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BRIEF REPORT

Long-Term Effects of Chemical Warfare on Post-traumatic Stress Disorder, Depression, and Chronic Medical Conditions in Veterans

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Abstract
We investigated the association between exposure to chemical warfare and chronic mental/physical conditions. This was a secondary analysis of data from a case–control study on Iranian male veterans. Participants with neuropsychiatric disorders other than depressive/anxiety disorders, anatomical defects, or malignancies were excluded. Compared to non-exposed veterans, exposed veterans demonstrated significantly higher odds of PTSD [OR (95% CI) = 5.23 (1.98–13.85)], hypertension [OR (95% CI) = 5.57 (1.68–18.48)], coronary heart disease [OR (95% CI) = 6.8 (1.62–28.49)], and diabetes [OR (95% CI) = 3.88 (1.35–11.16)], and marginally higher odds of moderate to severe depressive symptoms [OR (95% CI) = 2.21 (0.93–5.28)]. This study provides preliminary evidence on association of exposure to chemical warfare with long-term mental disorders as well as chronic medical conditions.

Keywords Chemical warfare · Post traumatic stress disorder · Hypertension · Coronary heart disease · Veterans

Introduction

Chemical warfare has been used since World War I (Evison et al. 2002), and in particular during Iran–Iraq war from 1983 to 1988 (Razavi et al. 2014). According to the reports by Foundation of Martyrdom and Veterans, about 30,000 chemically-injured Iranian veterans of Iran–Iraq war have received treatment yet with sulfur mustard (SM) and nerve agents comprising the major portion of chemicals (Razavi et al. 2014). It is documented that SM and its analogues has strong cytotoxic effects, decrease serum levels of albumin and paraoxonase-1 activity, and increase serum levels of C-reactive protein which may induce atherosclerosis and CHD (Faizi et al. 2007). There are numerous lines of evidence on acute and chronic effects of chemical warfare (Ghasemi et al. 2013; Razavi et al. 2012), among them reports on long-term mental disorders such as post-traumatic stress disorder (PTSD) and depression (Ahmadi et al. 2010; Hashemian et al. 2006), and chronic medical conditions such as hypertension (HTN), coronary heart disease (CHD), and diabetes mellitus (Balali-Mood et al. 2011; Faizi et al. 2007; Fujiyoshi et al. 2006; Gholamrezanezhad et al. 2007; Henriksen et al. 1997; Kehe and Szinicz 2005; Rohani et al. 2010).

There is strong evidence on the association of cardiovascular diseases, including myocardial infarction (Kubzansky et al. 2007) and ischemic heart disease (Ahmadi et al. 2011; Coughlin 2011; Vaccarino et al. 2013), with PTSD and depression in veterans which is discussed in detail elsewhere (Moazen-Zadeh et al. 2016). Meanwhile, there has been only few reports concerning long-term association of chemical warfare agents with comorbid PTSD, depression, and related cardiovascular diseases or diabetes mellitus (Ford et al. 2004; Kim et al. 2003; Schnurr et al. 2000), among which only one study compared exposed and non-exposed

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veterans regarding orange agent (Kim et al. 2003). Previously, Moazen-Zadeh et al. reported higher prevalence of exposure to chemical warfare as well as higher blood pressures and depressive symptoms in veterans with PTSD compared to control veterans (Moazen-Zadeh et al. 2016). We investigated potential association between exposure to chemical warfare and PTSD, depression, HTN, CHD, and diabetes in veterans of Iran–Iraq war.

Methods

This study was approved by institutional review board of Aja University of Medical Sciences based on World Medical Association (Declaration of Helsinki, as revised in Brazil 2013) code of ethics. Informed consent was obtained from all participants. It was a secondary analysis of data from a previous case–control study (Moazen-Zadeh et al. 2016). In the original study 50 patients with PTSD and 50 individuals as controls were selected based on convenience sampling from veterans of Iran–Iraq war who were referred to outpatient psychiatry clinic, Besat Medical Center, Aja University of Medical Sciences, from 2014 to 2015. Participants in both groups were matched based on age ± 3 years, and were excluded in case they met any of the following conditions: deployment duration of less than 3 months, malignancies, severe anatomical defects, history of PTSD before deployment to Iran–Iraq war, and concurrent psychiatric disorders except for anxiety/depressive disorders. PTSD diagnosis was confirmed by a military psychiatrist experienced in diagnosis and treatment of patients with PTSD for more than 10 years based on DSM-IV-TR criteria (American Psychiatric Association 2000). Medical records, available lab data, comprehensive and detailed history taking, and clinical examinations were sources of data for this study. In specific, exposure to chemical warfare and history of chronic diseases were extracted from the explicitly documented and archived medical records. The chemical warfare used during Iran–Iraq war mostly included SM and nerve agents such as Sarin. Participants were provided with essential explanations to fill the Beck Depression Inventory II (BDI-II) (Beck et al. 1996) by a trained author, who was also responsive to the participants' potential questions. This questionnaire is comprised of 21 items each scored 0–3 with higher scores indicating higher depressive symptoms. In this study, BDI-II scores were dichotomized to make a distinction between minimal to mild (BDI-II ≤ 19), and moderate to severe depressive symptoms (BDI-II > 19). Data were reported as median (range) or count (%) where appropriate. Odds ratio [OR (95% CI)] was the choice measure of effect size. Mann–Whitney U test, Fisher's exact test, and binary logistic regression models for prediction of chronic medical conditions were applied using SPSS 19.0 software (IBM CO., USA). Two-tailed p values < 0.05 were considered significant. History of HTN, CHD, and diabetes were the dependent variables for the three regression models. Status of PTSD, BDI-II score category, and exposure to chemical warfare were the independent variables in all the three models.

Results

The study sample included 30 veterans exposed to chemical warfare agents, and 70 non-exposed veterans. No significant difference was detected between the two groups concerning age [exposed = 52.00 (43.00–63.00); non-exposed = 49.00 (40.00–74.00); p = 0.654], body mass index [exposed = 27.35 (17.30–35.42); non-exposed = 26.88 (21.77–33.62); p = 0.542], or history of smoking [exposed = 13 (43.33%); non-exposed = 29 (41.43%); p = 1.000]. Frequency of moderate to severe depressive symptoms was marginally higher in veterans with exposure to chemical warfare compared to the non-exposed veterans [exposed = 17 (56.67%); non-exposed = 26 (37.14%); p = 0.082; OR = 2.21 (0.93–5.28)]. PTSD (exposed = 23 (76.67%); non-exposed = 27 (38.57%); p = 0.001; OR = 5.23 (1.98–13.85)], HTN [exposed = 9 (30.00%); non-exposed = 5 (7.14%); p = 0.005; OR = 5.57 (1.68–18.48)], CHD [exposed = 7 (23.33%); non-exposed = 3 (4.29%); p = 0.007; OR = 6.80 (1.62–28.49)], and diabetes (exposed = 10 (33.33%); non-exposed = 8 (11.43%); p = 0.020; OR = 3.88 (1.35–11.16)] were significantly more frequent in the veterans with history of exposure to chemical warfare agents compared to non-exposed veterans. Based on logistic binary regression models, exposure to chemical warfare was an independent predictor for HTN and CHD but not for diabetes, while PTSD and depression did not show such an independent predictive value for any of the chronic medical conditions.

Discussion

We found dramatically higher frequencies for PTSD, diabetes, CHD, and HTN in veterans exposed to chemical warfare agents compared to non-exposed veterans. Consistent with our findings, Rohani et al. (2010) reported higher frequency of ischemic heart disease in Iranian veterans with history of exposure to chemical warfare compared to the control group. Gholamrezanezhad et al. (2007) found a significant difference in scintigraphic pattern of myocardial perfusion between patients intoxicated with SM and controls, which was consistent with either coronary artery disease or cardiomyopathic changes.

Faizi et al. (2007) demonstrated higher rates of physical disability and lower age of coronary artery bypass grafting in veterans exposed to SM compared to non-exposed veterans; however, no difference was found for diabetes or HTN. Balali-Mood et al. (2011) reported positive correlation between severity of SM induced disability and blood pressure as well as diabetes. Henriksen et al. (1997) and Fujiyoshi et al. (2006) indicated correlation between dioxin exposure and diabetes mellitus. Furthermore, increased prevalence of PTSD and severe depressive symptoms is reported in civilians exposed to chemical warfare compared with those exposed to non-chemical/non-nuclear warfare (Hashemian et al. 2006). Also, a long term investigation of Tokyo metro sarin attack showed higher prevalence of PTSD in victims compared to normal population (Ahmadi et al. 2010). Finally, the only study similar to our study, demonstrated strong association of exposure to chemical warfare with PTSD, mood disorders, HTN, ischemic heart disease, and diabetes when comparing exposed and non-exposed Korean veterans; however, the investigated chemical was orange agent (Kim et al. 2003).

Inconsistent with other reports, a study on gulf war veterans exposed to low dose chemical agents did not found a prominent difference in health measures, hospitalization, or disability between exposed and non-exposed veterans (McCauley et al. 2002). As a potential explanation, it is important to consider that access to protective equipment during wartime and to post-exposure medical resources can considerably influence the consequences of exposure which would be a source of difference between findings of studies on Middle Eastern veterans and those by McCauley et al. (2002) on American veterans.

This study is subject to some limitations including relatively small sample size, using secondary analysis rather than an original design, lack of specific biological markers for chronic diseases, not using a scale for measurement of anxiety symptoms, lack of focused screening for potential current workplace exposure to chemicals or heavy metals, and lack of information on the exact chemical agent that each veteran was exposed to.

Hereby we provided further evidence on the potential link between exposure to chemical warfare, and long-term comorbid mental disorders as well as chronic medical conditions. Despite of the limitations, our findings have implications for future comprehensive investigations as well as further measures for improving the healthcare quality in this population. Veterans with exposure to chemical warfare may benefit from more frequent clinical assessments, as well as long term prevention programs for cardiovascular and related diseases.

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Compliance with Ethical Standards

Conflict of interest The authors of this study declare that they have no conflict of interest.

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