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HEPA filtration intervention in classrooms may improve some students' asthma

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Abstract

OBJECTIVE—The School Inner-City Asthma Intervention Study 2 (SICAS 2) tested interventions to reduce exposures in classrooms of students with asthma. The objective of this *post-hoc* analysis was limited to evaluating the effect of high-efficiency particulate (HEPA) filtration interventions on mold levels as quantified using the Environmental Relative Moldiness Index (ERMI) and the possible improvement in the students' asthma, as quantified by spirometry testing.

METHODS—Pre-intervention dust samples were collected at the beginning of the school year from classrooms and corresponding homes of students with asthma (n=150). Follow-up dust samples were collected in the classrooms at the end of the HEPA or Sham intervention. For each dust sample, ERMI values and the Group 1 and Group 2 mold levels (components of the ERMI metric) were quantified. In addition, each student's lung function was evaluated by spirometry testing, specifically the percentage predicted forced expiratory volume at 1 sec (FEV1%), before and at the end of the intervention.

RESULTS—For those students with a higher Group 1 mold level in their pre-intervention classroom than home (n=94), the FEV1% results for those students was significantly ($p<0.05$) inversely correlated with the Group 1 level in their classrooms. After the HEPA intervention, the average Group 1 level and ERMI values were significantly lowered, and the average FEV1% test results significantly increased by an average of 4.22% for students in HEPA compared to Sham classrooms.

CONCLUSIONS—HEPA intervention in classrooms reduced Group 1 levels and ERMI values, which corresponded to improvements in the students' FEV1% results.

Keywords

spirometry; mold; ERMI; dust; forced expiratory volume

Introduction

Asthma is among the most common chronic diseases of children in the United States (1). Indoor mold exposures have been linked to asthma development and exacerbations (2,3,4). Home exposures are known to be important triggers for asthma, but less is known about exposures at school. The observational School Inner-City Asthma Study SICAS 1 study demonstrated that students' classroom-specific exposures were associated with declines in lung function (5,6,7). Therefore, the School Inner-City Asthma Intervention Study 2 (SICAS 2) was conducted, which included school Integrated Pest Management and classroom High Efficiency Particulate Air (HEPA) filtration (8,9,10).

The primary results of the SICAS 2 intervention have been described in detail (10). Overall health benefits were not sustained during the school year; however, in *post-hoc* analysis the IPM schools demonstrated 63% reduction in asthma symptoms in the fall and winter. While

HEPA interventions in the classroom significantly reduced the levels of black carbon, coarse particulate matter (PM), $PM_{2.5}$ and airborne mouse and dog allergens compared to the Sham classrooms, it did not reduce symptoms (10). While the classroom and home allergen levels were balanced at randomization between groups in the trial, it is possible that home exposures could negate some of the benefit of a school-focused intervention. Therefore, we performed a *post-hoc* analysis based on whether mold levels were higher or lower in the classroom or home.

The mold levels in the school and home were compared using the Environmental Relative Moldiness Index (ERMI) metric (11). The ERMI was developed by the US Environmental Protection Agency (US EPA) in conjunction with the US Department of Housing and Urban Development (HUD) to standardize mold quantification in US homes. The ERMI metric has been used successfully in epidemiological studies to quantify the relationship between mold exposures in homes and asthma (12).

The ERMI is calculated based on the qPCR analysis of 36 common mold species, which include two groups: the 26 Group 1 molds are associated with indoor moisture damage, and the 10 Group 2 molds primarily originate from the outdoors (13). The ERMI value itself is the difference between the sum of the Logs of the Group 1 molds minus the sum of the Logs of the Group 2 molds (11).

In previous studies of the relationship between mold exposures and asthma, the lead author demonstrated that the relationship between different levels of mold exposures, based on the ERMI metric, and asthma health was best documented by the results of the spirometry testing, specifically the percentage predicted forced expiratory volume at 1 sec (FEV1%) (14,15). Therefore, in this study, FEV1% test results were used to compare the asthma health of students in HEPA versus Sham treated classrooms. Our hypothesis was that for students with higher mold levels (ERMI value, sum Logs of Group 1 and/or sum Logs Group 2 molds) in their classroom than home, HEPA filtration might improve the FEV1% test results compared to students receiving the Sham treatment.

Methods

Study design

The design of the SICAS 2 study has been described in detail previously (8,9). Briefly, SICAS 2 was an intervention study using HEPA filtration and/or integrated pest management (IPM) to reduce exposures in the classrooms of students with asthma. Each year of the five-year study, students with asthma in various schools were enrolled in the study for that year. Each year, the enrolled student’s classrooms were randomized to receive either HEPA filtration or Sham intervention (HEPA unit but without HEPA filter) (10). In most cases, only one student per classroom was enrolled but occasionally two.

Dust sample collection, quantitative PCR (qPCR), and ERMI analyses of molds

A pre-intervention dust sample was collected at the beginning of the school year in the classroom of students enrolled that year, using a Swiffer cloth, as previously described (16,17). Then the intervention was begun. A second dust sample was collected in each

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classroom in late Fall to early Winter and a third dust sample was collected in late Spring. However, in year five of the study, schools were closed in March due to a pandemic. The third sample from the classrooms that year was not able to be obtained. Therefore, for that year, the second dust sample results were substituted for the third sample in the analyses, which appeared to be satisfactory and the only reasonable alternative.

A dust sample was also collected in some (n=150) of the student's home during the study year, as previously described (9). (Homes of many of the SICAS 2 enrollees were not made available for sampling; some because the homeowner did not want anyone in their home and later because of the pandemic.) Each dust sample was analyzed by a commercial laboratory that performs the ERMI analysis (Mycometrics LLC, Monmouth Junction, NJ) using quantitative qPCR assays (11). The summed logs of the Group 1 molds (for short, Group 1 level), the summed logs of the Group 2 molds (for short, Group 2 level), and ERMI values were calculated, as previously described (11).

Spirometry testing

Spirometry testing was conducted, as previously described (10). Pre- and post-bronchodilator spirometry was performed according to American Thoracic Society guidelines (18). Briefly, at least three reproducible flow-volume loops were obtained using the portable KoKo® PFT Spirometer (CAREstream Medical, Longmont, CO), after which albuterol (2.5mg/0.5ml in 3mL normal saline) was administered via nebulizer. Approximately 10–15 min after completing the nebulized albuterol, spirometry was repeated to obtain post-bronchodilator FEV1%. The tests were conducted at the time of recruitment and after the intervention was completed. This was approximately at the beginning and at the end of school year. (In year five of the study, the mid-year FEV1% measurements were used in the analysis because schools were closed in March due to a pandemic.)

Statistical analysis

The Student's T-test was used to compare average Group 1 levels, Group 2 levels and ERMI values in the pre-intervention dust samples in the students' classrooms and their corresponding homes (n=150). Pearson correlation analysis was used to examine the relationship between the students' FEV1% test results with Group 1 levels, Group 2 levels or ERMI values in the classrooms and homes. Next, a Pearson correlation analysis was used to test the relationship between the students' FEV1% test results and classroom Group 1 levels, Group 2 levels and ERMI values for those students in classrooms where the Group 1 levels (n=94), Group 2 levels (n=121) or ERMI values (n=65) were <u>higher</u> than in their homes. In addition, a Pearson correlation analysis was used to test the relationship between the students' FEV1% test results and classroom Group 1 levels, Group 2 levels, and ERMI values for those students in classrooms when the Group 1 levels (n=56), Group 2 levels (n=29) or ERMI values (n=85) were <u>lower</u> than in their homes.

The pre-intervention distributions of FEV1% test results for the students in the HEPA intervention and Sham intervention classrooms were compared for normality of their distributions using the Kolmogorov-Smirnov test. In addition, the difference in mean

FEV1% test results and standard deviation in these two groups of students was evaluated using the Variance Ratio F-test.

A Student's T-test was used to evaluate changes in Group 1 levels, Group 2 levels or ERMI values post-intervention. A Pearson correlation was used to test the relationship between the changes in Group 1 levels, Group 2 levels and ERMI values and changes in FEV1% test results post-intervention. All statistical analyses were performed using SAS (SAS Institute Inc., Cary, NC).

Results

For the entire cohort of students with both a classroom and home dust sample (n=150), the average Group 1 and Group 2 levels were significantly ($p<0.001$) higher in their classrooms than their homes but not the average ERMI values (Table 1). However, there was no correlation between the students' FEV1% test results and the Group 1 levels, Group 2 levels or ERMI values in either the classrooms or homes (Table 2). Therefore, we examined the situation when Group 1 level, Group 2 level, or ERMI values in the pre-intervention classroom was higher in the students' classrooms compared to their homes (Table 3) and when they were lower (Table 4).

When the Group 1 mold level was higher in the pre-intervention classroom than home (n=94), the average Group 1 level was significantly ($p<0.05$) higher in the classroom than home (Table 3) and the students' FEV1% test results were significantly, inversely correlated with the Group 1 levels in these classrooms, i.e., the higher the Group 1 levels in the classroom, the lower the students' FEV1% test results (Table 3). For those classrooms with a higher Group 2 level than home (n=121) or a higher ERMI value than home (n=65), neither the average Group 2 level nor average ERMI value was significantly different from the homes' average Group 2 level or ERMI value. In addition, neither the Group 2 levels nor ERMI values were correlated with the students' FEV1% test results (Table 3).

Next, we examined the situation when the Group 1 level, Group 2 level, or ERMI value in the student's pre-intervention classroom was lower than in the corresponding home (Table 4). When the Group 2 mold level was lower in the pre-intervention classroom than home (n=29), the average Group 2 level was significantly ($p=0.01$) lower in the classrooms than homes (Table 4) and the students' FEV1% test results were significantly, inversely correlated with the Group 2 level in these classrooms, i.e., the lower the Group 2 level in the pre-intervention classroom, the higher the student's FEV1% test result (Table 4). For those classrooms with a lower Group 1 level than home (n=56) or lower ERMI value than home (n=85), neither the average Group 1 level nor average ERMI value was significantly different from the home's average Group 1 or average ERMI value. In addition, neither the Group 1 levels nor ERMI values were correlated with the students' FEV1% test results (Table 4).

Since the classrooms with higher Group 1 levels had students with poor FEV1% test results, the effect of HEPA versus Sham interventions on mold levels and FEV1% test results were evaluated for those students in the classrooms that had higher, pre-intervention Group 1

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levels than their homes (n=94). For these 94 students, 49 of their classrooms received the HEPA intervention treatment and 45 were Sham classrooms. After adjustments for missing data, the final comparison groups totaled 43 classrooms in the HEPA intervention group and 38 classrooms in the Sham intervention group.

The distributions of pre-intervention FEV1% values in the HEPA (n=43) and Sham (n=38) pre-intervention classrooms were normally distributed based on the Kolmogorov-Smirnov test results, 0.09 and 0.12, respectively. In addition, the averages, standard deviations and their variance were not significantly different (Table 5). Since the pre-intervention FEV1% test result distributions for students in HEPA and Sham intervention classrooms were comparable, the changes in FEV1% test results were compared to changes in mold measurements in these classrooms after interventions.

Table 6 shows the average, post-intervention decreases in Group 1 level, Group 2 level and ERMI value in the HEPA and Sham intervention classrooms. The average decrease in Group 1 level in the HEPA intervention classrooms was significantly (p=0.05) greater than the average decrease in the Sham classrooms (Table 6). Similarly, the average decrease in ERMI value in the HEPA intervention classrooms was significantly (p=0.03) greater than the average decrease in the Sham intervention classrooms. However, the average post-intervention Group 2 level in the HEPA and Sham intervention classrooms were not significantly different. Next, these post-intervention changes in mold measurements were assessed for their relationships to the post-intervention changes in the students' FEV1% test results.

Post-intervention, the average FEV1% test result of the students in the HEPA intervention classrooms increased 4.69% but only 0.47% for the students in the Sham intervention classrooms, for an increase of 4.22%, i.e., 4.69% for HEPA intervention minus 0.47 for Sham intervention classrooms. Therefore, the average spirometry test result was significantly improved (p=0.034, one sided T-test for improvements) for students in the HEPA compared to Sham intervention classrooms. This improvement corresponded to a significant reductions in average Group 1 level (p=0.05) and ERMI value (p=0.03) in the HEPA intervention classrooms (Table 6).

Discussion

In epi-studies of mold exposures and asthma, higher Group 1 levels and higher ERMI values were found to be associated with the increased likelihood of asthma occurrence, development, or exacerbation (3,16,19,20). However, the pre-intervention Group 1 levels, Group 2 levels and ERMI values in the classrooms or homes were not correlated with the students' pre-intervention FEV1% test results. Therefore, we examined the situation when the pre-intervention Group 1, Group 2 or ERMI value was <u>higher</u> in the classroom than home and when they were <u>lower</u> in the classroom than home.

When the pre-intervention Group 1 level was higher in the classroom than home, the students had a lower average FEV1% test result. Post-intervention, the average Group 1 level and ERMI value were both significantly lower in the HEPA compared to the Sham intervention classrooms. These reductions were correlated with an average improvement in FEV1% test results for students in the HEPA intervention classrooms of 4.2%

The 4.2% improvement in respiratory function compares favorably with the 3.0% improvement in FEV1% test results reported for improvements comparing omalizumab versus placebo treatments (21). Similarly, exercise training to improve respiratory function for people with asthma reported an average 3.0% increase in FEV1% test results for those receiving the training compared to the controls (22).

Although reductions in Group 1 levels and ERMI values and improvements in FEV1% test results were correlated, these findings should not be construed as evidence of causation, since many exposures were reduced in the HEPA intervention classrooms, including to black carbon, coarse and fine PM, and mouse and dog allergens (10). Interestingly, HEPA intervention did not result in a significant change in the average Group 2 levels in the classrooms.

The Group 2 molds, which primarily originate from the outdoor air, continued to infiltrate into the classrooms despite the HEPA intervention. However, in about 19% of the classrooms (29/150), the pre-intervention Group 2 level was lower than in the corresponding home. Whatever the pre-intervention conditions are that led to some classrooms with a lower pre-intervention Group 2 level, these conditions appear to be associated with better respiratory health for those students with asthma occupying those classrooms.

In summary, this analysis suggests that higher Group 1 levels and ERMI values are associated with poorer lung function, but lower Group 2 levels were associated with better lung function. However, there were many limitations in this exploratory study since it was not part of the original SICAS 2 study design. Also, some students failed to complete their final spirometry test. In addition, some students changed schools or classrooms, after the study began. Despite these limitations, it appears that measuring Group 1 levels and ERMI values in the classroom of students with asthma may be a useful biomarker of potentially problematic exposures.

Conclusion

When the pre-intervention Group 1 level was higher in the classroom than home, HEPA intervention reduced the Group 1 levels and ERMI values in the classrooms of students with asthma, which corresponded to improvements in the students' FEV1% test results.

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Data availability statement.

The data that support the findings of this study are available from the corresponding author, [SJV or WP], upon reasonable request.

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Table 1.

Comparison of mold levels in dust sample from classrooms and corresponding homes (n=150). (Significant differences are bolded.)

	Group 1 Average	Group 2 Average	ERMI[a] Average
Classrooms (n=150)	**20.11**	**15.81**	4.30
Homes (n=150)	**16.84**	**11.09**	5.75
T-test, p-value	**<0.001**	**<0.001**	0.12

[a]Environmental Relative Moldiness Index

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Table 2.

Relationship between students' spirometry test results and mold levels in classrooms and homes.

FEV1%[a]	**Classroom Group 1**	**Home Group 1**	**Difference**
Average (n=150)	**Average**	**Average**	**Average**
98.31	20.48	17.01	3.47
Pearson Correlation	−0.013	−0.016	0.004
Significance (p-value)	>0.2	>0.2	>0.2
FEV1%	**Classroom Group 2**	**Home Group 2**	**Difference**
Average (n=150)	**Average**	**Average**	**Average**
98.31	15.88	11.16	4.72
Pearson Correlation	0.041	0.013	0.017
Significance (p-value)	>0.2	>0.2	>0.2
FEV1%	**Classroom ERMI[b]**	**Home ERMI**	**Difference**
Average (n=150)	**Average**	**Average**	**Average**
98.31	4.59	5.85	−1.25
Pearson Correlation	−0.05	−0.03	−0.01
Significance (p-value)	>0.2	>0.2	>0.2

[a] percentage predicted forced expiratory volume at 1 sec

[b] Environmental Relative Moldiness Index

Table 3.

Relationship between students' spirometry test results and measures of mold when these mold measurements were higher in their classrooms than in their homes. (Significant differences are bolded.)

FEV1%[a]	**Classroom Group 1**	**Home Group 1**	**Difference**
Average (n=94)	**Average**	Average	**Average**
99.56	**22.62**	13.29	**9.38**
Pearson Correlation	**−0.20**	0.08	**−0.28**
Significance (p-value)	**<0.05**	>0.2	**<0.01**
FEV1%	**Classroom Group 2**	**Home Group 2**	**Difference**
Average (n=121)	**Average**	**Average**	**Average**
98.85	16.57	10.17	6.40
Pearson Correlation	−0.07	0.01	−0.06
Significance (p-value)	>0.2	>0.2	>0.2
FEV1%	**Classroom ERMI**[b]	**Home ERMI**	**Difference**
Average (n=65)	**Average**	**Average**	**Average**
98.2	7.14	2.43	4.71
Pearson Correlation	−0.10	0.03	−0.17
Significance (p-value)	>0.2	>0.2	>0.2

[a] percentage predicted forced expiratory volume at 1 sec

[b] Environmental Relative Moldiness Index

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Table 4.

Relationship between students' spirometry test results and measures of mold when these mold measurements were lower in their classrooms than in their homes (Significant differences are bolded.)

FEV1%[a]	**Classroom Group 1**	**Home Group 1**	**Difference**
Average (n=56)	**Average**	**Average**	**Average**
96.21	16.88	23.32	−6.44
Pearson Correlation	0.18	0.04	0.14
Significance (p-value)	0.2	>0.2	>0.2
FEV1%	**Classroom Group 2**	**Home Group 2**	**Difference**
Average (n=29)	**Average**	**Average**	**Average**
96.07	**13.03**	15.29	−2.26
Pearson Correlation	**0.51**	0.31	0.24
Significance (p-value)	**0.01**	0.1	>0.2
FEV1%	**Classroom ERMI**[b]	**Home ERMI**	**Difference**
Average (n=85)	**Average**	**Average**	**Average**
98.40	2.65	8.47	−5.81
Pearson Correlation	0.00	−0.08	0.09
Significance (p-value)	>0.2	>0.2	>0.2

[a] percentage predicted forced expiratory volume at 1 sec

[b] Environmental Relative Moldiness Index

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Table 5.

Distribution and assessment of differences in the students' initial spirometry test results in the intervention classrooms. (Significant differences are bolded.)

	Intervention	**Intervention**		
Student FEV1%[a]	**HEPA[b] (n=43)**	**SHAM (n=38)**	**T-test**	**p-value**
Average	98.5	100.5	−0.58	0.56
Standard Deviation	14.9	15.8	**F-test**	**p-value**
Variance	222	250	0.89	0.36

[a] percentage predicted forced expiratory volume at 1 sec

[b] Environmental Relative Moldiness Index

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Table 6.

Comparison of the change in mold levels after interventions. (Significant differences are bolded.)

	HEPA[b] (n=43)	**Sham (n=38)**	**T-test**
	Average	**Average**	**p-value**
Group 1	**−5.44**	**−3.30**	**0.05**
Group 2	−4.15	−3.93	0.67
ERMI [a]	**−1.29**	**+0.63**	**0.03**

[a]Environmental Relative Moldiness Index

[b]High-efficiency particulate air filtration