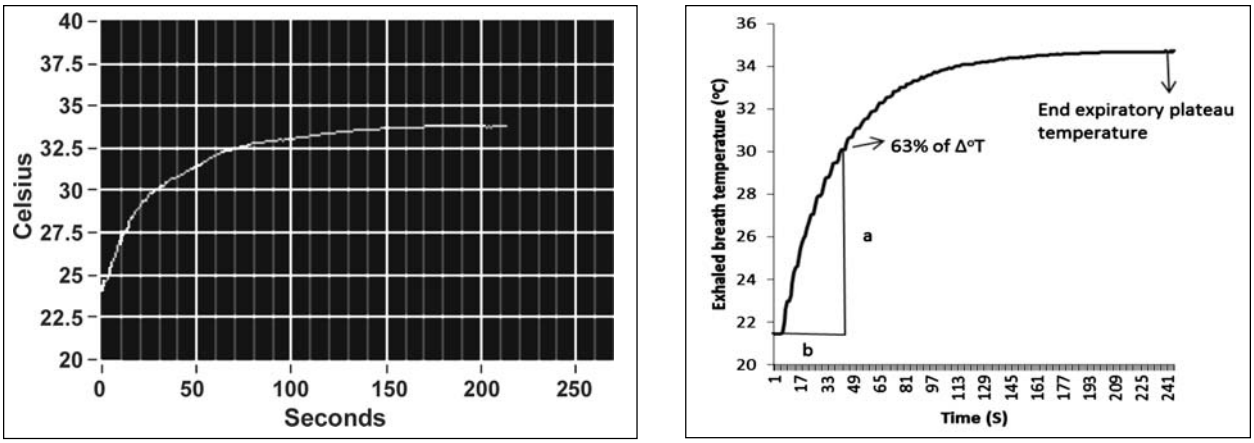
METHODS

This study was approved by the Ethics Committee of All India Institute of Medical Sciences, New Delhi. Prior informed written consent was obtained from parents/ guardians of all the participants.

The study was conducted in children/adolescents having CF and age- and gender-matched healthy controls recruited from pediatric out patient department of the hospital. Diagnosis of CF was made by clinical phenotype and documented sweat chloride ≥60 mmol/L on two occasions [7]. Consecutive children with CF who were able to perform spirometry as per ATS criteria [8] were enrolled in this study. All selected patients were in stable condition (not required antibiotics for last 1 month) and had FEV_1 >20% of predicted. Patients having any other respiratory or systemic disease were excluded from the study. Healthy controls were siblings accompanying the patients; pulmonary disease was ruled out by taking history, and by systemic examination.

The test for EBT was performed between 10 AM to 2 PM. All patients received their prescribed treatment on the day of performing the test, which included inhaled salbutamol, hypertonic saline followed by chest physiotherapy and inhaled budesonide. Measurements were done in an air-conditioned room (22-25 ^{o}C) after a rest period of at least half an hour. Participants were asked to abstain from eating or drinking for one hour prior to the test.

EBT was measured by multiple breath procedure using portable device X-halo (Delmedica Investments Pvt Ltd, Singapore) [9] in which expired thermal energy is accumulated in an insulated vessel containing a heat sink with high thermal capacity, thus making measurements less dependent on ambient temperature. Participants were instructed to purse their lips around the mouth piece, inhale through the nose and exhale freely into the device at a rate and depth suiting their normal tidal breathing pattern. The participant continued to exhale into the thermal chamber of the device till thermal equilibrium was reached inside the closed system and the stable



(a) *(b)*

FIG. 1: *Temperature curve obtained during recording of exhaled breath temperature (a); and Analysis of exhaled breath temperature (b).*

plateau temperature picked up by the silicon chip thermal sensor was reflected on the screen of the device. The incremental EBT curve was further analyzed (***Fig.* 1**).

Even though the cumulative temperature curve obtained by multiple exhalation method is different than that obtained in single breath method [2], both of them can be fitted by the same exponential model [10]. EBT tracings were analyzed in two ways; plateau (stable) temperature and rate of temperature rise i.e. slope of the curve (***Fig.* 1**). As the curve is exponential, it is difficult to determine the time at which final value is obtained because there may be a small change in temperature for long time as it approaches asymptote. It is easy to determine asymptote value and the time required to reach certain percentage of it using time constant (T), the most common is 63% rise time [1]. So the rate of rise of temperature was calculated from the beginning of exhalation to 63% of total temperature rise, which allows a reproducible mathematical characterization of the tracing before plateau. A better intera-session and inter-session variability has been observed by this method [2].

Inter group comparison was made by unpaired t test for slope of the EBT curve and by Mann Whitney test for plateau temperature. Data were expressed as mean (SEM) for slope of the curve and median (IQR) for plateau temperature. Statistical significance was set at $P<0.05$.

RESULTS

A total of 17 (13 males) children (6-18 yrs) with CF and 15 (12 males) age-matched healthy controls were enrolled in the study (***Table* I**). CF patients showed no significant difference in plateau temperature [34.4(32.3-34.6) *vs* 33.9 (33.0-34.4) ºC; $P=0.35$] while slope of the curve was significantly less in CF patients [0.09 (0.01) *vs* 0.14 (0.02) ΔºC/s ; $P=0.04$] as compared to controls (***Fig.* 2**).

DISCUSSION

In the present study, rate of temperature rise was slower in CF patients as compared to controls. Alteration of bronchial blood flow may affect either plateau temperature [9] or rate temperature rise [1]. Garcia, *et al*. [11] have also reported no difference in plateau temperature in adult CF patients. It could be speculated that transfer of heat energy from capillary bed to alveolar air may depend upon balance between two opposing factors *i.e.* inflammation [5] and remodeling [6] causing vasodilation, enlargement and tortuosity of bronchial arteries, increased bronchopulmonary anastomoses and other airways structural changes like thickening of reticular basement membrane which is present between lung alveoli and capillaries [6], deposition of collagen fibers in the interstitial tissue [12]; mucus hyper-secretion [13] and its adhesion to surface [14].

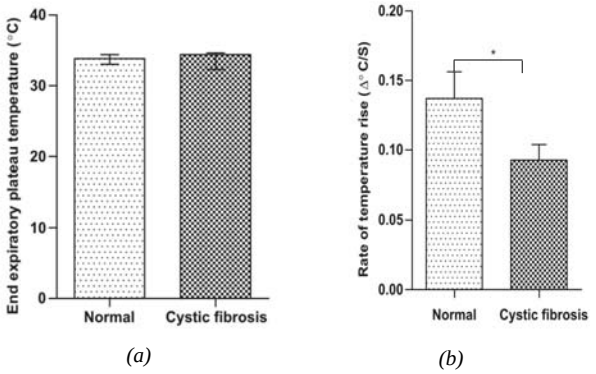
TABLE I DEMOGRAPHIC CHARACTERISTICS OF THE PARTICIPANTS IN THIS STUDY*

Parameter	*Cystic fibrosis (n=17)*	*Controls (n=15)*	*P value*
Age (y)	12.3 (3.14)	10.8 (2.11)	0.12
Gender (M:F)	13:4	12:3	–
Height (cm)	138.1(16.33)	140.1(14.10)	0.71
Weight (Kg)	29.3(13.18)	30.0 (7.26)	0.35
BMI (Kg/m^2)	14.7 (3.43)	15.1 (2.10)	0.38

**All values in mean (SD).*

WHAT THIS STUDY ADDS?

- There is a slower rise of exhaled breath temperature in children with cystic fibrosis.



(a) *(b)*

FIG. 2 *End expiratory plateau temperature (°C) in cystic fibrosis and healthy controls (a); and (b) Rate of rise in exhaled breath temperature Δ°C/s ; P<0.05.*

Thus, use of EBT – as a tool to monitor changes taking place in respiratory airways – requires more studies with higher sample size and correlation between EBT, various clinical parameters and objectively documented airway structural changes need to be explored.

Contributors: AT, GB and SK: conceived and designed the study; GB and SG: performed the experiments; AT, GB and SG: analyzed and interpreted the data, and manuscript; AT and SK; revised the manuscript. All authors approved the final manuscript.

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