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Comparison Spirometry Test with Related Factors on Pulmonary Complications in Exposed Persons to Mustard Gas.

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Abstract:

Back ground and objective: During the 8 year Iraq-Iran war (1980-1988) chemical weapons were frequently used against Iran .The aim of this study was to determine some related factors besides a spirometry test that can predict and evaluate late pulmonary effects on persons exposed to mustard gas.

Method: In a cross sectional study of 500 mustard gas exposed persons, we measured spirometric parameters with an assessment of their relationship with related factors including respiratory symptoms and signs, age, number of exposure episodes, length of post first exposure time and use of protective mask at time of exposure.

Findings: Of 500 exposed persons with the mean age of (45.6±6.5y), 91.6 %(n= 458) had lung Symptoms, dyspnea 88.2% (n=441, productive cough 36.2 % (n=181), dry cough 29.4 % (n= 147), haemopthesis 18.6 % (n= 93), and 8.2 % (n=41) had positive findings of the following in physical examination: wheezing 6.6 % (n=33), ronchi 1.2 % (n=6), and crackles 0.4 % (n=2). In a spirometry test, 52.4 % (n=262) had a dysfunction. Of these, 27.2 %(n=136) showed obstructive pattern, and 25.2 % (n= 126) showed a restrictive pattern. Prevalence of mild lung restrictive was 94.44% (n= 119) and mild obstructive pattern was 36.03 % (n=49). For moderate lung restrictive pattern prevalence was 5.56 % (n=7) and moderate obstructive pattern was 33.09 % (n=45). For moderate to severe lung obstructive pattern prevalence was 11.76 % (n= 16), and of severe lung obstructive pattern prevalence was 19.12% (n=26). Prevalence of dysfunction spirometry test increased with increasing the length of post first exposure time and no use of protective mask at the time of exposure. There wasn't any statistical significant relationship between respiratory symptoms and signs, the number of exposure episodes, and age with dysfunction spirometry test.

Conclusion: The most common type of dysfunction spirometry test is obstructive and then restrictive pattern in mustard gas exposed persons. The factors contributing to the increase of prevalence of dysfunction spirometry test include increasing the length of post first exposure time and no use of protective mask.

Keywords: Mustard gas, Prevalence rate, Spirometry test, Pulmonary complications.

Introduction:

During the Iraq-Iran war (1984-1988), Iraq used chemical warfare agents against Iran. Approximately more than 100,000 Iranians are now suffering from long term effects of mustard gas exposure.[1] Pulmonary complication is the most important and common complication in mustard gas exposed persons.[2] In numerous studies, a great number of pulmonary involvements have been reported by different methods (Spirometry test, Chest High Resolution Computed Tomography, lung biopsy) and related factors (length of post exposure time, nu mber of exposure episodes, use of protective mask at time of exposure, age). In one cohort study, a reduced pattern of pulmonary function test (PFT) was reported over a 10 year observation period in mustard gas exposed persons, but without correlations between the decrease in PFT and other factors including age, number of exposure episodes and time interval between exposure to SM and the study.(3) In another study, asthma was reported in 10.65%, chronic bronchitis in 58.88% and pulmonary fibrosis was seen in 12.18% of mustard gas exposed persons 10 years post exposure time.[4]

After 16-20 years post exposure time to mustard gas, high prevalence of respiratory complications (cough 100%, dyspnea 85%, and haemoptysis in 60%) in severe cases of mustard gas poisoning were reported. Respiratory signs were wheezing 95%, crackles 50% and stridor 10%. Spirometery test showed obstructive pattern in 57%, restrictive pattern in 22.5%, mixed pattern in 15%, and a normal pattern in 5% of mustard gas exposed persons.[5]

In recent studies, spirometry test showed more obstructive pattern [2, 4, 5] and dysfunction spirometry test increased over long term follow ups.[3]

In Bronchoalveolar Lavage (BAL), fluid in exposed patients to mustard gas with bronchiectasis, the CD4/CD8 ratio was significantly higher than in healthy controls and showed a negative significant correlation with Forced Expired Volume in 1 Second (FEV1) % predicted.[6]

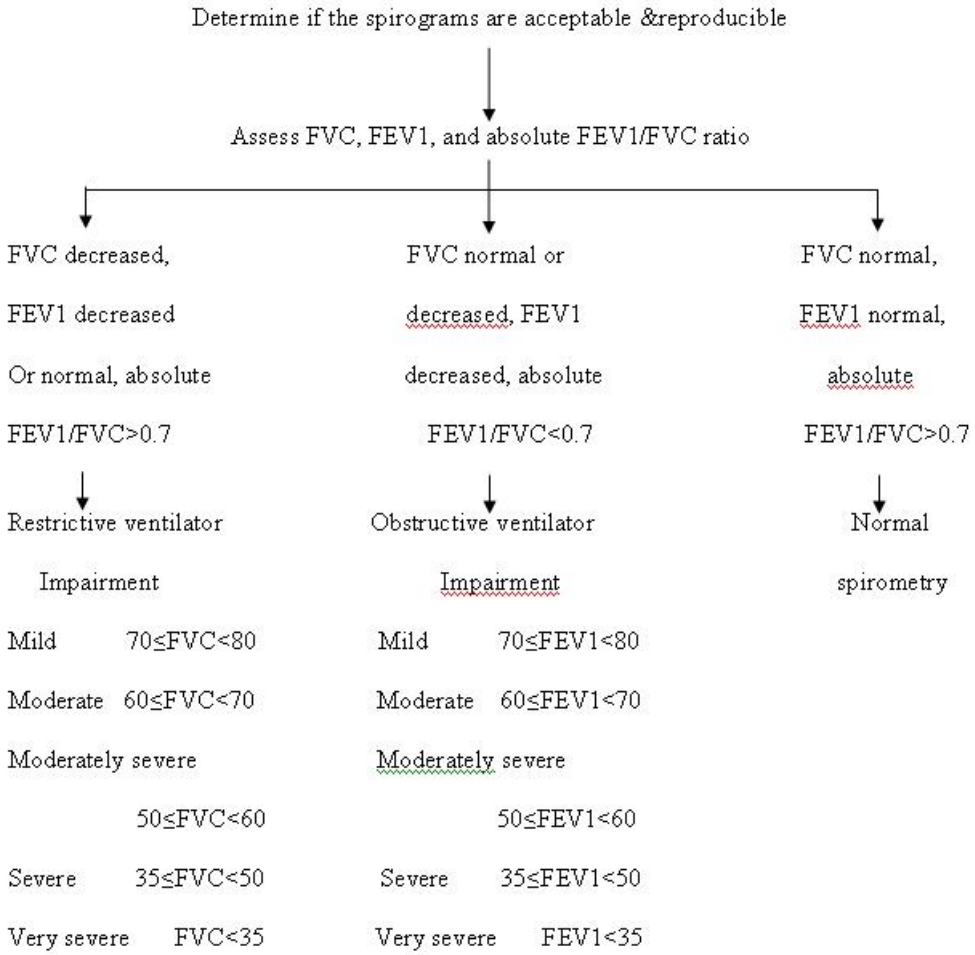
We were interested in determining a few related factors besides prevalence rate of dysfunction spirometry test that can predict and evaluate simply late pulmonary complication on exposed persons to mustard gas. After performing a spirometry test, we compared it with lung symptoms and signs, number of exposure episodes, length of post first exposure time, use of protective masks at time of exposure, and age.

Methods and study population:

In a cross sectional study between February 2006 and December 2008, 825 mustard gas exposed persons were referred to a pulmonary clinic at Emam Hospital. All of them had documented evidence of exposure to mustard gas but were referred for follow up or detection of new pulmonary involvement. Recorded information history and the results of their physical examination were entered in their questionnaires. The study was approved by the research ethics committee of Ahwas University of Medical Sci-

ences. The exposed persons then underwent a spirometry test (Portable jaeger spirometr, Germany) under the direction of physicians. Height and weight were measured before the test was conducted. The persons were seated with nose clip in place and asked to perform at least 3 forced expiratory maneuvers into a hand held spirometr. The Forced Expiratory Capacity (FVC) test was performed by having a patient inhale to Total Lung Capacity (TLC) and then make a maximally forced exhalation into the spirometer. Both the patient and technician received visual feedback from a monitor during the test, which was repeated until 3 technically satisfactory curves with acceptable and reproducible counters were obtained.[7] FEV1, FVC, and the ratio FEV1/FVC were derived from the same maneuver, which was the one with largest FVC. Then, participants were classified into 3 groups based on the spirometry data, as shown in the Algorithm 1.[8] Severities of dysfunction spirometry test were determined based on FEV1% and FVC% predict.[9]

Algorithm 1: Interpreting Spirometry Results



Inclusion criteria

Documentation of chemical exposure by military health services at the time of exposure.[14] M. Ghanei and Z. Allameh, Effect of chemical warfare agents on fertility, J. Med. Chem. Def [serial online]. (2003), p. 1…. .

Mustard gas exposed persons were under treatment temporarily stopped any bronchodilator drug based on their half life before the test (under the supervision of physicians).

Exclusion criteria

If they had a positive history for the following:

Smoking habit, history of lung disease before exposure to mustard gas, any occupational history of toxic fume, exposure or occupational risk factors that could lead to Interstitial Lung Disease(ILD), any associated chronic disease (such as heart failure or connective tissue disease) with potential pulmonary involvement, history of treatment with drugs that may

cause acute pneumonitis or ILD as a side effect.

Statistics and analyses

Statistical analyses were performed by using SPSS (Version 13.0). A p-value of ≤0.05 was considered as statistically significant. Methods of X2 , T-test and logistic regression were applied where necessary.

Results:

825 men who had been exposed to mustard gas performed spirometry test but 233 persons due to smoking history, 37 persons due to previously documented lung disease, and 55 persons due to not acceptable spirometr test were excluded from analysis of data. Finally, analysis was performed on 500 mustard gas exposed persons. All of them were male. Mean age group was 45.58±6.5 (range 36-85y). 50.2% (n=251) were between 35-44y, 41.4% (n=207) were between 45-54y, 6.2% (n=31) were between 55-64y and 2.2% (n=11) were equal or more than 65years. Persons were classified based on the length of post exposure time to mustard gas. Mean post first exposure time was 20.19±1.51 years (range 19-23y). 18.4% (n=92) were in group 19y, 10.2% (n=51) were in group 20y, 32.2% (n=161) were in group 21y, 25.6% (n=128) were in group 22y and 13.6% (n=68) were in group 23y post first exposure time. The number of exposure episodes was also classified. Mean number of exposure episodes was 1.27±0.59 times (range 1-4). 76.8% (n=384) had one exposure, 16.8% (n=84) had 2 exposure, 4.6% (n=23) had 3 exposure and 1.8% (n=9) had 4 exposure episodes. 37.6% (n=188) had used a protective mask at the time of exposure and 62.4% (n=312) did not.

In spirometry test, 52.4 % (n=262) had dysfunction spirometry test. Spirometry test study revealed more obstructive pattern 27.2 % (n=136) than restrictive pattern 25.2 % (n=126). 47.6 % (n=238) showed normal spirometry test. Mean spirometry data are shown in Table 1.

Table 1: Mean Spirometry data of mustard gas exposed persons based on spirometry patterns.

Mean Spirometry data	Dysfunction Spirometry Test (n=262)		Normal Spirometry Test (n=238)
	Obstructive Pattern (n=136)	Restrictive Pattern (n=126)	
FEV1%	58.22±17.61	73.77±5.65	98±11
FVC %	78.83±16.63	72.78±5.74	94.33±9.31
FEV1%/FVC%	59.45±6.66	92.33±5.74	92.24±15.82

Severities of dysfunction spirometry test in exposed persons to mustard gas are shown in Table 2.

Table 2. Severities of dysfunction spirometry test in mustard gas exposed persons.

Severity of dysfunction	Obstructive pattern	Restrictive pattern
test (n=262)	(n=136)	(n=126)
Mild	49(36.03%)	119(94.44)
Moderate	45(33.09%)	7(5.56%)
Moderate to severe	16(11.76%)	0
Severe	26(19.12%)	0

91.6% (n=458) had lung symptoms. Dyspnea 88.2% (n=441), productive cough 36.2% (n=181), dry cough 29.4% (n=147, and Hemopthesis 18.6% (n=93) were frequent clinical symptoms. There was no statistical significant relation between dysfunction spirometry test and positive respiratory symptom. (P.V=0.976) 8.2 %(n=41) had lung signs, wheeze 6.6 % (n=33), Ronchi 1.2 % (n=6) and crackles 0.4 (n=2) were the main respiratory signs. There was no statistical significant relation between dysfunction spirometry test and positive respiratory sign. (P.V=0.427) In this study, 48.85 % (n=128) of mustard gas exposed persons were between 35-44y had dysfunction spirometry test, 43.52% (n=114) between 45-54y, 5.73% (n=15) were between 55-64y, and 1.90% (n=5) were equal to or more than 65y. There was no statistical significant relation between dysfunction spirometry test and age groups. (P.V=0.777) The distribution of the percent patterns of spirometry test (separated to obstructive, restrictive and normal pattern) on the basis of the length of post first exposure time is shown in Table 3.

Table 3: The distribution of the percent patterns of spirometry test (separated to obstructive, restrictive and normal pattern) on the basis of the length of post first exposure time

Post exposure time	Obstructive pattern	Restrictive pattern	Normal pattern
(n=500)	(n=136)	(n=126)	(n= 238)
19Y	12(8.83%)	15(11.91%)	65(27.32%)
20y	11(8.09%)	12(9.52%)	28(11.76%)
21y	30(22.05%)	47(37.31%)	84(35.29%)
22y	45(33.08%)	41(32.53%)	42(17.65%)
23y	38(27.95%)	11(8.73%)	19(7.98%)

The distribution of the percent of patterns spirometry test (separated to obstructive, restrictive and normal pattern) on the basis of the protective mask is shown in Table 4.

Table 4: The distribution of the percent patterns of spirometry test (separated to obstructive, restrictive and normal pattern) on the basis of the protective mask

Use of protective mask	Obstructive pattern	Restrictive pattern	Normal pattern
(n =500)	(n=136)	(n=126)	(n= 238)
Yes	21(15.44 %)	40(31.75%)	127(53.36 %)
No	115(84.56%)	86(68.25%)	111(46.64%)

Between dysfunction spirometry test and no use of protective mask there was a statistically significant relation (P.V=0.000). When use of protective mask showed protective effect on the prevention of lung complications, a logistic regression test was applied on mustard gas exposed persons without protective mask at time of exposure. Then an odd ratio=1.38 was calculated for predicting dysfunction spirometry test chance with increasing length of post first exposure time(P.V=0.016).

Mean number of exposure episodes was 1.45±0.770 in dysfunction spirometry test and 1.16±0.42 in normal spirometry test by T test and a P.value was calculated close to a statistical significant relation. (P.V=0.056)

Discussion:

In this study, faced to obstructive pattern 27.2 % (n=136) as the most common pattern of dysfunction spirometry test, a similar finding in other studies.[2, 4, 5] But restrictive pattern 25.2 % (n=126) placed followed obstructive pattern by a close percentage. As indicated in the introduction part, other studies reported different prevalence of lung restrictive disease by considering different methods and samples. It seems our study was one of the rare studies that focused on detecting a dysfunction spirometry test on overall exposed persons to mustard gas. Maybe for this reason, most of them had mild dysfunction spirometry test 64.12 % (n=168), but we should emphasize on these points that some of the severe mustard gas exposed persons have lost during time while others have been hospitalized for a long time or living in nursing homes for supportive care. Mustard gas exposed persons are frequently visited in pulmonary clinics. For evaluating their most common complications we tried to find a few related factors and a simple way to predict and detect pulmonary complications based on the following: pulmonary symptoms and signs, number of exposure episodes, the length of post exposure time and use of protective mask at time of exposure were selected as the important related factors after reviewing mustard gas articles. In our study, although we reported a high prevalence rate of clinical respiratory symptoms, we did not find any statistical significant relation between them and the dysfunction spirometry test. Thus, respiratory symptoms may not be a reliable factor. Wheeze was detected as the most common sign as found in another study.[5] Since there was a low preva-

lence rate among mustard gas exposed persons with dysfunction spirometry test, we cannot rely on respiratory signs as a predictive factor.

However, no statistically significant relationship between older age and the dysfunction spirometry was found in the other study.[3] Finally, the most important factors associated with greater dysfunction spirometry test included the length of post first exposure time (PV=0.0016) and no use of a protective mask at time of exposure (PV=0.000). In clinic, we can be expected to face a dysfunction spirometry test in mustard gas exposed persons with history of long post first exposure time or no use of protective mask at the time of exposure.

Key messages:

(1) We determined the prevalence rate of clinical respiratory symptoms, signs and spirometry patterns in mustard gas exposed persons.

(2) We determined the prevalence rate of severities of dysfunction spirometry test in mustard gas exposed persons after 19-23y post first exposure time.

(3) No use of protective mask and the length of post first exposure time associate with greater risk of dysfunction spirometry test but older age and numerous exposure episodes don't seem to affect spirometry test.

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Conflict of interest:

None declared

References:

1. Aghanouri R, Ghanei M, Aslani J, et al, Fibrogenic cytokine levels in bronchoalveolar lavage aspirates 15 years after exposure to sulfur mustard, Am j physiol lung cell Mol physiol, 2004; 287: 1160-1164.

2. Balali mood M, Hefazi M, The pharmacology, toxicology, and medical treatment of sulphur mustard poisoning, Fundamental & clinical pharmacology, 2005; 19: 297-315.

3. Ghanei M, Eshraghi M, Peyman M, et al, Pulmonary function test trend in adult bronchiolitis obliterans, Tanaffos J, 2007; 6 (3): 40-46.

4. Emad A, Rezaian G.R, The diversity of the effects of sulfur mustard gas inhalation on respiratory system 10 years after a single, heavy exposure, chest J, 1997; 112: 734-38.

5. Balali Mood M, Hefazi M, Mahmoudi M, et al, long term complications of sulfur mustard poisoning in severely intoxicated Iranian veterans, Fundamental & clinical pharmacology, 2005; 19: 713-721.

6. Emad A, Emad Y, CD4/CD8 ratio and cytokine levels of the bronchoalveolar lavage fluid in patients with bronchiectasis caused by sulfur mustard gas inhalation, Inflammation J, 2007; 4: 2.

7. Miller M.R, Hankinson J, Brusasco V, et al, Standardization of spirometry, Eur respire J,2005; 26: 319-338.

8. Timothy J, Barreiro D.O, Irene P, An approach to interpreting spirometry, Am Fam Physician j, 2004; 69: 1107-1114.

9. Pellegrino R, Viegi G, Brusasco V, et al, Interpretative strategies for lung function tests, Eur Respir J, 2005; 26: 948-968.