

ENVIRONMENTAL DETERMINANTS

Effect of Dust Aerosol in Patients with Asthma

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Objective. Sandstorms frequently cause adverse health effects especially in patients with asthma. The aim of our research was to explore the mechanism of sandstorm-induced asthmatic exacerbation by administering dust aerosol through an environmentally controlled exposure chamber. **Methods.** Four samples of soil (Ganganagar clay, Bikaner sand, Jaipur sand, and Ganganagar sand) were collected from three sandstorm-prone areas of Rajasthan, the desert state of India. Twenty patients with asthma, who had stable disease with a forced expiratory volume in first second (FEV₁) more than 70% of predicted, volunteered to participate in this randomized single-blind placebo-controlled crossover study. The four samples of dust and placebo were administered randomly on 5 study days. FEV₁ was measured for the next 60 minutes and the maximal decline in FEV₁ (Δ FEV₁) from baseline was measured. The samples of dust were also analyzed for particle size and adhesiveness. **Results.** The maximal decline in FEV₁ was observed 15 minutes post-exposure with all dust samples. Mean Δ FEV₁ was 0.69 ± 0.08 liters for Ganganagar clay, 0.52 ± 0.06 liters for Bikaner sand, 0.39 ± 0.07 liters for Jaipur sand, and 0.32 ± 0.04 liters for Ganganagar sand dust aerosol samples. Decline in FEV₁ correlated with volume of dust particles with size $<10 \mu\text{m}$ (PM₁₀) and adhesiveness of the dust particles. **Conclusion.** Smaller-size sandstorm dust particles with higher adhesive properties have a greater potential of aggravating asthma.

Keywords Adhesion, FEV₁, particle size distribution, PM₁₀, sandstorm

INTRODUCTION

Asthma is an episodic disease with phases of sickness and well-being. The episodes of sickness are caused by various triggers. Triggers such as pollution, smoking, occupational sensitizers, infections, and indoor and outdoor allergens have been clearly linked with exacerbation of asthma (1). Some factors have been suspected to cause exacerbation of asthma but the definite mechanism is not clear.

Sandstorms have also been linked with asthma exacerbations leading to increased hospital admissions and strokes (2, 3). In Trinidad, pediatric asthma exacerbations were associated with Saharan dust cover and exhaust pollutants (3). Similarly, children in Seoul, South Korea, suffered from decline in peak expiratory flow (PEF) rates during Asian dust events (4). Various mechanisms have been suggested to explain the exacerbations of asthma during and after sandstorms, with changes in barometric pressure and temperature factoring in as important variables (5). Sandstorm particulate matter (PM) is understood to inflict oxidative damage (6) and therefore it exacerbates asthma and chronic obstructive airway disease (7). PM is generated by various sources like vehicular exhaust, burning of fossil fuels, and sandstorms (8). Elevated PM₁₀ (PM with size $\leq 10 \mu\text{m}$) levels released through vehicle exhaust, particularly those with size of less than $1 \mu\text{m}$, have long been associated with decrease in PEF rate and respiratory symptoms such as cough (7, 9).

Sandstorms are natural events occurring in arid and semi-arid areas. Rajasthan is a desert state in India where sandstorms occur frequently. Ganganagar and Bikaner are two districts within Rajasthan where the frequency of sandstorms is maximal (10). Ganganagar has the highest frequency of sandstorms in India, at 17.0 days per annum, while Bikaner experiences a frequency of 8.0 sandstorm days per annum (11). The aggravation of asthma due to sandstorms was measured, so far, indirectly by measuring the levels of dust in the environment and comparing it with the hospital visits, indoor admissions, or mortality rates due to asthma. However, the direct effect of dust inhalation has not been studied. We evaluated the effect of dust aerosol, equivalent to a sandstorm, under controlled conditions in patients with asthma. We also studied the physical properties of dust aerosol, including the particle size and adhesiveness, to find a possible correlation.

METHODS

Dust Sample Collection and Preparation

Four samples of dust were collected from areas of Rajasthan having high frequency of sandstorms. These included clay and sand samples from Ganganagar and samples of sandy soil from Bikaner and Jaipur. Of these regions, the district of Jaipur has the least number of sandstorms per year. The sampling was done 1 foot below the surface of sand dunes in order to obtain samples free of vegetation and deleterious material.

The soil sample was sieved through $45 \mu\text{m}$ filters (dry sieving) to exclude large-sized particles, and then autoclaved for sterilization. A wooden resuspension chamber

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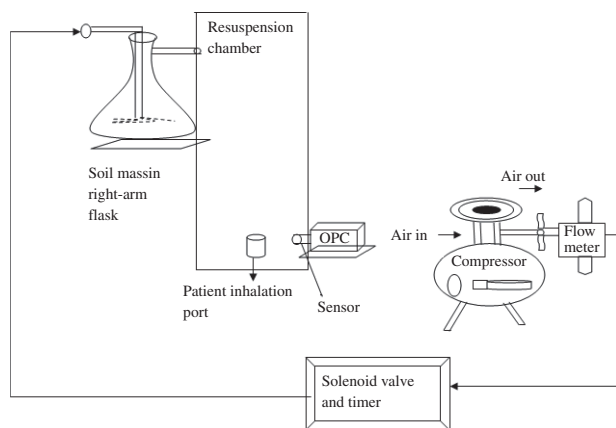


FIGURE 1.—Schematic representation of resuspension chamber.

(Figure 1), sized 72 cm × 51 cm × 107 cm, with a volume of 0.4 m³ was prepared (12). The chamber received dust aerosol from a 250 ml right-arm flask sealed with a rubber stopper. One arm of the flask was connected to the resuspension chamber while the other arm was attached to a compressor. A solenoid valve was connected to control the exit of air through the compressor which was opened once for 5 seconds every 2 minutes. A pulsed air jet was introduced from the compressor into the flask having sieved dust. It created a dust aerosol which was carried to the resuspension chamber. The pressure of the compressor was adjusted (~25 psi) to create a dust cloud equivalent to that of a sandstorm (PM₁₀ in range of 1500–2000 µg/m³/hour) (13). The dust cloud in the resuspension chamber was analyzed through optical particle counter (Grimm Optical Particle Counter (Model 1.108), GRIMM Aerosol Technik GmbH & Co. KG, Ainring, Germany). The patient inhaled through the opening on the opposite side of the resuspension chamber. Heavier particles settled faster than the lighter ones, with particles of size >10 µm settling within 4–5 minutes of sampling.

Size and Adhesiveness of Particles in the Dust Sample

The particle size distribution was carried out by the laser diffraction technique using a calibrated Malvern Master Sizer 2000 (Malvern Instruments, Ltd., Worcestershire, UK) (14). The dust sample was subjected to particle size analysis. The adhesive strength of the soil was determined using unconfined compressive strength (UCS) test (15). The UCS test was performed using a compression tester apparatus which consisted of a small load frame fitted with a ring to measure the vertical stress applied to the soil specimen. Deformation of the sample was measured with the help of a separate dial gauge. Strain was calculated by dial readings (for deformation) and load dial readings. Stress, which is equivalent to the adhesiveness value, was calculated by strain and area of soil sample.

Subjects and Methodology

This single-blind, placebo-controlled, interventional, crossover study was conducted at SMS Hospital, Jaipur, India. The study was approved by the Institutional Ethics

Committee and registered with the Clinical Trial Registry of India (CTRI No.: CTRI/2010/091/000513).

Twenty patients with mild asthma and a forced expiratory volume in first second (FEV₁) > 70% of predicted were recruited for the study. Asthma was diagnosed on the basis of an appropriate clinical history of episodic cough and dyspnea or wheeze with reversible airway obstruction (≥12% and more than 200 ml reversibility in FEV₁ from pre-bronchodilator value) at least once in preceding 12 months. After thoroughly explaining study protocol, volunteer subjects gave their informed consent to participate in the study. Patients younger than 15 years and older than 60 years of age were not included in the study. Subjects having other systemic illnesses such as valvular heart disease, ischemic heart disease, congestive heart failure, uncontrolled hypertension, diabetes mellitus, pregnancy, liver failure, or renal failure were excluded from the study. Patients with asthma who had a history of upper respiratory infection in the 6 weeks prior to study initiation were also excluded.

Of the five study days, 4 days were attributed to dust aerosol inhalation and 1 day to placebo. Placebo consisted of the patient inhaling from the resuspension chamber with the compressor running on an empty flask. The allocation of days was random. All study days were separated by 2-week intervals, resulting in each patient having at least five visits over 8 weeks. The patients were advised to avoid short-acting beta agonists for 6 hours, and long-acting beta agonists, theophylline, and smoking for 12 hours before the scheduled visit. Baseline FEV₁ was taken at the onset of each visit, after which the patient inhaled three times from the resuspension chamber. Serial FEV₁ was measured thereafter at 5-, 15-, 30-, and 60-minute intervals. The maximum decline in ΔFEV₁ from baseline was taken as an index of provocation. Patients whose FEV₁ did not return to baseline were administered 200 µg of salbutamol through a nebulizer.

Statistical Analysis

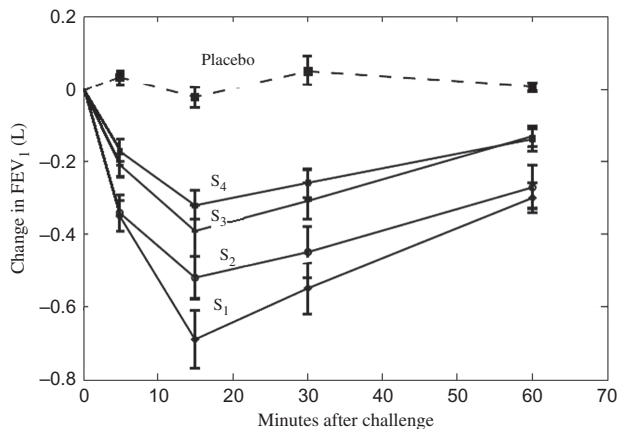
The results were statistically analyzed at 0.05 levels through one-way analysis of variance using SPSS software. Further, Tukey HSD test was used as a post hoc analysis to compare the means in ΔFEV₁ values at particular time intervals for placebo and the four different types of dust aerosol particles. Coefficient of correlation (R^2) was calculated between the decline in FEV₁ and various properties of dust aerosol.

RESULTS

Twenty patients with mild asthma, whose baseline characteristics are shown in Table 1, participated in the study. The mean age of participants in the study was 26.6 ± 7.3 years. Of the 20 participants, 100% had history of atopy and tested positive in a skin-prick test for one or more common antigens (dust mite, grass pollen, *Holoptelia integrifolia*). Baseline FEV₁ values of the patients were not significantly different from each other. Maximal decline in mean ΔFEV₁ was observed 15 minutes after inhalation of dust on all the 4 days (Figure 2). The percent

TABLE 1.—Demographic variables of the patients.

Baseline parameters		N = 20
Age		26.6 ± 7.3 years
Gender	Females	4 (20%)
	Males	16 (80%)
Smoking history	Smokers	3 (15%)
	Non-smokers	17 (85%)
Atopy		20 (100%)
Duration of asthma		12.4 ± 2.2 years
FEV ₁		3.09 ± 0.6 liters
		88.8 ± 7.2%
FEV ₁ /FVC		78.8 ± 2.5%

FIGURE 2.—FEV₁ (liters) change (mean ± SEM) with dust aerosols and placebo. S₁ – Ganganagar clay, S₂ – Bikaner (Lunkaransar), S₃ – Jaipur, S₄ – Ganganagar sand.

decline in FEV₁ (Δ FEV₁/baseline FEV₁) was also plotted and showed similar results (Table 2 and Figure 3). There was no significant decline in FEV₁ when the patient inhaled placebo. Mean declines in FEV₁ 15 minutes after dust inhalation for Ganganagar clay, Bikaner sand, Jaipur sand, and Ganganagar sand were 0.69 ± 0.08 , 0.52 ± 0.06 , 0.39 ± 0.07 , and 0.32 ± 0.04 liters, respectively. Post hoc analysis was done with 15-minute values of Δ FEV₁. When one-way analysis of variance was applied to Δ FEV₁ values between placebo and patients with asthma, a significant *p*-value was observed (*p* < .001).

Table 3 shows the volume distribution of particles according to their size in the four soil samples. In the

TABLE 2.— Δ FEV₁/baseline FEV₁ for the four soil samples.

	5 minutes	15 minutes	30 minutes	60 minutes
Placebo	0.99 ± 1.01	-0.44 ± 1.19	2.05 ± 1.39	0.14 ± 0.63
Ganganagar clay	-10.74 ± 1.31	-20.22 ± 1.95	-15.93 ± 1.79	-8.96 ± 1.09
Bikaner sand	-9.82 ± 1.46	-14.99 ± 1.5	-12.79 ± 1.81	-7.57 ± 1.54
Jaipur sand	-6.57 ± 1.11	-12.23 ± 2.02	-9.8 ± 1.69	-4.08 ± 0.96
Ganganagar sand	-5.35 ± 0.96	-9.85 ± 1.24	-7.9 ± 1.23	-4.31 ± 0.91

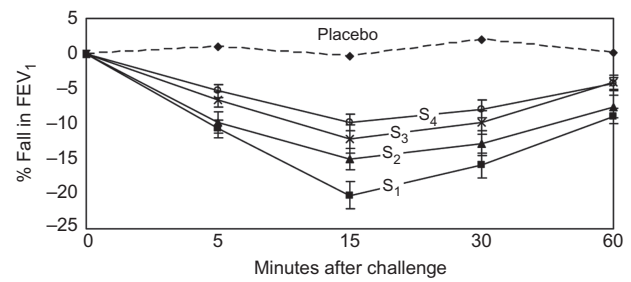
FIGURE 3.—Changes in Δ FEV₁/baseline FEV₁ (y-axis) with time (x-axis). S₁ – Ganganagar clay, S₂ – Bikaner sand, S₃ – Jaipur sand, S₄ – Ganganagar sand.

TABLE 3.—Distribution of particle size in four different soil samples.

Size of particles	Volume percentage			
	Ganganagar clay	Bikaner sand	Jaipur sand	Ganganagar sand
<2.5 μ m	13.23	6.04	3.35	3.04
2.5–10 μ m	35.32	10.87	5.63	4.8
PM ₁₀ (<10 μ m)	48.55	16.91	8.98	7.84
10–45 μ m	51.45	83.09	91.02	92.16

TABLE 4.—Adhesiveness of four dust samples.

Sample no.	Sample of soil dust aerosol	Adhesiveness (kPa)
1	Ganganagar clay	33.73
2	Bikaner sand	17.72
3	Jaipur sand	9.80
4	Ganganagar sand	6.8

increasing order they were Ganganagar sand < Jaipur sand < Bikaner sand < Ganganagar clay. There was also significant difference between a decline in FEV₁ of Ganganagar clay and Ganganagar sand dust samples (*p* < .01).

The adhesiveness of the various soil samples in increasing order were Ganganagar sand < Jaipur sand < Bikaner sand < Ganganagar clay (Table 4). Thus, soil with greater adhesiveness was found to cause a greater decline in FEV₁. A positive correlation was found between the decline in FEV₁ and volume of dust PM₁₀ ($R^2 = 0.89$) and adhesiveness ($R^2 = 0.98$) (Figures 4 and 5).

DISCUSSION

Storms and their association with asthma has been long speculated and studied. In the 1980s, Packe et al. (16) observed that a thunderstorm was followed by an epidemic of asthma. This finding was subsequently reported in various parts of the world (17–20). Changes in temperature (5), humidity (5), barometric pressure (5), pollens (21), and cold air outflow (21) have been the postulated mechanisms. However, there are studies that have not found an

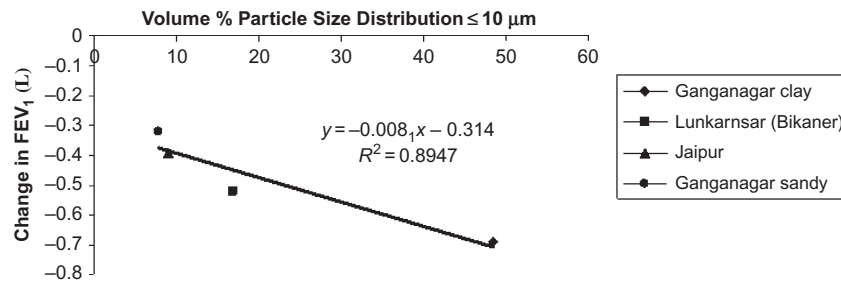


FIGURE 4.—Correlation between decline in FEV₁ (liters) with volume percentage of PM₁₀ particles.

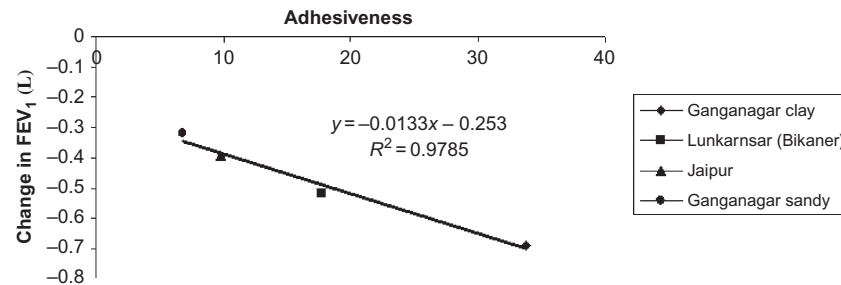


FIGURE 5.—Correlation between decline in FEV₁ (liters) and adhesiveness of dust particles.

association between pollen levels and asthma exacerbations (22). Fungal spores have also been studied as possible etiological factor of thunderstorm-induced asthma (23).

Studies validating the association between sandstorms and exacerbation of asthma have thus far been indirect (2–4, 8), where increased levels of dust aerosol in the environment were associated with either declines in PEF in patients or increases in hospital admissions or visits due to asthma. Due to the lack of direct data, the bias toward other environmental conditions or viral infections was perpetuated. This is the first study in which direct effect of dust aerosol inhaled through environmentally controlled exposure chamber was studied in patients with mild asthma. We created an artificial sandstorm in the laboratory with a controlled number of particles and found that dust aerosol caused a significant decline in FEV₁ compared with placebo. The strength of the study was the removal of bias due to changes in environmental conditions. Second, the direct association between dust aerosol and the decline in FEV₁ was calculated. Third, it was a placebo-controlled, single-blind study. Fourth, we went a step further and studied the properties of dust aerosol which are responsible for the decline in FEV₁ and found that smaller and more adhesive dust particles correlated with a steeper decline in FEV₁.

Sandstorms originate when huge amounts of clay and silt particles are deflected from the surface and carried away in suspension by wind in the form of PM (24). Air quality is commonly assessed by the ambient concentration of PM₁₀ particles. The dry climate and reduced rainfall in deserts allow a long floating time for the aerosol particles in the atmosphere. Consequently, the PM levels in the air quality of the desert region are seasonally and episodically

increased (25). Sandstorms, which are common in deserts, are associated with a rise in PM₁₀ levels (8).

PM₁₀ have been divided into two fractions depending on their size, namely coarse (2.5–10 μm) and fine (<2.5 μm). Most of the studies (7, 9) had found that adverse respiratory effects were associated with fine particle fraction of PM₁₀ of air pollutants. It was postulated that fine particles reach the alveoli and cause inflammation (26). Schwartz et al. (27) did not find that increased concentration of coarse particles, released primarily from burning of fossil fuels, causes an increase in mortality. However, asthma is a disease of proximal airways and the PM need not reach the peripheral alveoli to cause inflammation (1). In our study, we found that PM₁₀ in the soil sample also caused a decline in FEV₁. The maximum decline in FEV₁ was due to Ganganagar clay which had the largest volume of both fine and coarse particles. It, however, had the smallest volume of particles with size >10 μm. We also found that the volume of both fine and coarse particles correlated with a decline in FEV₁. Thus, PM₁₀ particles including both fine and coarse particles are responsible for the decline in spirometric variables.

We also studied the adhesion of dust particles and found that the soil sample causing the maximum decline in FEV₁ were the most adhesive. The decline in FEV₁ correlated strongly with the adhesiveness of the soil sample ($R^2 = 0.98$). Therefore, the greater the adhesiveness, the greater the sticky nature of dust sample. There have been no previous studies considering the adhesiveness of soil particles and its effect on respiratory system. It can be postulated that particles with higher adhesiveness stick to the inflamed bronchial mucosa of asthmatic patients, causing mechanical irritation, thereby resulting in bronchoconstriction.

CONCLUSION

Our data demonstrated a clinically significant decline in FEV₁ after exposure to dust aerosol as compared with placebo. The decline in FEV₁ was greater in soil sample that had smaller and more adhesive particles. The decline in FEV₁ correlated with the volume percentage of fine and coarse particles.

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DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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