*Original Article*

# DIFFUSING CAPACITY FOR LUNG CARBON MONOXIDE (DLCO) IN CHEMICAL LUNG INJURIES DUE TO THE USE OF MUSTARD GAS IN THE POISONED SOLDIERS OF IRAN-IRAQ WAR 2006

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**ABSTRACT**

***Objectives:*** To assess the Mustard gas exposure effects on pulmonary system, particularly on diffusing capacity for lung carbon monoxide (DLCO) and simple spirometry .

***Methodology:*** Sixty-five sulfur mustard- poisoned soldiers from Mostazafan and Janbazan organization were referred to our center in 2005. Complete history, physical examination, chest X ray, Echocardiography, Arterial blood gas, high – resolution computerized tomography, diffusion capacity for lung carbon monoxide and spirometry of these were performed and compared this result with normal value.

***Results:*** The mean value of indices in studied injured subjects was: Spirometry: forced expiratory volume in one second (FEV1) = 70.4, Forced vital capacity (FVC) = 66.5, EFE 25-75= 81.1, FEV1/FVC=101.9, Flow 25% = 28.7, Flow 50%= 72.9, Flow 75%= 100.1, Sample volume: Functional residual capacity of lungs (FRC) = 131.5, residual volume (RV) = 157.3, RV/TLC= 169.1, Total lung capacity (TLC) = 91.3, KCO= 131.6, TLCO= 116.3. No significant correlation was observed between TLCO values with HRCT, echocardiography, ABG and spirometry values (P>0.05).

***Conclusion:*** We recommend TLCO & RV/TLV tests to assess severity of Injuries as there is no a suitable criterion to measure the real consequences of mustard gas on affected combatants. and Biological markers are also needed to determine cause- effect relations.

**KEY WORDS:** Mustard gas, Chemical injuries, Pulmonary function test (PFT), Diffusing capacity for lung carbon monoxide (DLCO).

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## INTRODUCTION

The threat of chemical warfare used by various governments despite Geneva commitment in 1925 which forbid the use of chemicals is undeniable. Mustard gas was used in Iran – Iraq war (1980 -1988) against militaries and civilians. Thirty-four Iranian people were exposed to mustard gas and are still alive after nearly two decades.

Toxic effects of mustard gas have been recognized from 100 years ago.[1,2] Mustard gas or

sulfur mustard is a highly reactive agent that alkylates cellular components. The acute effects of mustard gas result from irreversible alkylation of proteins and nucleic acids, this causes loss of structural and functional integrity of cells and tissues (Ghavami). This gas causes chronic pulmonary disorders in exposed persons.[3-5] Pulmonary disorders, are the most common late symptoms in SM-exposed persons.[6] Mustard gas has proven mutagenic, carcinogenic, cytotoxic and vesicant properties, therefore designing an interventional study is impossible according to ethical issues. Thus, SM- poisoned veterans offer an opportunity to recognize chemical warfare gas effects and make progressive attempts to minimize their difficulties.

There are a large number of chemical affected combatants in Iran that have complicated pulmonary problems. As such conducting studies to complete diagnosis will lead to a better scanning of pulmonary disorders and then minimize their respiratory complication. This' study surveys chronic complication of SM- poisoned combatants and DLCO index changes in SM-poisioned subjects. Result of pulmonary function test (PFT), involve DLCO, is very useful in disease progress assessment. Spirometry test results are highly dependent on subject participation and in order to overcome this problem, it is recommended to perform PFT with DLCO, to increase reliability of the results.

Following some studies, it is recommended that in SM- poisoned subjects, more attention should be paid to bronchioltis obliterans (late respiratory complication of chemical gas poisoning), rather than pulmonary fibrosis, since the former is more common in chemical poisoned subjects.[7-10] This study is an attempt to diagnose late respiratory complications of mustard gas poisoned Iranian veterans.

## METHODOLOGY

This s is a descriptive cross sectional analytical study performed in sixty-five SM- poisoned soldiers. Inclusion criteria were:

1. Confirmed chemical injury with mustard gas in Iran – Iraq war episodes
2. Injury index (this index determined by janbazan and mostazafan organization according to history and physical examination and HRCT and explanatory of debility ) must be more than 25%, since pulmonary lesions are certain in-patient with injury index up to 25%. This should note that 20% of this index is merely attributable to pulmonary lesion.
3. Signed informed written consent was taken from all chemical injured subjects to enroll in the study after agreement and participation of janbazan & mostazafan organization

*Exclusion criteria:*

1. History of cigarette smoking or occupational exposure to pulmonary toxic agents
2. Evidence of prior pneumonia, tuberculosis, lung cancer, or other respiratory infections

All patients underwent through history and physical examination to detect ocular, skin and pulmonary lesions. Then they underwent simple spiromentry and echocardiography. Subjects were referred to a clinic in Isfahan to undergo DLCO assay.

To maintain conformity and to minimize bias in study, all DLCO assays were conducted in a single clinic in Isfahan, then the results of DLCO, spirometery and PAP data from echocardiography were codified and analyzed using SPSS software and spearman statistical test.

## RESULTS

In this study, we followed determination of relationship between DLCO using pulmonary experimental & diagnostic tests, in 65 mustard – poisoned soldiers during Iran – Iraq war. The findings are as follows:

* Injury percent of studied subjects fall in 25-65%, mean ± standard deviation (mean±SD): 29.6 ± 9.9. All of the studied subjects were male and poisoned during the period of 1984-1988.
* 89.2% of all subjects had no systemic disease, 7.7% had a pulmonary disorder and 1.5% had collagen vascular disease before mustard – poisoning.

* In Echocardiography: right ventricular pressure in 25-75 statistical range, mean and SD were 28.3±7.5mmHg, left ventricular Ejection fraction (LVEF) in 50-83 statistical range was 61.2±6.3% (Mean ±SD).

Pulmonary arterial pressure in 66% of studied subjects was in normal range and 33% of them was abnormal (Table-I).

*ABG (arterial blood gas) results were:*

PO2 (arterial oxygen pressure) in the range of 62-88 was 69.8±7.7 (means ± SD). PCO2 (arterial carbon dioxide pressure) in the range of 29.2-42.5 was 36.9±3.4mmHg (mean ± SD), Hemoglobin saturation (O2 sat) in the range of 93.7-97% was 93.4 ±2 (mean ± SD) and attrite blood pH in the range of 7.3-7.5 was 7.41±0.02 (Mean ± SD) (Table-II).

Simple spirometry was performed for all subjects (Table-III). (The results are expressed as a proportion of obtained results to the predicted value of the healthy with same gender, race, age, height, weight group).

Pulmonary volumes and capacities, KCO (CO diffusion index, an indirect estimate of DLCO) and TLCO (use as a substitute index for DLCO), measured precisely using sample volume method (Table-IV). (Results of pulmonary volume of capacity are recorded as the proportion of obtained results to predicted value of reference group).[18,19]

There was no significant correlation between right ventricular pressure, left ventricular Ejection fraction, pulmonary arterial pressure and TLCO (P>0.05). There was no significant correlation between PO2, PCO2, O2 sat, blood PH and TLCO (P>0.05). There was significant positive correlation between FEV1, FVC, Flow 50% and TLCO (P<0.05). There was no significant correlation between FEF25, flow 25%, flow 75% (spearman rank correlation test), FEV1/FVC and TLCO (P>0.05).

There was significant positive correlation between RV, TLC, FKC and TLCO (P<0.05), but there was no significant correlation between RV/TLC proportion in both measurement methods with TLCO (P>0.05). There is a highly significant positive correlation between KCO and TLCO (P<0.0001).

Table-I: Echocardiography results of Mustard soldiers in Iran – Iraq war

| | Mean | SD | Min | Max |
|---|---|---|---|---|
| Right ventricular pressure(RVP) in echocardiography | 28.3 mmHg | 7.2 | 25 | 75 |
| Left ventricular ejection fraction (LVEF) | 62.2% | 6.3% | 50% | 83% |

## DISCUSSION

In this study, we assess late respiratory complications of SM- poisoned soldiers in Iran – Iraq war, using ABG, echocardiography and DLCO by sample volume tests.Following performance of simple spirometry of 65 subjects, the proportion of pulmonary function indices to predicted value were: FEV1: 70%, FVC: 66%, FEF 25-75:81%, FEV1/FVC: 101%, flow 25%: 58%, flow 50%: 72% and flow 75%: 100%. These results indicated that most patients had obstructive and restrictive lung disease. FEV1 and FVC indices were lower than expected value (80-120%).

FEF 25-75% was in the lowest level of normal range, among studied subjects. Flow 50% was lower than expected value, but flow 75% was in normal range in the studied subjects. FEV1/FVC proportion was in normal range but FEV1 and FVC were lower than expected values, therefore FEV1/FVC falling in normal range does not mean that patients' pulmonary function is a normal and healthy one.Janghorbany et al, using simple spirometry, surveyed respiratory situation of chemical poisoned soldiers, 5-10 years after exposure.They concluded that 54.8% of studied subjects had impaired pulmonary function tests (PFT). In 37.3% obstructive disorders, in 13.4% restrictive and in 4.1% disorders were observed.

Table-II: ABG results of SM- soldiers in Iran – Iraq war

| | *Mean* | *SD* | *Min* | *Max* |
|---|---|---|---|---|
| PO2 | 69.8 | 7.7 | 62 | 88 |
| PCO2 | 36.9 | 3.4 | 29.2 | 42.5 |
| O2 Sat | 93.4 | 2 | 93.4 | 97 |
| Blood pH | 7.41 | 0.02 | 7.3 | 7.5 |

Table-III: Simple spirometry results of SM- soldiers in Iran – Iraq war

| *Statistical* | *Mean* | *SD* | *Min* | *Max* |
|---|---|---|---|---|
| FEV1 | 70.4 | 17.4 | 20 | 106 |
| FVC | 66.5' | 16.1 | 30 | 98 |
| FEF25-75 | 81.1 | 28.1 | 11 | 133 |
| FEV1/FVC | 101.91 | 16.3 | 36 | 121 |
| Flow 25% | 58.7 | 22.1 | 11 | 116 |
| Flow 50% | 72.9 | 23.9 | 11 | 122 |
| Flow 75% | 100.1 | 37 | 21 | 192 |

Table-IV: Pulmonary capacities, volumes, and determination of KCO and TLCO in SM soldiers in Iran – Iraq war using sample volume

| | *Mean* | *SD* | *Min* | *Max* |
|---|---|---|---|---|
| FRC | 131.5 | 36.5 | 81 | 285 |
| RV | 157.3 | 50.2 | 94 | 446 |
| RV/TLC | 169.1 | 39.8 | 115 | 298 |
| TLC | 91.3 | 19.3 | 54 | 140 |
| KCO | 131.6 | 23.2 | 86 | 209 |
| TLCO | 116.3 | 26.4 | 71 | 209 |

A significant decrease in vital capacity was observed in chemical poisoned, compared with normal persons.[11]

A survey concluded that 47.2% of studied patients had obstructive, 25.4% had obstructive – restrictive, and 7.8% restrictive and 9.6% had normal patterns in spirometry.[12]

Comparison of mentioned studies with our study showed that, after 20 years, SM- affected soldiers had pulmonary disorders that cause impairment & restriction in pulmonary volumes and capacities. This finding is more obvious in DLCO results using sample volume.

This method is a precise one in measurement of pulmonary volumes and capacities (despite of simple spirometry) and it showed that functional residual capacity of lungs (FRC), residual volume (RV) and proportion of residual capacity to total lung capacity (RV/TLC) were significantly higher than expected values. This means air trapping (that indicates obstructive pulmonary disease) is highly observed in chemical – injured soldiers, however, patient TLC was in normal range.

According to the obtained results from Echocardiography, in 33% of studied subjects, PAP increased and mean value of right ventricular pressure was higher than normal value, but left ventricular ejection fraction of patients fell in the normal range. In most relevant studies it has been concluded that chemical injured soldiers have evidences of late & chronic respiratory complications.[11-14] .This occurs by impacts on lung perfusion, leads to destruction of pulmonary capillaries, affects pulmonary vasculature, results in increase vascular resistance in pulmonary arteries, therefore right ventricle encounters long term increasing load hence intraventricular and pulmonary artery pressure increased. The impairment severity of right ventricle in most studied subjects were not affected left ventricle significantly, but this may occur in future and echocardiography may show advanced impairment in right ventricle and start of left ventricle impairment.

ABG results in SM- poisoned solders shows that mean values of PO2 was 66.8, PCO2 was 37.9, O2 sat was 93.4 and arterite blood PH was 7.41, all of these were in the normal range. TLCO is an alternative option for DLCO in clinical studies. TLCO mean value is 116.3% that is in normal range, upper limit is in normal range too.

Rezaiean concluded that in subjects that branchoalveolar lavage shown lung fibrosis evidences, merely DLCO can show fibrosis severity, and PFT does not help much.[15] Agusti concluded that DLCO and FVC could be employed in idiopathic lung fibrosis diagnosis.[16] Another study has reported that in patients with lung fibrosis, DLCO values decrease 30-50%.[13]

As mentioned, a complete detailed study that survey DLCO in chemical-poisoned soldiers has not been published, but in a review of relevant studies, we concluded that in lung fibrosis cases, DLCO values decrease. Results of this study showed a positive correlation between TLCO and FVC, FEV and flow 50%.

TLCO values decrease is in relation with FRC, RV and TLC decreasing but there is no significant correlation between TLCO and other stud-

ied indices.The following points were extracted:

1- Decrease of TLCO values (as index for lung obstructive disease diagnosis) following FEV1 and flow 50% indices decrease (showed that in obstructive disease blood flow rate decreases, destruction of capillary bed occurs, therefore this damages gas interchange surface and TLCO decreases finally.

2- TLCO decrease following TLC, FRC and RV decrease showed that TLCO value is affected by alveolar volume, as the same decrease in mentioned volumes and capacities that occurs frequently in lung restrictive diseases, reflects lower TLCO values in lung restrictive patients.

Lung fibrosis that is one of the major lung restrictive disease group, in SM- poisoned soldiers particularly, is followed by DLCO decrease that is shown in various studies.[16-18]

This study results confirm those study findings indirectlywhich means that in lung fibrosis cases, in which RV, FRC and TLC decrease occurs, TLCO decreases too, therefore TLCO is a valuable index in lung fibrosis severity determination and in SM- poisoned soldiers with lung fibrosis, TLCO decreases significantly.

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