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Cornea & External Disease

Wildfire Smoke Induces Eye Surface Inflammation and Tear Film Changes in a Human Experimental Model

Sukanya Jaiswal[1], Blanka Golebiowski[1], Meagan Porter[2], Ha T. Duong[1], Michele C. Madigan[1,3], Fay H. Johnston[2,4], and Isabelle Jalbert[1]

[1] School of Optometry and Vision Science, University of New South Wales, Sydney, NSW, Australia
[2] Fire Centre, School of Natural Sciences, University of Tasmania, Hobart, Tasmania, Australia
[3] Save Sight Institute, University of Sydney, Sydney, NSW, Australia
[4] Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia

Correspondence: Sukanya Jaiswal, School of Optometry and Vision Science, Faculty of Medicine and Health, Room 3.029, North Wing, Rupert Myers Building, UNSW Sydney, 2052, Australia. e-mail: suki.jaiswal@unsw.edu.au

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Purpose: To investigate the short-term impact of exposure to smoke from vegetation burns on ocular surface symptoms and signs.

Methods: Woody bushfuels were burnt in an enclosed room (Flammability Laboratory, University of Tasmania, Australia) to generate particulate matter and monitored in real time (Dust Trak II). Eighteen participants (aged 20–63 years, 8 males and 10 females) fitted with respirators were seated 1.5 m from the burn for 15 minutes. Clinical ocular surface measurements were conducted in the right eye. Tears were collected from the left eye and analyzed for the cytokine interleukin-1β (enzyme-linked immunosorbent assay). Pre- and postexposure differences were analyzed using paired *t* tests or Wilcoxon signed rank tests. Associations between symptoms and signs were analyzed using Spearman's correlation.

Results: Mean particulate matter with a diameter of 2.5 µm or smaller exposure was 1903 µg/m^3. After smoke exposure, an increase in symptoms (median change, 2; interquartile range [IQR], 1–6; $P = 0.001$), ocular surface staining (median change, 1; IQR, 0–1; $P = 0.007$), limbal redness (mean change, 0.28 $\pm$ 0.36; $P = 0.02$), palpebral conjunctival redness (mean change, 0.35 $\pm$ 0.36; $P = 0.009$), palpebral conjunctival roughness (mean change, 0.3 $\pm$ 0.4; $P = 0.046$), and decrease in tear breakup time (mean change. 1.4 $\pm$ 2.6 seconds; $P = 0.03$) occurred. The change in bulbar conjunctival redness correlated with the change in dryness symptoms (r = 0.70; $P = 0.001$). The interleukin-1β concentration increased in the majority of participants post exposure (median change, 6.6 pg/mL; IQR, 2.2–21.1 pg/mL; $P = 0.01$).

Conclusions: This study demonstrated that short-term wildfire smoke directly and adversely affects the ocular surface and induces symptoms.

Translational Relevance: This study used a unique enclosed experimental laboratory to simulate ocular exposure to wildfire smoke and demonstrates the need to elucidate the role of anti-inflammatory therapies in mitigating the impact of smoke on the ocular surface.

Introduction

Wildfires are increasing in frequency and severity worldwide.[1] With growing populations living at wildfire-urban interfaces, an increasing number of people are exposed to wildfire smoke.[2,3] Smoke can be transported to locations thousands of kilometers away from the wildfire site,[4,5] resulting in exposure of many more millions of people.

Wildfire smoke can dramatically reduce air quality by increasing particulate matter (PM) in air. Smoke from the recent (2023) Canadian wildfires resulted in PM with a diameter of 2.5 µm or smaller (PM2.5) daily average concentration in northeastern United States of 258 µg/m^3.[6] During the 2019

and 2020 wildfires, the daily average PM2.5 concentration reached 1146 μg/m^3 in Australia's capital city.[7] These concentrations were 20-fold and 75-fold higher, respectively, than the World Health Organization global air quality recommended maximum PM2.5 concentration of 15 μg/m^3 averaged over a 24-hour period.[8]

The ocular surface is directly exposed to smoke during wildfires, yet the impact of wildfire smoke on eyes remains largely unknown. Up to 73% of adults experience ocular symptoms described as eye irritation or watery eyes during periods of poor air quality owing to wildfire smoke, and more symptoms are reported by those with a history of respiratory conditions.[9,10] Children with and without asthma were found to have nine- versus three-fold greater odds of itchy watery eyes, respectively, after local wildfires.[11,12] Chronic exposure to PM2.5 in urban air pollution has also been associated with altered meibomian gland function and poorer tear stability; however, whether these occur after wildfire smoke exposure is unknown.[13]

Elevated PM2.5 in the air during wildfire episodes is associated with deaths and increased presentations to hospitals.[14] More than 400 additional deaths and 4500 hospital presentations and admissions for cardiovascular and respiratory conditions were attributed to smoke from the 2019 and 2020 Australian wildfires.[14] PM2.5 from wildfire smoke can cause up to 10 times greater respiratory presentations to hospitals, compared with PM2.5 from nonwildfire periods.[15] Animal studies attribute this to the lung inflammation induced by wildfire PM2.5 causing greater damage to alveoli and airways, compared with the inflammatory response induced by nonwildfire PM2.5.[16] Wood smoke-induced inflammation in human respiratory cells and the resultant cell death has been attributed in part to the activation of the pro-inflammatory cytokine interleukin-1 beta (IL-1β) and its downstream signalling.[17] IL-1β is also implicated in reduced cell viability and increased oxidative stress of human corneal cells exposed to PM2.5.[18]

Investigations of the impact of wildfire smoke on the ocular surface have been hampered in part by a lack of suitable models able to generate smoke and safely and effectively expose the ocular surface. In animal studies, the ocular surface has, for example, been exposed to atmospheric PM2.5 using eyedrops; however, this strategy does not truly mimic real-life human eye exposure to wildfire PM2.5.[19,20] Studies seeking to expose human participants to wildfire smoke are constrained by an inability to predict the occurrence of wildfires and the direction of smoke transport. Ocular surface smoke exposure studies to date have used PM2.5 from cigarette smoke or diesel exhaust.[21,22] However, as has been shown for respiratory tissues, PM2.5 from these sources may impact the ocular surface differently than wildfire PM2.5 owing in part to differences in the inflammatory response.[15]

The aim of this human exposure study was to demonstrate that wildfire smoke causes adverse changes to the ocular surface. For this purpose, a newly developed model using a wildfire simulator was used (https://firecentre.org.au/firelab3/).

Methods

Participants

Healthy participants between 18 and 65 years of age were recruited from University of Tasmania, Sandy Bay Campus (Hobart, Australia), and from Hobart's local community. Written consent was obtained from the participants before participation. This study was approved by University of New South Wales Human Research Ethics Committee (Project ID 230169) and University of Tasmania Human Research Ethics Committee (Project ID 29137).

Participants with the following conditions were excluded from participating in the study: used artificial tears in the 48 hours before the study or therapeutic eye drops in the month prior, or had a current or previous history of severe ocular surface disease, corneal surgery, chronic medical conditions such as respiratory disease (e.g., asthma), cardiovascular disease (e.g., heart disease or previous stroke) or metabolic conditions (e.g., diabetes), had experienced emotional distress or anxiety during previous wildfire events, or were pregnant or breastfeeding at the time of study participation.

After verbal confirmation of the eligibility criteria, current ocular and systemic medications used by participants were recorded, along with participants' location in the prior 24 hours and whether they had been exposed to any smoke such as from campfires, tobacco smoke, wood heaters, or incense during this period. The maximum PM2.5 concentration at that location was then extracted from the state Environmental Protection Authority's online database of air pollution (https://epa.tas.gov.au/environment/air/monitoring-air-pollution/monitoring-data/real-time-air-quality-data-for-tasmania) and examined for levels exceeding background concentration (10 μg/m^3), which is the concentration of ambient air pollution that is not attributable to any local emission sources.

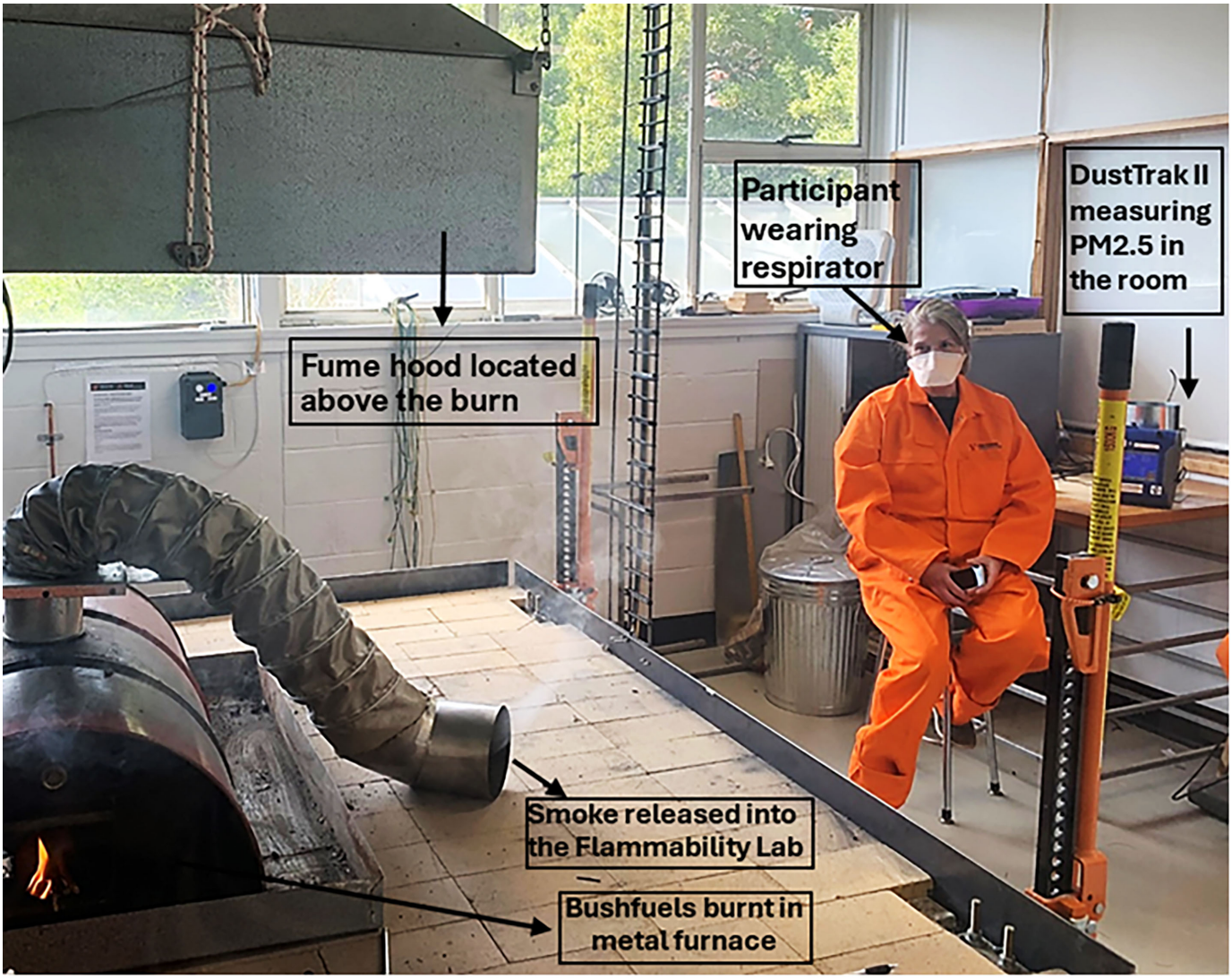

Figure 1. Setup of the Flammability Laboratory (FireLab[3], Bushfires, Bioenergy and Emissions Research Laboratory (University of Tasmania Hobart, Australia) showing how participants' ocular surface was exposed to smoke. The participant pictured gave permission for the photo to be taken and used for publications.

Smoke Exposure

This exposure study was conducted in the Flammability Laboratory at the FireLab,[3] Bushfires, Bioenergy and Emissions Research Laboratory at the University of Tasmania (Hobart, Australia). The Flammability Laboratory is a purpose-built room approximately 3 × 4 m in size. Coarse and fine woody bush fuels were burnt in a metal furnace fitted with an exhaust pipe that released smoke into the Flammability Laboratory, where it naturally dispersed (Fig. 1). The fire was fed and monitored by a trained technician with the aim to generate and maintain a rolling average PM2.5 concentration of 2000 μg/m^3 in the Flammability Laboratory for 15 minutes of exposure. Combustion is a dynamic process where fire activity alternates between phases of active combustion, which typically result in a decrease in PM and phases of smoldering combustion, which are associated with spikes in PM concentrations. The target of 2000 μg/m^3 was selected to recreate the maximum PM2.5 concentration in community that occurred during to the Black Summer wildfires in Australia.[23]

PM2.5 concentrations were monitored in the laboratory using a smoke calibrated DustTrac II device (Model no. 8530, TSI Incorporated, Shoreview, MN) located near the participant (Fig. 1). A secondary DustTrac II device was located near the technician. These devices sampled the air every 10 seconds and displayed PM2.5 concentration in

real time. If excessive PM2.5 was generated from the burn, a fume hood located above the metal furnace was operated to rapidly exhaust smoke out of the room. The Flammability Laboratory was ventilated between participants to reduce PM2.5 concentration in the room to less than 10 $\mu g/m^3$ before a new fire was generated for subsequent participants.

Participants were seated approximately 1.5 m from the furnace. Spectacles if habitually worn were removed. To prevent respiratory and dermal exposure, participants were fit checked with P2 masks[24] by a trained technician and wore fire-retardant overalls. Participants were instructed to leave the Flammability Laboratory at any time if they felt uncomfortable.

Outcome Measures

The following outcome measures were recorded immediately before and after smoke exposure; impression cytology was performed after smoke exposure only. Measurements were carried out in the order of least to most invasive. Ocular surface symptoms were measured for each eye and findings from the right eye only are presented. Visual acuity (VA) measurement and ocular surface examination were conducted on the right eye only. Tear film and impression cytology samples were collected from the left eye only.

Ocular Surface Symptoms

The Instant Ocular Symptoms Survey (IOSS),[25] which measures the intensity of discomfort and dryness, was modified to also include stinging or burning and sore eyes. These two additional symptoms are commonly reported by Australian firefighters after exposure to wildfire smoke.[26] This modified IOSS was administered verbally by the examiner and scored on a scale of 0 to 5 for each of the four symptoms, where 0 represented none at all and 5 represented very intense. The total score was calculated as the sum of responses to the four questions and ranged from 0 to 20.

Visual Acuity

Habitual VA was measured using a 3-m Snellen chart and converted into logMAR scores before analysis. Pinhole VA measurement was conducted for any results poorer than 6/9.

Ocular Surface Clinical Signs

The ocular surface was examined with a portable slit lamp (Shin Nippon XL-1, Tokyo, Japan). Redness of the inferior limbus, the nasal and temporal bulbar conjunctiva, and the inferior palpebral conjunctiva, in addition to roughness of the inferior palpebral conjunctiva, were graded in 0.1 steps using the 0 to 4 BHVI grading scale.[27] Tear break up time after instillation of sodium fluorescein (Fluorets 1 mg strips, Bausch + Lomb, Bridgewater, NJ) was averaged over three measurements (in seconds). Ocular surface staining was graded in whole steps using the 0 to 5 Oxford grading scale.[28]

Tear Analysis

Approximately 10 µL of basal (unstimulated) tears were collected using glass microcapillary tubes (BLAUBRAND 10-µL micropipettes, Merck, Rahway, NJ) applied gently to the temporal inferior eyelid tear meniscus. Tear samples were transferred to and centrifuged in sterile microcentrifuge tubes and stored at −80°C until analysis. The tear concentration of IL-1β was measured by enzyme-linked immunosorbent assay (IL-1β Human ELISA Kit #BMS224-2, Invitrogen Thermo Fisher Scientific, Waltham, MA) as per the manufacturers' instructions. Briefly, basal tears were diluted with assay diluent to a final volume of 50 µL, the minimum volume required for analysis, after which the assay was performed. Absorbance was measured at 450 nm with a 630 nm reference wavelength using a TECAN safire[2] plate reader and Magellan 7.2 SP1 software. IL-1β concentration (pg/mL) was calculated using a standard curve, prepared with the assay standards.

Conjunctival Impression Cytology

Impression cytology samples were collected twice: immediately after smoke exposure and 48 hours later. Participation in the second cytology sample collection was optional so as to not adversely affect study recruitment. Impression cytology was not performed before smoke exposure, because the collection of bulbar conjunctival epithelial cells disrupts the epithelial surface. Conducting this procedure beforehand could have introduced residual effects that would confound the interpretation of post-exposure samples.

A drop of proxymetacaine hydrochloride 0.5% (Alcaine, Alcon, Fort Worth, TX) was instilled in the left eye to anaesthetize the ocular surface. A Biopore membrane (0.4 µm pore size, 8 mm diameter, Merck Millipore, Cork, Ireland) was gently held against the temporal bulbar conjunctiva for approximately 5 seconds as described previously,[29,30] then removed and immediately immersion fixed in 95% ethanol in 24-well plates and stored at 4°C until processed.[31] The ethanol was replenished weekly to prevent samples drying owing to evaporation. For staining, impression cytology samples were rinsed with Milli-Q water three times for 2 minutes each, then incubated in 0.5% w/v

periodic acid (H_5IO_6, Muraban Laboratories, Kuringgai, Australia) for 10 minutes. Goblet cells were stained with periodic acid-Schiff reagent (Muraban Laboratories) for 3 minutes in the dark at room temperature, followed by staining of cell nuclei with hematoxylin (Gill No. 1, GHS132, Sigma-Aldrich, St. Louis, MO) at 37°C for 1 hour on an orbital shaker. After rinsing in 2% sodium hydrogen carbonate ($NaHCO_3$) (BDH, Sydney, Australia) for 2 minutes, membranes were further washed in Milli-Q water before imaging.

Stained membranes were placed on a clean glass microscope slide with a drop of Milli-Q water to prevent drying and viewed using an Olympus IX71 inverted light microscope (20× objective). Images were taken with a DP73 Olympus camera and cellSens Standard (Olympus 4.2.1, Tokyo, Japan) software. Approximately 10 randomly selected areas were imaged for each membrane by an investigator who was masked to the time point at which the samples were collected. Multilayering refers to samples where several of the 5 to 10 layers of conjunctival epithelium plus goblet cells are visible on impression cytology membranes.[32–34] Three images with greatest multilayering of epithelium were selected and a grid of 200 × 200 µm squares was overlaid on each image using Image J software (Version 1.54d, National Institutes of Health, Bethesda, MD). Three squares containing multilayering of epithelium and highest goblet cell density were chosen per image and the number of periodic acid-Schiff positive goblet cells were counted in each square by two observers, and averaged to calculate goblet cell density for each membrane.[33]

Statistical Analyses

A sample size of 18 participants was estimated to be required to detect a clinically significant change in bulbar conjunctival redness (0.5 ± 0.7 grade[32]) with a 5% probability of a false positive ($\alpha = 0.05$) and 80% power. A paired t test was performed to confirm ocular symptoms did not significantly differ between the right and left eyes ($P = 0.65$), and ocular symptoms from the right eye only were used in all subsequent analyses. Cronbach's alpha test was performed to confirm the internal consistency of the modified IOSS questionnaire. The intraclass coefficient was calculated to assess the consistency of goblet cell density measurements conducted by two different observers.

The effect of smoke exposure on symptoms and signs was analyzed using paired t tests and Wilcoxon signed rank tests for parametric and nonparametric data, respectively. Spearman's correlation was used to analyze associations between symptoms and signs. The resulting P values for symptoms, signs, and their correlations were adjusted for multiple comparisons using step-down Holm method.[35,36] Linear mixed models with random intercept for participant were used to examine the impact of age and gender and exposure on the outcome measures. Fixed effects of time point, gender, and age, as well as their interactions, were included.

Results

Eighteen participants (8 males and 10 females) aged 20 to 63 years were enrolled. PM2.5 did not exceed background concentrations for any of the locations where participants had spent time outdoors in the 24 hours before participating in this study. Three participants reported less than 30 minutes of exposure to woodfire smoke 15 to 24 hours before study participation.

PM2.5 Concentrations

The mean PM2.5 concentration (measured every 10 seconds, Supplementary Figure S2) across all burns was 1903 ± 942.2 µg/m^3 with range of 292 to 6560 µg/m^3 (Fig. 2, Supplementary Figure S2). Participant 3 was removed from the Flammability Laboratory at 9 minutes on advice of the fire technician owing to inconsistencies with smoke generation. For this participant, ocular surface measurements after 9 minutes of exposure are presented and were used in the statistical analyses in place of the 15-minute data.

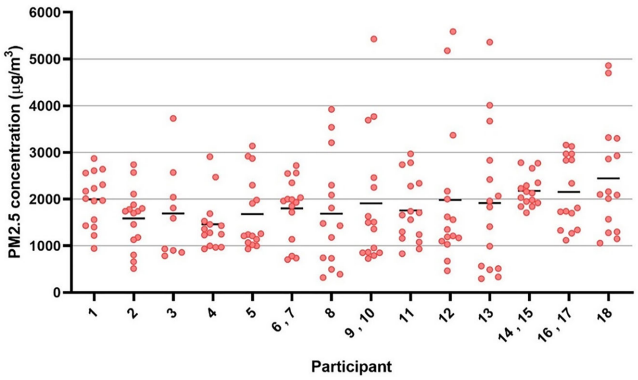

Figure 2. PM2.5 concentration (y axis) inside the Flammability Laboratory during the 15 minutes of smoke exposure for each participant (x axis). Measurements at 1-minute intervals are indicated by filled *red circles* and mean PM2.5 concentrations over 15 minutes are indicated by the *black horizontal bars*. In some instances, two participants were exposed to smoke at the same time (x axis, participants 6 and 7, 9 and 10, 14 and 15, and 16 and 17).

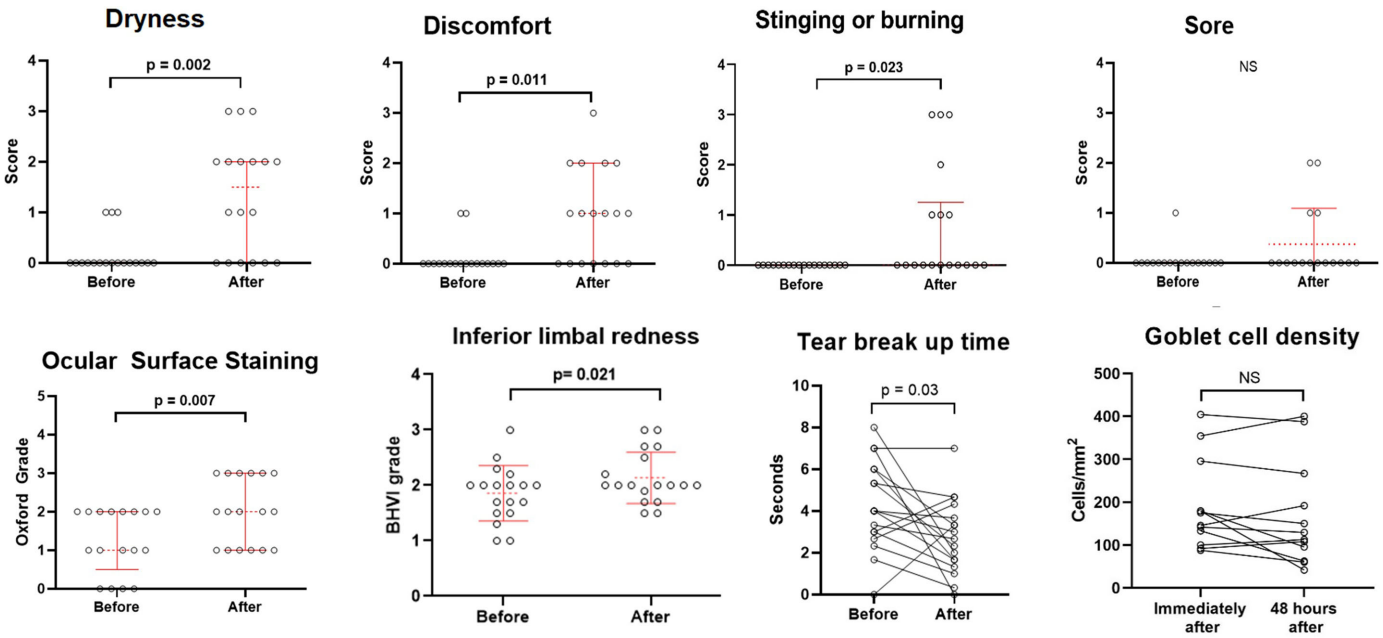

Figure 3. Ocular surface symptoms ($n = 18$, *top*) and signs (*bottom*, $n = 18$ except tear break up time [$n = 17$]) before and after 15 minutes of simulated wildfire smoke exposure. Goblet cell density was measured immediately after and 48 hours after exposure. *Red lines* indicate mean and standard deviation (symptoms and inferior limbal redness) or median and interquartile range (staining). NS, not significant. *P* values shown are adjusted for multiple comparisons.

Ocular Surface Symptoms and Clinical Signs

The modified IOSS (with four questions) demonstrated good internal consistency with a Cronbach's alpha value of 0.71. The median modified IOSS score (sum of discomfort, dryness, stinging or burning and sore eyes) increased from 0 (interquartile range [IQR], 0–0.75) to 3 (IQR, 1–6) ($P = 0.001$). The intensity of discomfort ($P = 0.01$), dryness ($P = 0.002$), and stinging or burning ($P = 0.02$) worsened after smoke exposure, but sore eyes did not change significantly (Fig. 3).

VA did not change significantly with smoke exposure with median VA of 0.04 (IQR, 0.02–0.22) before exposure and 0.02 (IQR, 0.00–0.06) after exposure ($P = 0.18$) (Supplementary Figure S3).

Limbal redness increased after exposure ($P = 0.02$; Fig. 3), as did inferior palpebral conjunctival redness ($P = 0.009$) and roughness ($P = 0.046$) (Supplementary Table S1 and Supplementary Figure S1). The change in nasal and temporal bulbar conjunctival redness was not significant (Supplementary Table S1 and Supplementary Figure S1).

Ocular surface staining increased after exposure ($P = 0.007$; Fig. 3). Staining before and after smoke exposure was most often observed at the limbus and nasal and temporal bulbar conjunctiva.

Tear break up time decreased from before exposure of 4.3 ± 2.1 seconds to 2.8 ± 1.8 seconds after smoke exposure ($P = 0.03$; Fig. 3). Tear break up time measurement was excluded from analysis for one participant who experienced rhinitis and reflex tearing after smoke exposure.

Tear Inflammatory Markers

Tear samples were collected from 16 of 18 participants because for 2 participants no tears could be extracted during the prescribed collection time. The median tear IL-1β concentration significantly increased from 22.50 pg/mL (IQR, 9.7–59.3 pg/mL) before smoke exposure to 33.38 pg/mL (IQR, 14.9–70.9 pg/mL) after smoke exposure ($P = 0.01$; Fig. 4). After short-term smoke exposures, the IL-1β concentration increased in 12 participants, did not change in 2 participants, and decreased in 2 participants (Fig. 4).

Conjunctival Cytology

Conjunctival cell samples were collected from 12 of 18 participants and the Intraclass coefficient was 0.947 (95% confidence interval, 0.915–0.967) for goblet cell counts between the 2 observers. The median goblet cell density was 160.4 cells/mm^2 (IQR, 125.0–208.3 cells/mm^2) immediately after smoke exposure

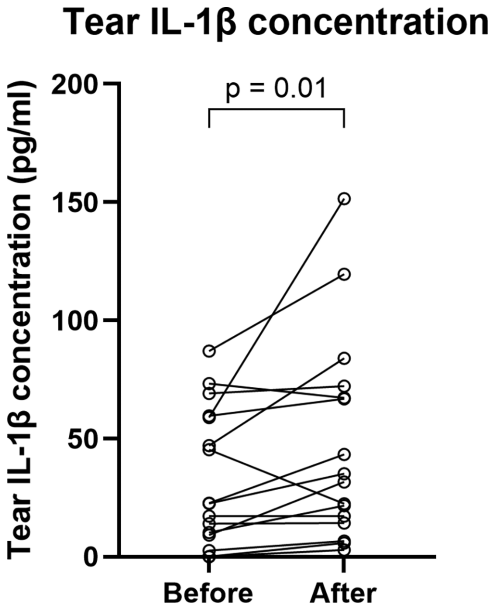

Figure 4. IL-1β concentration (pg/mL) in tears of participants ($n = 16$) before and after 15 minutes of simulated wildfire smoke exposure. Tears could not be collected from participants 13 and 17.

and 120.8 cells/mm^2 (IQR, 87.5–210.4 cells/mm^2) 48 hours after smoke exposure (Fig. 3), but this change was not statistically significant ($P = 0.18$). Goblet cell density decreased in 8 of 12 participants and increased in 4 participants.

Associations Between Signs and Symptoms and the Effects of Age and Gender

The increase in dryness after smoke exposure was significantly associated with the increase in temporal conjunctival redness ($r = 0.70$; $P = 0.001$). No other significant correlations were found.

The increase in discomfort before and after smoke exposure differed with age ($F = 7.327$; $P = 0.017$) but the three-way Time × Gender × Age interaction was not significant. Thus, older participants were more likely to experience discomfort from smoke exposure compared with younger participants, but there was no difference for males and females. No other signs or symptoms significantly interacted with gender, age, and exposure to smoke.

Discussion

This study is the first to demonstrate the adverse ocular surface effects of exposure to wildfire smoke in humans by successfully simulating the air quality (including PM2.5 concentration) of severe wildfires. Increased ocular symptoms reported after acute exposure to simulated wildfire smoke were accompanied by increased corneal and conjunctival staining, limbal and conjunctival redness, palpebral roughness, and upregulation of tear film pro-inflammatory cytokine IL-1β.

The finding of increased ocular symptoms after smoke exposure aligns with observational studies showing that ocular symptoms are commonly reported after exposure to different types of smoke.[11–13,37–39] Eye irritation was the leading symptom reported by adults and children after wildfire episodes in South America, whereas dry and stinging eyes were commonly reported by Australian wildland firefighters after occupational smoke exposure.[11,12] Ocular surface discomfort and irritation has also been reported in women using open fire stoves for cooking and in children exposed to second-hand tobacco smoke.[13,37]

The increase in ocular surface staining and worsening of tear stability observed provides the first evidence of damage to the ocular surface caused by exposure to wildfire smoke in humans. Based on animal and in vitro studies, these changes could be attributed to oxidative stress-mediated apoptosis of corneal and conjunctival cells.[40,41] A longer duration of exposure (weeks to months) to PM2.5 has been found to induce meibomian gland obstruction and dropout of glands in mice, which reduces the quality and quantity of meibum production.[42,43] These adverse changes are not exclusive to wildfire PM2.5; ocular surface staining, tear evaporation, tear instability. and increased tear lipid spread time have also been reported with tobacco smoke exposure.[44] Goblet cell density was also found to be reduced after cigarette smoke exposure[44] and may not recover within 48 hours after exposure based on the current study results. The current study was not sufficiently powered to detect whether goblet cell density recovers 48 hours after exposure. The findings of this study, however, have shown that future investigations with a larger sample size (minimum $n = 46$) would be required to confirm how goblet cell density is affected and recovers over time (48 hours) after smoke exposure.

The increase in conjunctival and limbal redness and tear proinflammatory IL-1β in this study suggests that wildfire smoke exposure induces an inflammatory response of the ocular surface, confirming previous findings only shown in vitro and in animal studies.[19,20] In rodent models, the NLRP3-inflammasome pathway, which includes IL-1β, has been shown to be involved in mediating the ocular surface inflammatory response to PM2.5.[18,43] Allergic, neurogenic, and cytokine-based immune responses at the conjunctiva can trigger release

of vasodilatory mediators, resulting in acute conjunctival hyperemia.[45] The association of ocular dryness symptoms with bulbar conjunctival hyperemia in this study suggests that the burden of ocular symptoms associated with wildfire smoke could be reduced therapeutically by targeting the ocular surface inflammatory response.

Inferior palpebral conjunctiva changes found in this study are consistent with allergic conjunctivitis cases previously shown to occur with increased PM2.5 concentrations.[46,47] This finding is supported by mouse studies showing increased eosinophils and histamine at the palpebral conjunctiva after PM2.5 exposure.[20,48] The increased inferior palpebral redness and roughness measured in the current study may be a precursor for similar immune cell infiltration of the palpebral conjunctiva. Further research is required for a more comprehensive understanding of the inflammatory process, including the atopic response occurring at the human ocular surface after wildfire smoke exposure. This work could help to explain how environmental exposure to wildfire smoke can cause ocular surface dysfunction and disease.

Human exposure to controlled levels of fresh biomass smoke achieved in this study established a new tool for research on the health impacts of wildfire smoke. The exposure technique at the Flammability Laboratory offers a significant improvement over existing models, which have previously delivered human ocular exposure to cigarette smoke through improvised cardboard box chambers, and animal exposure to PM2.5 through eyedrops.[44] Furthermore, the controlled environment inside the laboratory ensures that participants are not exposed to adverse airflows caused by outdoor wind, ventilation, or air conditioning systems that can affect ocular surface symptoms and signs. The use of natural bushfuels also ensures that any impacts measured at the ocular surface represent the true effects of wildfire smoke on the ocular surface in community.

A limitation of this study was the inability to mask participants and examiners, and this factor could have biased the measurement of symptoms and signs. Sham exposure studies have inherent challenges owing to the distinct smell and visibility of smoke. Investigator masking could be achieved by conducting ocular assessments in a location distant from the Flammability Laboratory, ensuring that examiners remain unaware of which participants have been exposed to smoke. Furthermore, noxious gas concentrations, which are known to be released during biomass burns, were not measured in the Flammability Laboratory. Their possible impact on the ocular surface was, therefore, not characterized.

Implications for Research and Policy

This study explored the impact of short-term exposure to very high levels of PM2.5 on the ocular surface. The PM2.5 concentrations that communities are exposed to during wildfire events are typically lower; however, the duration of exposure can sometimes extend to weeks. Further research is needed to evaluate the impacts of a longer duration of exposure as well as ascertaining the PM2.5 concentration thresholds at which the observed ocular surface responses occur. Further characterization of the tear inflammatory response to smoke exposure is required to develop a comprehensive understanding of the pathophysiology driving the clinical response. This process includes assessing changes in other tear inflammatory mediators involved in the inflammatory cascade using multiplex methods. Such mediators include those identified in vitro and in cohort studies to be implicated in urban air pollution-related ocular surface disease.[49] Challenges related to low tear volumes collected may be overcome with advanced proteomics analyses such as Olink technology, which can be used to conduct multiplex immunostudies with tear sample volumes of less than 4 µL.[50]

This study highlights a previously unrecognized need to understand and generate better guidance on how best to avoid, mitigate, and manage the effects of wildfire smoke on the ocular surface. Eye washing with a commercial solution has been shown to reduce tear film inflammatory mediators and prevent ocular surface staining in mice exposed to PM.[51] Many questions, however, remain unanswered. Indoor air filtration devices can improve respiratory health outcomes during wildfire episodes[52]; however, whether air filtration can similarly protect the ocular surface from wildfire induced damage is not known. Artificial tears and medicated eye drops, including those with anti-inflammatory action, may also prove useful in mitigating the adverse effects of wildfire smoke. Smoke exposure laboratories such as the Flammability Laboratory could be used to investigate these questions. Generating this evidence so that guidance can be developed for practitioners involved in managing wildfire smoke-induced ocular surface damage is urgently needed.

Conclusions

This study is the first to demonstrate that exposure to wildfire smoke causes ocular symptoms and adversely affects the ocular surface. Given the increase in frequency and severity of wildfires globally, public

health warnings regarding the adverse effects of wildfire smoke on the ocular surface may now be warranted. In addition, further investigations as to which therapeutic options may best prevent or mitigate smoke induced ocular surface damage are urgently needed.

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