

Delayed Neurological Complications of Sulphur Mustard and Tabun Poisoning in 43 Iranian Veterans

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Abstract: Delayed neurotoxic complications of chemical warfare agents (CWA), such as sulphur mustard (SM) and tabun, in human beings have not been reported in detail. We thus aimed to investigate possible neurotoxic complications of these agents in Iranian veterans 22–27 years after exposure. After co-ordination with the veteran foundation and obtaining the approval of the medical research ethics committee, 43 Iranian veterans with late complications of CWA exposure during the Iran–Iraq conflict were studied after obtaining signed written informed consent. Demographic and clinical findings were recorded on pre-designed forms. Neurological examination was performed by a neurologist. Routine biochemical tests were performed for all the patients. Electromyography (EMG), nerve conduction velocity (NCV) and electroencephalography (EEG) were carried out as clinically indicated. The majority of the patients (38) had been exposed to SM and only five patients to tabun. Hyperaesthesia was the most objective finding (72.1%). Fatigue (93%), paraesthesia (88.3%) and headache (83.7%) were the most common subjective findings in the patients. Sensory nerve impairments, including paraesthesia (88.3%), hyperaesthesia (72.1%) and hypoesthesia (11.6%), were the most common observed clinical complications. EMG and NCV were impaired in seven patients (16.3%) who were all SM-exposed patients but did not show any significant correlation with organ complications. EEG was negative even in the seized patients. Cholesterol, LDL and triglyceride levels were significantly above the normal ranges. Late neurological complications of CWA, particularly SM poisoning, are considerable even after three decades of exposure and require medical attention.

Chemical warfare agents (CWA) have caused considerable damage to mankind and are still a major concern worldwide, especially as terroristic menace. According to the World Health Organization (WHO), CWA have induced 1.3 million casualties, including 90,000 deaths [1]. CWA were widely used during World War I and in the Iran–Iraq conflict between 1983 and 1988. Widespread chemical war gas attacks by the Iraqi army against the Iranian combatants left more than 100,000 military and even civilian casualties [2] as well as 25,000 mortalities [3]. The first use of a nerve agent (tabun) in the war by the Iraqi army was in February 1984 in Majnoon Island poisoning several thousands and caused 300 deaths within just 30 min. of exposure [4]. The first use of sulphur mustard (SM) by Iraq was in November 1980 in Susangerd, which was continued by several attacks in Halabja (March 1988) as well as in Hawizah Marsh (March 1985), Sumar/Mehran (October 1987), Al-Faw (February 1986 and April 1988) and on many west border cities of Iran. Over 30 chemical attacks in civilian areas were reported during the war. The last SM attack by Iraqi troops was in July 1988 at the south central border of Oshnavieh. A chemical war attack in March 1988 in Halabja, a Kurdish town in Iraq, caused rapid deaths from exposure to sarin and other CWAs, including SM [4–6].

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Nerve agents (NA) are organophosphorous (OP) compounds, which irreversibly bind the enzyme acetylcholine esterase (AChE) leading to accumulation of toxic levels of neurotransmitter acetylcholine (ACh) at the neuromuscular junction. ACh stimulates muscarinic and nicotinic receptors in the autonomic nervous systems at the neuromuscular junction [5]. There is also evidence proposing non-cholinergic mechanisms in the central nervous system at a dose approaching LD₅₀ [5]. Soman and tabun inhibit catabolism of GABA, which explains the occurrence of seizures as a complication [7]. It seems that amygdala is more affected than other parts of the CNS [8]. Compared with sulphur mustard, nerve agents have relatively high acute lethal toxicity and are known as lethal agents and the deadliest CWA [9]. Initial neurological symptoms and signs of nerve agent poisonings are vast, including ataxia, anxiety, headache, insomnia, apathy, tremor, giddiness and amnesia [4,10–12]. The acute toxicity of OP is attributable to the inhibition of AChE and the consequent accumulation of ACh in the central and peripheral nervous system synapses [13]. Balali and Navaeian [14] have reported CNS excitation-caused convulsions in six Iranian veterans who were hospitalized for acute OP nerve agent intoxication. Koc *et al.* [15] have also reported segmental demyelination and axonal degeneration in distal parts of the lower extremities in two patients with acute organophosphate intoxication. Besides, depression of the respiratory and vasomotor centres as a result of this may be life-threatening [4,16].

Sulphur mustard is an alkylating agent that induces more delayed complications than nerve agents on different organs,

particularly the respiratory tract, the nervous and immune systems, skin and eyes [17]. SM absorption will lead to chromatin aberration as well as inhibition of DNA, RNA and protein synthesis [18].

Balali-Mood *et al.* [19] observed 77% abnormal NCV pattern, especially in the sensory nerves and lower extremities, and incomplete interference with normal amplitude in 15% of 43 patients who underwent EMG for possible delayed neuromuscular complications of SM poisoning.

Inactivation of neurotoxic esterase can lead to organophosphate-induced delayed neuropathy (OPIDN) within 2–4 weeks after exposure and characterized by distal paraesthesia, impaired reflexes and progressive weakness [20]. The other late neurological effect that occurs 1–4 days after exposure and is characterized by reversible weakness in proximal muscles, particularly chest muscles, is called intermediate syndrome [21]. Mechanisms of IMS include prolonged AChE inhibition, muscle necrosis, down-regulation or desensitization of post-synaptic ACh receptors, failure of post-synaptic ACh release and oxidative stress-related myopathy [13]. Inhibition of an enzyme in the central nervous system called neuropathy target enzyme (NTE) may pull the trigger in these two syndromes [22]. However, it has recently been reported that determination of NTE is not valid for the evaluation of OPIDN [20]. Delayed onset encephalopathy and coma have also been reported by Peter *et al.* [23] in acute organophosphate poisoning.

Despite early treatment and the use of urgent countermeasures (atropine and oxime for OP nerve agents), it may take long to recover from or even alleviate the complications. Although neurotoxic complications of OP nerve agents are considerable, there are only sparse reports in the literature. Delayed neurological complications of SM have previously not been investigated in detail. We thus aimed to study delayed neurological complications of sulphur mustard and tabun poisonings in Iranian veterans, by means of standard neurological investigations.

Materials and Methods

After co-ordination with the veteran foundation of Korassan Razavi and approval of the University Medical Research Ethics Committee, the patients with more than 25% disabilities caused by CWA poisoning and who had signed the informed consent were investigated. Disability percentages were determined by a medical committee of the foundation for all CWA veterans using severity of the complications in different organs. There are in fact three kinds of disability: physical, chemical and total. Physical includes all physical injuries and post-traumatic stress disease (PTSD). Chemical contains disabilities attributable to CWA exposure, either SM or the nerve agent tabun. Total means the sum of both physical and chemical disabilities. Disability percentages are updated regularly by the foundation and any changes in percentages are recorded. Patients with a history of diabetes mellitus, chronic alcoholism and opium administration, uraemia and any other systemic disorders, including malignancies and congenital malformations, were excluded from the study.

Every Saturday, 4–5 CWA veterans were recruited from the veteran foundation to the medical toxicology research centre, Emam Reza hospital, Mashhad, Iran, for about 3 months in early 2010. As the first step, 5-ml blood samples were taken from the brachial vein in the morning after 12-hr fasting for laboratory tests including liver function

tests and lipid profile. Biochemical tests were performed by auto analyser (Abbott Analyzer, Chicago, IL, USA) in the biochemical laboratory of Emam Reza hospital, Mashhad, Iran. After breakfast serving, demographic and CWA exposure information as well as clinical history and primary clinical general examinations including vital signs and BMI were entered onto pre-designed forms by a senior medical student (1st author). Complete neurological examination was performed by an experienced neurologist (2nd author) for all the patients and recorded by the senior medical student on the clinical forms. Further para-clinic experiments, including EMG, NCV and EEG, were performed as clinically indicated. EMG and NCV were carried out by a physiatrist (3rd author). EMG was performed for all four extremity muscles. NCV was also carried out in both upper (ulnar and median nerves) and lower (peroneal and tibial nerves) extremities. EMG and NCV were performed by the Myoto & TOENNIES Multiliner device and interpreted by the physiatrist.

Data on quantitative characteristics are expressed as mean \pm standard deviation (S.D.). Data on qualitative characteristics are expressed as numbers and percentage values as indicated. The patients were divided into two groups according to the type of exposure, SM and tabun. Comparisons between the two groups were made using the independent sample Student *t*-test (continuous data) and Fisher's exact test (nominal data). Spearman correlation coefficients and linear regression models were used for evaluation of the correlations between two quantitative variables. Test of significance was two-tailed. Comparison of the average laboratory tests with their maximum standard levels was performed by the one-sample Student *t*-test and Wilcoxon's test, and the test of significance was one-tailed. The Alpha error was set at 0.05. Analyses were carried out by the Statistical Package for the Social Sciences software (SPSS version 16, Chicago, IL, USA) and Prism Version 3.02 (Graph Pad Software, San Diego, CA, USA) for the Wilcoxon test.

Results

Subjects.

Forty-three patients with late complications of CWA exposure and with mean disability percentage of $56 \pm 1.31\%$ were investigated. The patients were all married men with a mean age of 50.6 ± 9.1 years. The majority of the patients (38 cases) had been exposed to SM and only five patients had nerve agent poisoning acquired in Majnoon Island, which was subsequently diagnosed as tabun. Demographic data and clinical history of the patients are summarized in table 1.

Late clinical neurological complications.

Subjective findings were more common than the observed neurological disorders. Hyperaesthesia (72.1%) was the most objective finding in the patients, while chronic fatigue was the most common subjective finding and observed in 93% of the patients. Paraesthesia (88.3%) and chronic headache (83.7%) were in the next places of subjective findings.

As described in table 2, sensory nerve impairment was the most striking late neurological clinical complication because hyperaesthesia and hypoesthesia (as a sign) were observed in 72.1% and 11.6%, respectively, and paraesthesia (as a symptom) in 88.3% of the patients.

Olfactory and auditory nerves were the most involved cranial nerves, because 53.4% reported some degree of hearing loss and 41.9% reported hyposmia. High blood pressure (sys-

Table 1.

Summary of demographic and clinical history findings of 43 male veterans with delayed neurological complications of sulphur mustard (SM) and tabun poisonings in Mashhad, Iran.

Demographic characteristics (unit)	Results (mean ± S.D.)	Clinical histories (unit)	Results (mean ± S.D.)
Age (years)	50.3 ± 8.7	Type of exposure	
		SM	38
		NA	5
Height (cm)	169 ± 0.052	Age at exposure time (mean ± S.D.)	23.5 ± 8.1
Weight (kg)	75.75 ± 12	Physical disability percentage (mean ± S.D.)	4.36 ± 8.5
BMI (kg/cm ²)	26.56 ± 4	Chemical warfare agents (CWA) disability percentage (mean ± S.D.)	53.2 ± 17
Number of children (median)	3	Total disability percentage (mean ± S.D.)	56.8 ± 13.12
Educational status		History of hypertension	17 (39.5%)
More than 11 years	11		
Less than 11 years	32	History of myocardial infarction	4 (9.3%)
Employed	30	History of intraocular pressure (IOP)	31 (72.1%)
Retired & unemployed	13		

Table 2.

Common observed signs and symptoms in 43 male veterans with delayed neurological complications of sulphur mustard and tabun poisonings in Mashhad, Iran.

Symptoms	N (%)	Signs	N (%)
Fatigue	40 (93.0)	Hyperaesthesia	31 (72.1)
Paraesthesia	38 (88.3)	Impaired Deep-tendon reflex	25 (58.1)
Headache	36 (83.7)	Tremor	23 (53.4)
Weakness	35 (81.3)	high blood pressure	17 (39.5)
Impotency	32 (74.4)	Palmomental reflex	11 (25.5)
Loss of concentration	28 (65.1)	Babinski reflex	8 (18.6)
Loss of memory	25 (58.1)	Glabella reflex	6 (13.9)
Emotional stability	23 (53.4)	Hypoesthesia	5 (11.6)
Hearing loss	23 (53.4)	Paresis	5 (11.6)
Depression	19 (44.1)	Dysarthria	3 (6.9)
Hyposmia	18 (41.9)	Ataxia	2 (4.7)
Insomnia	13 (30.2)	Nystagmus	1 (2.3)
Anxiety	12 (27.9)	Paralysis	1 (2.3)
Sphincter disorder	10 (23.2)		
Loss of libido	8 (18.6)		
Seizure	2 (4.6)		

tolic pressure >139 and diastolic pressure >89) was observed in 39.5% of the cases. Cyanosis, coma, myoclonus, speech disorders, sleepiness and apathy were not observed in any of the patients. Clinical neurological complications are presented in table 2.

Mean cholesterol, LDL and triglyceride profile were significantly above the cut-off points among the biochemical assays (*p*-values of 0.002, 0.017 and 0.041, respectively). Data on biochemical findings are presented in table 3. Means of the liver function test enzymes were not higher than the upper limits of normal range.

Electrophysiological findings.

Electromyography and NCV findings showed abnormal pattern in seven patients (16.3%) of twelve who had the clinical indication for the experiments. The chemical exposure was SM in all of the seven patients. Three patients had pure

Table 3.

Biochemical findings in 43 male veterans with delayed neurological complications of sulphur mustard and tabun poisonings in Mashhad, Iran.

Findings	Mean ± S.D.	Normal ranges ¹	<i>p</i> -value
SGPT	26.25 ± 1.18	0–40 U/l (optimal = 21)	0.999
SGOT	22.90 ± 9.80	0–31 U/l (optimal = 24)	0.999
LDH	460 ± 103.2	94–500 U/l	0.435
Total bilirubin	0.61 ± 0.26	0–1 mg/dl	0.999
Direct bilirubin	0.19 ± 0.06	0–0.3 mg/dl	0.999
Cholesterol	222.90 ± 3.47	<200 mg/dl	0.002
HDL cholesterol	38.57 ± 7.7	>39 mg/dl	0.258
LDL cholesterol	149.05 ± 3.33	<130 mg/dl	0.017
Triglyceride	188.44 ± 1.15	<150 mg/dl	0.041

¹Normal ranges are according to National Health and Nutritional Examination Survey, conducted by the National center for Health Statistics (NCHS), USA. SGPT, serum glutamate pyruvate transaminase; SGOT, serum glutamic-oxaloacetic transaminase; LHD, lactic dehydrogenase.

sensory polyneuropathy and four patients had sensory-motor distal polyneuropathy of axonal type. NCV-disrupted patterns were symmetric in both upper and lower extremities. EMG pathologies contained chronic polyphasic MUAP (motor unit action potential) in distal tested muscles, including tibialis anterior, peroneus longus, gastrocnemius, first dorsal interossei and opponens pollicis muscles.

Electroencephalography was performed in two patients according to their history of seizure. Type of epilepsy was idiopathic generalized tonic-clinic (history) and both the EEGs were normal at the time of experiment, when the patients took anti-epileptic medications. Both patients were intoxicated by tabun.

Correlations of demographic findings with the other data.

There was a significant correlation between the age and physical disability percentage ($r = 0.340$, $p = 0.038$) of the patients. The patients' age had also a significantly negative correlation with SGPT ($r = -0.353$, $p = 0.021$), total bilirubin ($r = -0.313$, $p = 0.038$) and direct bilirubin ($r = -0.367$, $p = 0.010$). BMI

and CWA disability percentages were negatively correlated ($r = -0.438$, $p = 0.015$). CWA disability percentages significantly differed from physical injuries ($p < 0.001$) but were correlated with the overall disability percentages ($r = 0.884$, $p < 0.001$). Patients with cranial nerve disorders (hearing loss and hyposmia) and positive palmomental reflexes had significantly higher age than the others at the exposure time ($p < 0.001$ and $p = 0.020$, respectively). Patients with chronic fatigue had lower age than the others at the exposure time ($p = 0.008$).

Correlations between neurological complications and disability percentages.

In this study, some neurological complications correlated with higher rates of disability percentages. Paraesthesia had correlation with overall, chemical and physical disability percentages ($p < 0.001$, $p < 0.001$, $p = 0.002$, respectively). Paresis and loss of libido showed significant correlations with physical disability percentage ($p = 0.002$ and 0.020 , respectively). Hypertension significantly correlated with chemical disability percentage ($p = 0.008$). Palmomental reflex significantly correlated with chemical and physical disability percentage ($p = 0.017$ and 0.013 , respectively). Glabella reflex had also significant correlations with overall war disability percentage ($p = 0.029$) and chemical disability percentage ($p = 0.006$). Babinski reflex did not have any significant correlation with disability percentages. Those who had disruption in both palmomental and glabella reflexes (six patients, 13.9%) were significantly older than the others ($p = 0.005$). They had more chemical and overall disability percentages ($p = 0.006$ and 0.029 , respectively) and also a higher SGPT value ($p = 0.019$). SM-exposed veterans were significantly older ($p = 0.008$) and had significantly more sensory nerve impairment ($p = 0.039$) in comparison with the patients exposed to tabun. Impaired EMG and NCV did not reveal any correlation with any other parameter. In the biochemical results, LDL showed significant reverse correlation with chemical disability percentage ($r = -0.442$, $p = 0.010$).

Discussion

Chemical warfare attacks by Iraqi troops during the Iran–Iraq war were atrocious acts, and organ complications of SM-exposed veterans can still be observed after three decades. The respiratory system, skin and eyes were reported to be the mainly affected organs after exposure [17]. Psychiatric disorders were also recorded but neurological complications were not reported at the late-phase of intoxication in SM poisoning [14]. However, neurological manifestations after nerve agent exposure as cholinergic syndromes and CNS depression are prominent [5]. Nerve agents trigger a much higher mortality rate than the blistering agent of SM and are less likely to cause chronic diseases. Mixed intoxication with both of the agents was not recorded, though not conclusively proved. All the NA patients were exposed in Majnoon Island in February 1984 and subsequently diagnosed as having been exposed to tabun. SM patients were intoxicated in different areas of the

country because of several SM attacks by Iraqi troops during the war. The dose of SM and tabun gas experienced by the veterans was sufficient to cause acute severe reactions (i.e. skin blistering), which were defined as high-dose exposure [24]. So, in this study, exposure is defined as high-dose exposure. However, the exposure dose cannot be measured exactly during warfare, especially when the gas spreads through the area and the combatants remain in the field for several days. In addition to the exposed dose, other factors can affect the severity of the complications such as temperature, humidity, wind direction, personal protective equipment and activity level of the soldier [25,26]. Hence, disability percentages that are estimated and routinely followed up by the veteran foundation can be an appropriate predictor to select severely exposed patients for this study.

All the veterans were poisoned via gas inhalation, and thus, influence of the other routes of entry [9,27] on neurological complications was eliminated.

Neurological examinations and diagnostic procedures revealed that late neurological complications of CWA poisoning are notable. However, subjective findings were more common than the observed neurological disorders, possibly due to financial gaining (malingering) of the veterans. Fatigue was the most observed symptom in our study (93%). Newmark [9] mentioned hypoxic encephalopathy as the most significant long-term neurological effect of organophosphates, caused by respiratory depression. Fatigue was also previously reported in other studies as one of the major late manifestations of organophosphate poisonings [11,28,29]. Engel *et al.* [30] described fatigue as one part of ‘post-war syndrome’ beside depression and chronic pain. Although fatigue probably occurs more often at higher age, we observed it to be significantly more prevalent in patients of lower age at the time of exposure (who were younger than the others at the time of the investigation). It could be explained by greater impact of ‘post-war syndrome’ at earlier age, with fatigue as one of its physical manifestations [30]. Sensory nerve impairments, including hyperaesthesia, hypoesthesia (as sign) and paraesthesia, (as a symptom) were the most common clinical complications and were observed significantly more often in the SM patients. In comparison with the adult neuropathy prevalence of 3.3–8% [31,32], we observed a prominently higher prevalence (72.1% hyperaesthesia and 11.6% hypoesthesia) of objective clinical sensory nerve impairment. The aetiology of neuropathy is related to both ageing processes and pathologies. It is difficult to separate ageing-associated changes and pathological manifestations. Diabetes mellitus, vitamin B12 deficiency, chronic alcoholism and cancer are the most commonly reported aetiologies [33]. Diabetes mellitus is the most common cause of neuropathy worldwide [34]. We excluded the patients with diabetes mellitus, alcoholism and any other systemic disorders including malignancies in this study. Age-related sensory neuropathy named as chronic idiopathic axonal polyneuropathy (CIAP) also includes neuropathies insidious, bilateral, of unknown aetiology which represents 15% of neuropathies in the elderly population beyond 60 years of age [33]. Average age in our study was 50.3, so CIAP does not appear to be a

contributing factor in the patients' neuropathies. Balali-Mood *et al.* [19] formerly reported 77.5% peripheral neuropathy in 43 severely SM-intoxicated Iranian veterans with more sensory than motor nerve dysfunctions. Even after electrophysiological procedures, approximately 50% of polyneuropathies remain unrevealed [34]. Thus, despite ruling out pathological and senile aetiologies of sensory neuropathy, we cannot thoroughly assume CWA exposure as the main aetiology. OPIND is the most significant delayed organophosphate-induced neuropathy, however, very rare [20]. It is a symmetrical sensorimotor axonopathy that is an extremely disabling condition in severe cases [5]. However, as the nerve agents are more lethal than disabling, there is no indication that survivors of nerve agents are at greater risk of neuromuscular problems [9].

Headache was the third most common symptom of the veterans, which is compatible with a previous report by Balali-Mood and Hefazi [18].

Impotency was recorded in 74.4% of the veterans, which is higher than reported by Amirzargar (2009). In his cohort study of 64 CWA patients two decades post-exposure, 14 cases of infertility (22.6%) were observed. Based on hormonal assay and histopathological evaluation of testes, he claimed that SM can be gonadotoxic and its chronic toxicity may be permanent. He assumed germ cells as the most susceptible gonadal cells to SM [35]. Ghanei *et al.* (2004) observed 10.3% of infertility among individuals 17 years post-SM exposure who were single at exposure and subsequently married. He concluded that SM exposure compared with a worldwide rate of 10–15% failed to correlate with increased risk of infertility [36]. We also observed loss of libido in 18.6% of the patients. The mechanism of intoxication in fertility problems is not well defined. As confounding variables, such as diabetes mellitus and chronic opium administration, were negative in all the patients, these could be attributed to chronic glucocorticoid treatments for their respiratory problems. In a review article by Moghadam-Kia and Werth [37], impotency, muscle weakness and high levels of lipid profiles were mentioned as side effects of chronic glucocorticoid administration. Overall, data addressing the reproductive toxicities of SM in human models are both lacking and contradictory [25].

Lack of concentration, which was observed in 65.1% of the patients, is in accordance with a previous report by Balali-Mood and Hefazi [18] as a common late complication in SM veterans. Page [38] also reported two significant complications of lacking concentration and sleep disturbances after CWA exposure in a telephone survey of 4022 military volunteers, which is similar to our findings of 30.2%.

In an observation on workers accidentally exposed to tabun and sarin (49 patients, 53 controls), CNS effects such as sleeping disorders, mood changes and easy fragility were reported as common complications [39]. In another study on 72 workers accidentally exposed to sarin, loss of concentration, mental confusion, giddiness and insomnia were common complications [40]. Common symptoms observed in up to 10 years' follow-up between affected and unaffected citizens in the Matsumoto incident in Japan were asthenopia and psychic symptoms including flashback, nervousness and loss of

concentration [11]. The latter complication was also high (65.1%) in our patients.

Hypertension had significant direct correlation with chemical disability percentage in our patients. High blood pressure can be a late complication of pulmonary diseases such as COPD (chronic obstructive pulmonary disease), which is a major problem among SM-intoxicated veterans. Considering the reverse correlation of BMI and chemical disability percentage, we unseemly can assume over-ranged BMI as the main reason for hypertension in the veterans. Young *et al.* [41] reported significant correlation between body-weight loss and plasma cholinesterase levels of sarin in poisoned rats. We did not measure plasma cholinesterase level as it returns to normal a few weeks after OP exposure and thus is not considered as a marker for late complications of tabun poisoning.

We observed two epileptic patients with a history of seizures after the combat with normal EEG, which should be due to anti-epileptic medications. Prolonged seizures in connection with the sarin attack in the Tokyo subway was also reported in severely intoxicated patients [42], which is a common finding in the early-phase of nerve agent poisoning [43].

Seven patients had abnormal EMG and NCV pattern in our study. All of the impaired NCVs were of the axonal type and observed in both upper and lower extremities. In a study of 43 severely intoxicated Iranian veterans, Balali-Mood *et al.* [19] claimed that although late complications of SM are usually because of its direct toxic effect, neuromuscular complications are probably the result of systemic toxicity. More recently, in a cross-sectional study in 100 CWA Iranian veterans, Holisaz *et al.* [44] reported five patients suffering from axonal neuropathy, which is significantly higher than what is found in the normal population. In a cohort study of 74 OP-poisoned patients 13 years post-exposure, EMG and NCV were normal except for two severely affected patients [45]. Newmark [9] also stated that electrodiagnostic findings of OP intoxication are time-dependent. Wadia *et al.* [46] observed normal NCV pattern but reduced sensory nerve action potentials and compound motor action potential amplitude during OPIDN. In another study, EMG showed denervation with reduced recruitment. We did not find any late peripheral neuropathy in cases of tabun poisoning and in fact all the patients with impaired EMG and NCV patterns were intoxicated by SM. Small changes in EMG with no late clinical neuromuscular symptoms were formerly reported in sarin-exposed cases [13]. Considering the significantly higher occurrence of sensory nerve impairment in SM than in NA patients, SM may induce more delayed complications than the nerve agents in the nervous system as well as in other organs. Nevertheless, supported by previous reports on late effects of SM exposure in comparison with nerve agents, further studies of more nerve agent cases are required.

LDL, cholesterol and triglyceride profiles were significantly above the cut-off points. With regard to cardiovascular diseases as the first reason of CWA patients' death [47], this result could be an alarm sign in the life of the veterans. LDL showed reverse correlation with chemical disability percentage. Yanagisawa *et al.* [11] previously observed lower levels

of triglyceride, as a late sign, in severely affected sarin patients in connection with the terrorist attack in Matsumoto. He assumed affected adrenal medulla as the reason of the event; however, we did not observe any corroborant in our study.

Comparison of the two groups (SM and NA) showed higher mean age and more sensory nerve impairment (including hypoesthesia, hyperaesthesia and paraesthesia) in the SM group. Because of the low number of NA cases, only few results were achieved. Both of the seized patients were in the NA group and all seven impaired EMG and NCV patients were in the SM group but statistical correlation between the groups was not found. Life-threatening complications decrease as the time passes. Nevertheless, neurological complications are still notable and may disturb the life of the veterans, and therefore, they should be considered as part of their medical care.

Unfortunately, no further cases of pure nerve agent poisoning were found among the veterans. During the Iran-Iraq war, there was only one nerve agent attack, occurring in Majnoon island, whereas chemical war gas attacks with SM happened repeatedly. Therefore, our report is a cross-sectional descriptive study focused on the neurological complications of SM and tabun poisonings in these war veterans.

Further studies are needed to determine the underlying mechanisms of neurological complications and molecular aspects of both SM and tabun poisonings. Case-control studies with a higher number of patients are warranted to compare late neurological effects of SM and NA in the veterans.

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