Ocular Surface Symptoms in Veterans Returning From Operation Iraqi Freedom and Operation Enduring Freedom

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PURPOSE. To correlate situational exposures and psychiatric disease with self-reported ocular surface symptoms in a younger veteran population involved in Operation Iraqi Freedom and Operation Enduring Freedom (OIF/OEF).

METHODS. Cross-sectional study of all veterans evaluated in the OIF/OEF clinic between December 2012 and April 2013 who completed the dry eye questionnaire and screening evaluations for environmental exposures, posttraumatic stress disorder (PTSD), and depression. The main outcome measures were the influence of environmental exposure and psychiatric disease on ocular surface symptoms.

RESULTS. Of 115 participants, the average age was 33 years. While overseas, exposure to incinerated waste (odds ratio [OR] 2.67, 95% confidence interval [CI] 1.23–5.81, $P = 0.02$) and PTSD (OR 2.68, 95% CI 1.23–5.85, $P = 0.02$) were associated with self-reported ocular surface symptoms. On return to the United States, older age (OR per decade 2.66, 95% CI 1.65–4.31, $P = 0.04$) was associated with persistent symptoms and incinerated waste was associated with resolution of symptoms (OR 0.25, 95% CI 0.07–0.90, $P = 0.04$). When evaluating symptom severity, 26% of the responders complained of severe ocular surface symptoms, with PTSD (OR 3.10, 95% CI 1.22–7.88, $P = 0.02$) and depression (OR 4.28, 95% CI 1.71–10.68, $P = 0.002$) being significant risk factors for their presence.

CONCLUSIONS. PTSD was significantly associated with ocular surface symptoms both abroad and on return to the United States, whereas air pollution in the form of incinerated waste, was correlated with reversible symptoms.

Keywords: dry eye symptoms, depression, posttraumatic stress disorder, PTSD, environmental exposure

Dry eye syndrome (DES), a multifactorial disease of the ocular surface, affects nearly 4.9 million Americans aged 50 years and older.^{1,2} The estimated direct fiscal burden of DES approaches \$3.8 billion annually in the United States, with calculated indirect costs exceeding \$55 billion.³ Affected patients commonly complain of irritation, burning, foreign body sensation, and intermittent blurry vision.^{4,5} In addition to causing ocular morbidity, this disease has been shown to diminish work productivity and disrupt activities of daily living.^{3,6–9}

The global prevalence of DES has been estimated between 3.5% and 34.0%, with significant variation attributable to age and by the diagnostic criteria used.⁵ Recent reports have specifically identified a high prevalence of DES in US veterans, with 5-year period prevalence estimates ranging from 12% to 19%.^{7,10} In this population, an increased risk of DES was associated with female sex, older age, and psychiatric disease.^{7,10} Specifically, depression and posttraumatic stress disorder (PTSD) were associated with nearly a 2-fold increased risk of DES. The veteran population is unique due to their environmental and situational exposures. Specifically, veterans

with combat exposure have increased rates of PTSD and depression,^{11,12} which may make them more susceptible to developing DES.

As the prevalence of disease increases with age, most DES studies have focused on the elderly,^{13,14} with fewer studies concentrating on younger individuals.¹⁵ As our younger veterans, with situational risk factors and potential psychiatric disease, return from Iraq and Afghanistan, closing this knowledge gap is critical. This study, focusing on younger veterans involved in Operation Iraqi Freedom and Operation Enduring Freedom (OIF/OEF), correlated situational exposures and psychiatric disease with self-reported ocular surface symptoms.

METHODS

Study Population

The Miami Veterans Administration (VA) ophthalmology service initiated this study as a quality improvement project. Miami VA

Institution Review Board approval was later obtained to perform a chart review and link patient data to the questionnaires. The study was conducted in accordance with the principles of the Declaration of Helsinki. All veterans evaluated in the OIF/OEF clinic between December 2012 and April 2013 were eligible to participate. This clinic consists of all veterans who were abroad in either Iraq or Afghanistan and presented to the Miami VA for any form of medical assistance. All patients were invited to complete a dry eye questionnaire. Of the 500 patients seen in the OIF/OEF clinic during the time period, 28% (142) elected to fill out the questionnaire. To evaluate potential biases associated with incomplete patient ascertainment, demographic characteristics of nonresponders were collected weekly (every Tuesday).

Determination of DES

To assess for new and persistent symptoms, patients were asked two questions: (1) Did you experience NEW eye dryness/discomfort when you were overseas? (2) If yes, have these symptoms PERSISTED since your return? Furthermore, to assess symptom severity, each patient filled out the dry eye questionnaire 5 (DEQ5). The DEQ5 is a validated questionnaire consisting of five questions regarding the presence and severity of dryness, tearing, and discomfort over a 1-month recall period.¹⁶ The score ranges from 0 to 22, with 0 reflecting no ocular surface symptoms and 22 reflecting maximal symptoms. Per previously established guidelines, the presence of mild symptoms was defined as a score of 6 or greater and severe symptoms as a score of 12 or greater.

Determination of Patient Exposures and Comorbid Illness

Upon presentation to the OIF/OEF clinic, patients undergo a comprehensive screening process for environmental and combat-related exposures. Environmentally, veterans are asked about a history of exposure to incinerated waste. This exposure is a form of air pollution secondary to a warzone practice of burning organic waste with the release of noxious gases into the atmosphere. All patients are additionally screened for PTSD, depression, alcohol use, and traumatic brain injury (TBI). The validated screening tests used for the above disorders include PTSD 4-Questionnaire (PTSD 4Q; PTSD), Patient Health Questionnaire-2 (PHQ-2; depression), Alcohol Use Disorders Identification Test-Consumption (AUDIT-C; alcohol), and the traumatic brain injury screening questionnaire, respectively. Of the 142 patients who filled out the DEQ5, 115 had undergone the above screening assessment.

Medication information on the use of antidepressants and anxiolytics was extracted from the Miami VA administrative database. Antidepressants included selective serotonin reuptake inhibitors (e.g., citalopram, duloxetine), tricyclics (e.g., amitriptyline), atypicals (e.g., venlafaxine, trazodone, bupropion, mirtazapine), and monoamine oxidase inhibitors (e.g., selegiline, phenelzine). Anxiolytics included benzodiazepines (e.g., alprazolam), buspiron, and hydroxyzine.

Main Outcome Measures

The main outcome measure was the effect of environmental exposures and psychiatric disease on the risk of DES.

Statistical Analysis

All statistical analyses were performed using the SPSS 20.0 (SPSS Inc., Chicago, IL) statistical package. Logistic regression analyses (using ocular surface symptoms overseas, persistence

on return, and severe ocular surface symptoms [$DEQ5 \geq 12$] as the dependent variables) were used to evaluate the effect of environmental exposure and comorbid disease on DES. Multiple logistic regression analyses were performed to assess if the associations with each risk factor remained after adjusting for demographic and other clinical factors.

RESULTS

Study Population

Of the 115 patients included, mean age was 33 years (Table 1). Discharge information was available in 81 patients and ranged from 2001 to 2012, with most discharges occurring in the latter 4 years ($n = 66$, 81%). Twenty of the 115 respondents had a documented eye examination from the VA eye clinic. Of those, two carried an ocular diagnosis other than DES (i.e., pterygium and glaucoma). Fourteen of 76 patients were noted to be contact lens wearers. Clinical records were sampled on a weekly basis and a list of DEQ5 nonresponders was compiled. The mean age of the sampled 27 nonresponders (mean 45 years, SD 14) was significantly higher than that of the responders ($P < 0.0005$). There were no significant differences between the groups with respect to sex, race, and ethnicity.

Risk Factor Analysis for New Ocular Surface Symptoms While Abroad

Exposure to incinerated waste, PTSD, and depression were all individually associated with a 2.7-fold increased risk of reporting new symptoms that started while abroad (incinerated waste: 95% confidence interval [CI] 1.23–5.81, $P = 0.02$, PTSD: 95% CI 1.23–5.85, $P = 0.02$, depression: 95% CI 1.14–6.26, $P = 0.03$). Demographics, alcohol use, and TBI were not found to be significant risk factors. When all significant and nonsignificant variables were included in a forward stepwise logistic regression analysis (including antidepressant and anxiolytic use), exposure to incinerated waste and PTSD remained significant risk factors, each conferring an approximate 3-fold increased risk of reporting new symptoms (OR 3.17, 95% CI 1.30–7.77, $P = 0.01$ and OR 2.81, 95% CI 1.17–6.79, $P = 0.02$, respectively).

TABLE 1. Demographic and Clinical Characteristics of the Study Population

Number	115
Age, y, mean (SD)	33 (10)
Sex, male % (<i>n</i>)	87 (102)
Race	
White, % (<i>n</i>)	50 (71)
Black, % (<i>n</i>)	30 (43)
Ethnicity, Hispanic, % (<i>n</i>)	49 (69)
Dryness/discomfort started overseas, % (<i>n</i>)	40 (57)
Dryness/discomfort persisted upon return, % (<i>n</i>)	63 (36/57)
Mild or greater dry eye symptoms at clinic visit (DEQ5 ≥ 6), % (<i>n</i>)	61 (70)
Severe symptoms (DEQ5 ≥ 12), % (<i>n</i>)	26 (30)
Exposure to incinerated waste, % (<i>n</i>)	50 (55)
PTSD, % (<i>n</i>)	50 (55)
Depression, % (<i>n</i>)	31 (34)
Alcohol use, % (<i>n</i>)	22 (25)
TBI, % (<i>n</i>)	36 (34)
Antidepressant use, % (<i>n</i>)	27 (31)
Antianxiety use, % (<i>n</i>)	8 (9)

TABLE 2. Association Between Demographic and Clinical Factors and Severe Dry Eye Symptoms (DEQ5 $\geq$ 12) at the Time of OIF/OEF Clinic Visit

	OR	95% CI	P Value
Age, decade	1.38	1.14–1.67	0.10
Sex, female/male	0.83	0.21–3.26	0.79
Race, black/white	0.34	0.12–0.95	0.04
Ethnicity, Hispanic/Non-Hispanic	2.26	0.94–5.43	0.07
Exposure to incinerated waste, yes/no	0.90	0.37–2.20	0.82
PTSD, yes/no	3.10	1.22–7.88	0.02
Depression, yes/no	4.28	1.71–10.68	0.002
Alcohol use, yes/no	1.24	0.46–3.38	0.67
TBI, yes/no	1.30	0.49–3.46	0.60

Risk Factor Analysis for Ocular Surface Symptoms Persisting After Return to the United States

Older age was found to be a risk factor for persistent symptoms with each additional decade of age conferring a 2.7-fold increase in risk (95% CI 1.65–4.31, $P = 0.04$). On the other hand, exposure to incinerated waste was found to be protective, with a 75% reduced risk for persistent symptoms in those exposed (95% CI 0.07–0.90, $P = 0.04$). PTSD, depression, alcohol use, and TBI were not found to be significant risk factors. When all variables were included in the regression analysis, older age (per decade) remained a significant predictor of persistent symptoms (OR 4.49, 95% CI 2.25–8.94, $P = 0.03$).

Risk Factor Analysis for Severe Ocular Surface Symptoms During the Clinic Visit

DEQ5 scores were used to evaluate severity of ocular surface symptoms. The mean DEQ5 score was 7.77 (SD 5.5). Sixty-one percent of patients reported mild or greater ocular surface symptoms (DEQ5 $\geq$ 6) and 26% reported severe symptoms (DEQ5 $\geq$ 12). Black race, as compared with white, was associated with a 66% reduced risk of reporting severe symptoms (Table 2). Hispanic ethnicity, on the other hand, was associated with a 2-fold higher risk of reporting severe symptoms, although this was not statistically significant. PTSD and depression were associated with a 3.0- and 4.3-fold increased risk of reporting severe symptoms, respectively. When all variables were included in a regression analysis, depression (OR 4.53, 95% CI 1.40–14.5, $P = 0.01$) and antidepressant use (OR 7.5, 95% CI 2.13–26.4) remained significant predictors of severe symptoms.

Contact lens (CL) information was available in 76 patients (67%). In this limited subset, there was no difference in any DES metrics between CL wearers and nonwearers. Military discharge information was available in 81 patients (70%). In this subset, a longer duration between OIF/OEF clinic presentation to discharge was associated with 1.3-fold increased risk of severe ocular symptoms (95% CI 1.03–1.64, $P = 0.03$).

DISCUSSION

Limited data are available on DES prevalence in younger patients. Using a three-question symptom-based definition of DES, Uchino et al.¹⁵ evaluated Japanese high school adolescents between the ages of 14 and 18 and found that 22% reported symptoms. Using the same questions, Schaumberg et al.¹ found a prevalence of 3.9% in men (age 50 to 54)² and 5.7% in women (younger than 50) in a US population. A prior study

using the DEQ5 questionnaire to assess ocular surface symptoms in older veterans found that 26% complained of severe symptoms.¹⁷ Although the current study was not designed as a prevalence study, the finding that 26% of younger veterans reported severe symptoms suggests that they may be as susceptible to DES as older veterans.

Our study is unique, as it evaluated ocular surface symptoms in a young veteran population with recent combat and environmental exposure. We found that the presence of PTSD and depression affected the risk of having ocular surface symptoms both abroad and on return to the United States. Three prior studies, all detecting PTSD and depression via International Classification of Diseases (ICD) coding,^{7,10,18} found a positive correlation between both psychiatric disorders and DES. This study adds to the existing literature, as PTSD and depression were systematically screened for as opposed to relying on ICD coding. Relative to the general population, patients with depression and PTSD report higher rates of body pain.^{19,20} Via a similar mechanism, it is plausible that these psychiatric disorders alter the perception of ocular surface discomfort with a resultant increase in reported ocular surface symptoms.

Exposure to incinerated waste, a practice of burning organic refuse with release of dioxin and furan emissions, is a unique exposure in veterans.²¹ Both gases are considered noxious by the Environmental Protection Agency but their effect on the ocular surface is not well understood. In our population, exposure to incinerated waste significantly increased the risk of ocular surface symptoms while abroad. It can be postulated, however, that the exposure had a transient effect on the ocular surface, given its association with symptom resolution. Previous studies have also demonstrated the importance of environmental factors in DES, such as air pollution,^{22,23} volcanic eruption,²⁴ saw mill dust,^{25,26} industrial chemicals,²⁷ and sulfur mustard exposure during warfare.²⁸ Taken together, these findings suggest that air pollution does play a role in DES, and our study suggests that extrication from pollution can be a potential therapeutic solution.

As with all retrospective reports, however, our study has limitations that need to be considered when interpreting the study results. Our study relied on patient self-report without an examination to confirm objective findings of dry eye. As such, there may have been variables other than DES (e.g., pterygium, allergy) that could have affected symptoms. Additionally, all patients with asymptomatic dry eye symptoms would be missed in this study. We also did not have information on other environmental factors that may have affected the ocular surface, such as low humidity and/or exposure to sand storms. Furthermore, the response rate in the OIF/OEF clinic was low, which may have introduced bias. The aim of our study, however, was to assess for DES risk factors in a younger veteran population, a goal that does not rely on complete ascertainment. Finally, our patient population, with a higher proportion of individuals of Hispanic ethnicity, a group previously recognized to have increased dry eye symptoms,¹² may not be representative of other US veteran populations.

With these limitations in mind, this study supports an association between PTSD and depression and ocular surface symptoms in a young veteran population. This study highlights the need for further research to examine the mechanisms by which mental illness affects ocular surface symptoms. In the meantime, with nearly 900,000 OIF/OEF veterans accessing VA health care since 2001,²⁹ a large number of returning veterans may have unrecognized morbidity secondary to DES. This study suggests that veterans with PTSD and depression, irrespective of age, should be systematically screened for ocular surface symptoms and potentially referred to an eye care provider for further evaluation.

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