ERJ open research
THE BEST IN OPEN ACCESS BASIC, TRANSLATIONAL & CLINICAL RESPIRATORY RESEARCH

Early View

Research letter

Chronic effects of occupational exposure to mineral fibers and recurrent chest infections in insulators

Subhabrata Moitra, Ali Farshchi Tabrizi, Linda Henderson, Fadi Khadour, Mohamed Osman, Lyle Melenka, Paige Lacy

Please cite this article as: Moitra S, Tabrizi AF, Henderson L, *et al*. Chronic effects of occupational exposure to mineral fibers and recurrent chest infections in insulators. *ERJ Open Res* 2022; in press (https://doi.org/10.1183/23120541.00095-2022).

Chronic effects of occupational exposure to mineral fibers and recurrent chest infections in insulators

Subhabrata Moitra[1], Ali Farshchi Tabrizi[1], Linda Henderson[2], Fadi Khadour[2], Mohamed Osman[3], Lyle Melenka[2], Paige Lacy[1]

[1]Alberta Respiratory Centre, Division of Pulmonary Medicine, Department of Medicine, University of Alberta, Edmonton, Canada

[2]Synergy Respiratory & Cardiac Care, Sherwood Park, Canada

[3]Division of Rheumatology, Department of Medicine, University of Alberta, Edmonton, Canada

Correspondence to:

Paige Lacy, Alberta Respiratory Centre, Division of Pulmonary Medicine, Department of Medicine, 559 Heritage Medical Research Centre, University of Alberta, 11207 87 Avenue, Edmonton, AB T6G 2R3, Canada.

Telephone: 1-780-492-6085

Fax: 1-780-492-5329

Email: placy@ualberta.ca

Part of this report was presented at the Annual Congress of the European Respiratory Society, held on 5-7 September 2021.

Word count: 1,418 (except the title page, abstract, references, and table)

Tables: 1

Key message: Mineral fibers, a man-made form of vitreous fibers commonly used as insulating material are risk factors for recurrent chest infections among workers which underscores the necessity of workplace surveillance to protect workers from hazardous substances.

Mineral fibers, which are types of commercially produced man-made vitreous fibers (MMVFs) with a woolly consistency, are industrially manufactured by passing air through molten glass, rock, or slag, and are commonly known as glass, slag, or rock wool. Although all these materials are grouped together as mineral fibers, there are differences in their composition and physical properties. Glass wool/fiberglass is made from borosilicate glass which is composed of sand, soda ash dolomite, limestone, ulexite, and anhydrite, while rock and slag wools are produced of naturally occurring igneous rock (basalt or dolomite rocks), and molten furnace slag, respectively [1]. These disorganized, interlocking fibers were reported to deliver potentially deleterious health effects, particularly on the skin and upper respiratory tract to workers occupationally exposed to these materials, such as during installation or removal of insulation [2, 3]. While a few studies reported no evidence of pneumoconiosis in the industrial workers exposed to glass, rock, or slag wool [4], several case reports appeared in recent years describing a long biopersistence of MMVFs leading to the development of pulmonary fibrosis at a later stage [5-8]. However, evidence of mineral fiber-associated respiratory tract infections has been limited. In this study, we aimed to investigate whether occupational exposure to mineral fibers was associated with recurrent chest infections.

We used baseline and follow-up data in this longitudinal study of unionized insulators that were enrolled in the Wellness of Workers (WoW) program in Alberta between 2011 and 2017. Details of the study population and methodologies were reported previously [9]. Briefly, out of 990 workers who were recruited at the baseline visit, we removed participants who had chest infections at baseline (n=457), were diagnosed with asthma or chronic obstructive pulmonary disease (COPD) (n=206), and were lost to follow-up (n=55). Finally, we recruited 272 insulators for this current analysis. The demographic profile, smoking history (ever vs. never smokers, and smoking pack-years), exposure to second-hand smoke (SHS) in childhood (yes/no), and family history of lung disease in either or both the parents (yes/no) were recorded using a structured questionnaire as described elsewhere [9]. Occupational exposure to mineral fibers was self-reported (yes/no) and was recorded at the baseline visit. Self-reported chest infection, as defined previously [9], was recorded at the follow-up visit, and episodes of chest infections in the past three years were considered as the primary outcome. In a subsample, we also collected venous blood samples at the baseline, and follow-up visits, and complete blood cell count, were performed.

We created univariable and multivariable Poisson regression models (for count outcome variable) to examine the association between baseline mineral fiber exposure and episodes of recurrent chest infections at follow-up. Multivariable models were adjusted for baseline age, sex, ethnicity, BMI, marital status, education, smoking pack-years, the time between baseline and follow-up visit, and use of personal protective equipment [PPEs]). We checked for multicollinearity among the confounding variables using variance inflation factor (VIF). The goodness of fit of the models was tested by Akaike's information criteria (AIC). We also performed some secondary analyses. We tested the potential effect modification of smoking habits (active vs. former/never smoker), exposure to SHS in childhood, and parental lung disease on the association between mineral fiber exposure and chest infections. In a subgroup (n=157), we also tested the mediation effect of monocyte to lymphocyte ratio (MLR) and neutrophil to lymphocyte ratio (NLR) on the association between mineral fiber exposure and chest infections. All analyses were performed as a complete case approach in STATA v.17 (StataCorp, College Station, TX, USA).

This study was approved by the Health Research Ethics Board of Alberta (HREBA.CTC-17-0067) and Health Research Ethics Board (Pro00079792), University of Alberta, and was conducted according to the Declaration of Helsinki. All participants provided signed informed consent forms before taking part in the study.

Descriptive statistics of the study participants are presented in **Table 1**. Most participants were male (91%) with a mean [SD] age of 46.9 [13.6] years. 64% were active smokers at baseline with a median (interquartile range [IQR]) of 3 (0-16.4) pack-years. Participants were followed-up at a median (range) interval of 3.8 years (3-8 years) from their baseline visit. In the follow-up visit, 95% of the participants reported occupational exposure to mineral fibers at baseline and reported to have a median (IQR) of 2 (0-2) episodes of chest infections that occurred between the baseline and the follow-up visits.

In the univariable analysis, we found that being exposed to mineral fibers was associated with increased episodes of chest infections (regression coefficient [β]: 1.56; 95% confidence interval [CI]: 0.16-2.95). After adjusting for confounders in the multivariable model (except for PPEs), the association remained consistent although the magnitude of the estimate was increased marginally (1.95; 0.55-3.35). However, adding the use of PPEs in the model did not alter the magnitude of the estimate significantly

(1.84: 0.41-3.26). We did not observe any effect modification by smoking, exposure to SHS in childhood, or parental lung disease on the association between mineral fiber exposure and recurrent chest infections. In a subgroup analysis, we did not observe any mediating effects of LMR or NLR on the association between mineral fiber exposure and recurrent chest infections.

Our study demonstrates that mineral fiber exposure can lead to recurrent chest infections in a group of insulators. We did not observe any potential involvement of active or passive smoke exposure, family history of lung diseases, or immune cell modulators (LMR/NLR) on this association. Our findings of mineral fiber exposure-associated chest infections are supported by the only available report of increased risk of infectious pneumonia due to exposure to inorganic dust containing mineral fibers [10]. A case of pneumonia with anthracofibrosis was reported in which the investigators found that the patient had a history of mineral fiber exposure. While previous studies have demonstrated LMR and NLR as biomarkers for influenza and pneumonia-like infections in our subgroup analysis [11-14], we did not observe any mediating role of LMR or NLR on the pathway between mineral fiber exposure and recurrent chest infection. This presumably indicates that mineral fiber exposure might trigger infections other than pneumonia or influenza, although the detailed pathophysiology of such infections is not fully understood yet [15]. One possible hypothesis of such aggravated risk of chest infections is that MMVFs can damage alveolar macrophages [16], thus reducing the lung's capacity to counter pathogens. Lastly, our study also emphasizes the use of proper PPEs for controlling exposure. As we mentioned previously, PPEs should be quality-checked for different exposures, as PPEs are product-specific, and not all PPEs provide uniform protection from different classes of materials.

One of the strengths of this study lies in the longitudinal design of the study which suggests an association between mineral fiber exposure and the event of concomitant chest infections for the first time. Moreover, we investigated other factors (potential effect modifiers and mediators) which could influence the association between mineral fiber exposure and chest infections. However, the study has some limitations. Firstly, the exposure was self-reported, and we could not determine individual exposure to mineral fibers and were also unable to calculate the cumulative exposure index, as participants were

unable to provide exact information about their exposure history (years of said exposure). Secondly, chest infections were self-reported and were not clinically examined. Due to longitudinal nature of the study design, we could not determine the exact time of onset of such infections and could only obtain reports of chest infections at the time of follow-up. Therefore, the possibility of over- or under-reporting could not be eliminated. Thirdly, blood cell profiles were not available from all participants, and we did not have information about other immunological markers or bacterial/viral infections in participants. Moreover, we could not determine any possible deviation in the LMR and NLR values of our study population due to the lack of standard reference ranges of those variables in healthy adult population. Lastly, the plausible involvement of other factors such as exposure to physical, chemical, or biological agents in the workplace or residence could not be estimated, and thus more robust studies are required in the future.

In summary, we may conclude that our study provides a potential link between occupational exposure to mineral fibers and recurrent chest infections in insulators. This underscores the deleterious yet undetermined health effects of such insulating materials and warrants proper and safe handling of insulating materials. Moreover, continuous surveillance of workplaces as well as personnel health is necessary to minimize the risk of exposure to such hazardous substances, as well as facilitate compensation and medical assistance in case of adverse events due to exposure.

DATA SHARING POLICY

The datasets used and/or analyzed during the current study contain sensitive personal data and cannot be made publicly available. However, a de-identified dataset with limited variables is available from the corresponding author on reasonable request.

FUNDING

This research was supported by grants from the Wellness of Workers (WoW) Program, Local 110 Heat & Frost Insulators & Allied Workers, and Synergy Respiratory Care Limited. However, the funder was not involved in the design of the study and did not influence the dissemination of the study outcomes.

COMPETING INTEREST

SM reports personal fees from Synergy Respiratory & Cardiac Care (Canada), related to this work; and Apollo Gleneagles Hospital (India) and Permanyer Inc. (Spain) outside this work. PL reports grants from Wellness of Workers (WoW) Program, Local 110 Heat & Frost Insulators & Allied Workers, and Synergy Respiratory Care Limited (Canada) that supported this work; and personal fees from AstraZeneca (Canada) and GlaxoSmithKline (Canada) outside this work. Other authors do not have any conflict of interest to declare with this work.

AUTHORS' CONTRIBUTION

SM carried out the formal analysis, validated and interpreted the results and drafted the original version. AFT was involved in data curation and revised the manuscript. DF was involved in data curation and revised the manuscript. LH was involved in project administration and revised the manuscript. FK was involved in the clinical investigation, project administration, resource acquisition and reviewing the draft. MO provided intellectual content and reviewed the draft. LM conceptualized and administered the project, acquired funding, and was involved in clinical investigation and revision of the draft. PL was involved in project administration and resource acquisition, supervised the project, and edited the draft.

ACKNOWLEDGEMENTS

The authors thank all the volunteer insulators contributing to the WoW survey program as well as members of Synergy Respiratory and Cardiac Care: Bill Stowe, Carrie McPhee, Jennifer Spring, Melanie De Pruis, Lindsay Simmonds, Celeste Hernandez, Kylie Haydey, Blake MacDonald, Linda Ferguson, Michael Krause, Heather Ryan, Michele McKim, Alana Goodall, Shirley Carr, Kevin Lecht, William Spring, Melanie Holowach, and Dina Fathy. We would also like to thank Meghan Dueck, Lei Pei, Samineh

Kamravaei, Noushin Miandashti, and Kawtar Idrissi Machichi for their support in data collection and management.

REFERENCES

1. Willoughby J. Insulation. In: Snow DA, editor. Plant Engineer's Reference Book (Second Edition). Oxford: Butterworth-Heinemann; 2002. p. 30-1--18.

2. Fireman E. Man-made mineral fibers and interstitial lung diseases. Curr Opin Pulm Med 2014;20(2):194-8.

3. Marsh GM, Gula MJ, Youk AO, Buchanich JM, Churg A, Colby TV. Historical cohort study of US man-made vitreous fiber production workers: II. Mortality from mesothelioma. J Occup Environ Med 2001;43(9):757-66.

4. De Vuyst P, Dumortier P, Swaen GM, Pairon JC, Brochard P. Respiratory health effects of man-made vitreous (mineral) fibres. Eur Respir J 1995;8(12):2149-73.

5. Takahashi T, Munakata M, Takekawa H, Homma Y, Kawakami Y. Pulmonary fibrosis in a carpenter with long-lasting exposure to fiberglass. Am J Ind Med 1996;30(5):596-600.

6. Yamaya M, Nakayama K, Hosoda M, Yanai M, Sasaki H. A rockwool fibre worker with lung fibrosis. Lancet 2000;355(9216):1723-4.

7. Guber A, Lerman S, Lerman Y, Ganor E, Trajber I, Edelstein E, et al. Pulmonary fibrosis in a patient with exposure to glass wool fibers. Am J Ind Med 2006;49(12):1066-9.

8. Drent M, Bomans PH, Van Suylen RJ, Lamers RJ, Bast A, Wouters EF. Association of man-made mineral fibre exposure and sarcoidlike granulomas. Respir Med 2000;94(8):815-20.

9. Moitra S, Farshchi Tabrizi A, Idrissi Machichi K, Kamravaei S, Miandashti N, Henderson L, et al. Non-Malignant Respiratory Illnesses in Association with Occupational Exposure to Asbestos and Other Insulating Materials: Findings from the Alberta Insulator Cohort. Int J Environ Res Public Health 2020;17(19):7085.

10. Toren K, Qvarfordt I, Bergdahl IA, Jarvholm B. Increased mortality from infectious pneumonia after occupational exposure to inorganic dust, metal fumes and chemicals. Thorax 2011;66(11):992-6.

11. Zhang HF, Ge YL, Wang HY, Zhang Q, Li WQ, Chen Y, et al. Neutrophil-to-Lymphocyte Ratio Improves the Accuracy and Sensitivity of Pneumonia Severity Index in Predicting 30-Day Mortality of CAP Patients. Clin Lab 2019;65(10).

12. Huang Z, Fu Z, Huang W, Huang K. Prognostic value of neutrophil-to-lymphocyte ratio in sepsis: A meta-analysis. Am J Emerg Med 2020;38(3):641-7.

13. Piotrowski D, Saczewska-Piotrowska A, Jaroszewicz J, Boron-Kaczmarska A. Lymphocyte-To-Monocyte Ratio as the Best Simple Predictor of Bacterial Infection in Patients with Liver Cirrhosis. Int J Environ Res Public Health 2020;17(5):1727.

14. Patel B, Oye M, Norez D, Isache C. Peripheral blood lymphocyte-to-monocyte ratio as a screening marker for influenza infection. J Investig Med 2021;69(1):47-51.

15. Naccache JM, Monnet I, Nunes H, Billon-Galland MA, Pairon JC, Guillon F, et al. Anthracofibrosis attributed to mixed mineral dust exposure: report of three cases. Thorax 2008;63(7):655-7.

16. Donaldson K, Brown RC, Brown GM. New perspectives on basic mechanisms in lung disease. 5. Respirable industrial fibres: mechanisms of pathogenicity. Thorax 1993;48(4):390-5.

Table 1: Demographic, exposure, and clinical characteristics of study participants

	N=272
Demographics	
Age (years), mean (SD) †	46.9 (13.6)
Sex (male), n (%)	248 (91)
BMI (kg/m^2), mean (SD) †	29.6 (6.0)
Ever smokers at baseline, n (%)	173 (64)
Smoking pack-years at baseline, median (IQR)	3 (0-16.4)
Ethnicity (Caucasian), n (%)	219 (81)
Educational qualification, n (%)	
Grade school	8 (3)
High school	36 (13)
Trade school	128 (47)
College/university	100 (37)
Marital status, n (%)	
Single/unmarried	82 (30)
Married/with a partner	172 (63)
Divorced/separated/widowed	18 (7)
Exposure history	
Childhood smoke exposure, n (%)	182 (67)
Parental lung condition, n (%)	74 (27)
Exposure to mineral fibers, n (%) †	259 (95)
Use of PPEs for mineral fibers, n (%) †	161 (59)
Clinical profile	

Episodes of chest infection in the past 3 years, median (IQR)*	2 (1-2)	
WBC profile	***Baseline***	***Follow-up***
Neutrophil (%), mean (SD)	58 (10)	59 (10)
Eosinophil (%), mean (SD)	3 (2)	3 (2)
Lymphocyte (%), mean (SD)	30 (8)	30 (9)
Monocyte (%), mean (SD)	8 (2)	8 (2)
LMR (ratio of absolute count), mean (SD)	3.84 (1.31)	3.76 (1.45)
NLR (ratio of absolute count), mean (SD)	2.26 (1.45)	2.31 (1.19)

Data presented as mean (standard deviation [SD]) or median (interquartile range [IQR]) for numerical variables or frequency (%) for categorical variables. † Data taken at the baseline visit and *at the follow-up visit (median interval between baseline and follow-up visit: 3.8 years). Abbreviations: BMI: body mass index; LMR: lymphocyte/ monocyte ratio; NLR: neutrophil/lymphocyte ratio; PPE: personal protective equipment. WBC: white blood cells.