Assessment of Spirometric Parameters Changes Before and After of Protective Interventions among Workers of Chlorine Production Plant in Iran

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Running Title: Spirometric Parameters and Protective Interventions

Abstract

Objectives: To assess of the spirometric parameters changes before and after of protective interventions among workers of Semnan chlorine production plant during 2012 – 2016.

Methods: The study was a quasi-experimental study which was performed on 100 workers of chlorine production plant of Semnan city (Iran) during 2012 – 2016. Spirometric parameters (FVC, FEV1, FEV1/FVC, PEF, and PEF (25-75%)) were measured for all workers before intervention in 2012. Then, the protective interventions were implemented for four consecutive years and parameters were measured annually. The multivariable linear regression model were used to assess the effective factors on spirometric parameters before and after protective interventions by SPSS 24.

Results: The mean of all spirometric parameters had significantly increased after protective interventions (P-Value <0.05). The multivariable linear regression model showed that age (β = -0.40), BMI (β = 0.71; %95 CI: 0.11 to 1.31) and type of mask (β = -7.88; %95 CI: -15.96 to -0.46) had significant effect on mean difference of FVC. Similarly, the age (β = -0.35; %95 CI: -0.70 to -0.01), BMI (β = 0.80; %95 CI: 0.20 to 1.41) and type of mask (β = -8.88; %95 CI: -16.98 to -0.79) had significant association with the mean difference of FEV1. Also, the type of mask (β = -12.81; %95 CI: -25.01 to -0.60) had significant effect on mean difference of PEF.

Conclusions: The all spirometric parameters had significantly increased in workers after protective interventions. Therefore, the protective interventions to prevent respiratory disorders in workers exposed to chlorine gas are suggested.

Key Words: Chlorine Gas, Spirometric Parameters, Protective Interventions, Quasi-Experimental Study, Iran
Introduction

Occupational health is always one of the most important priorities of the World Health Organization (WHO). Occupational health focuses on various aspects of occupational health and safety, and its more actions is associated to primary prevention of hazards in the workplace. However, according to the report of the International Labour Organization (ILO), nearly 2.78 million worker die annually due to occupational injuries and work-related illnesses in the world [1, 2]. Occupational diseases are caused by exposure to chemical, biological agents and physical hazards in the workplace [3]. Among occupational diseases, respiratory diseases are the most common work-related diseases and also account for about 17% of all deaths [2, 4]. Among the chemical agents that cause occupational respiratory diseases, chemical vapors, especially chlorine, are one of the most important risk factors for these diseases [5, 6].

The major route of exposure to chlorine gas is the inhalation route. Exposure to this gas can irritate the eyes, skin, nose, throat and mucous membranes. Eye injuries may be permanent [7]. Poisoning by chlorine can be lead to various consequences and outcomes which involves simple respiratory irritation, spasm and bronchial contractions, damage to bronchioles and the walls of the air sacs (alveoli) and many other pulmonary diseases. Although, there is a high chance of recovery after disconnection and remedial action, however, severe and prolonged exposure can be lead to permanent and irreversible damage to lung function especially in related industries workers [8, 9]. Chronic exposure to 15 ppm chlorine causes cough, hemoptysis, chest pain and sore throat [10]. Various studies have suggested that chronic and prolonged exposure to chlorine is the important factor in the development of occupational asthma. Some studies have also shown that long-term exposure to chlorine causes chronic rhinitis in the industrial workers, which can eventually lead to reactive airway dysfunction syndrome (RADS) [11, 12]. Other long-term effects of exposure to chlorine and chlorinated compounds on the respiratory system including shortness of breath, irregular breathing, irregular heartbeat, chest pain, reactive upper airways dysfunction syndrome, tooth decay and increased colds and many other respiratory diseases [8, 10].

Given that the numerous complications and consequences of exposure to chlorine, design and implementation of the effective and protective interventions that can be the basis for preventive measures in the related industries workers seems essential. Therefore, according to the above
description and also the limited studies conducted about the effect of protective interventions on lung function and spirometric parameters in the chlorine factories workers in Iran, the aim of this study was to assess the changes of spirometric parameters before and after of protective interventions among workers exposed to chlorine gas in Semnan Chlorine Production Plant (Iran) during 2012 -2016.

**Methods and Materials**

1. **Study Design and Participants**

   This research was a quasi-experimental study which was performed on 100 workers of chlorine production plant of Semnan city (Iran) during 2012 – 2016. In this study, given that the all workers were investigated, therefore, sampling was in the form of a census. **Inclusion criteria** including working in factory production unit throughout the study period, having an active occupational-medical record and healthy lung function at time of employment. **Exclusion criteria** including prohibition of spirometric testing for the worker (such as stroke or heartache in the last 6 weeks, active bloody sputum, pneumothorax, abdominal or cerebral aneurysm, recent eye surgery, abdominal or thoracic surgery, pulmonary embolism, recent cerebrovascular events), having respiratory diseases (such as asthma, rhinitis, bronchitis and emphysema) and concurrent employment in other industrial plants.

2. **Data Collection**

   To collect the data, we used a checklist including variables of demographic (age, sex, weight, height, and smoking) occupational (work experience, family history of respiratory diseases, environmental risk factors such as enzyme, vapors, type of masks and solvents and dust ) and the spirometric parameters including Forced Vital Capacity (FVC), Forced Expiratory Volume during first second (FEV1), Peak Expiratory Flow (PEF), Peak Expiratory Flow occurring in the middle 50% of the patient's exhaled volume PEF (25-75%) and FEV1/FVC. To perform the study, spirometric parameters were measured for all workers before intervention in 2012. Then, the protective interventions were implemented for 4 consecutive years and spirometric parameters were measured annually. These protective intervention measures were as follows:
1- Electrolysis chamber insulation (overhaul of electrolysis machine, fix small and intangible device leakage using high pressure pump and create exhaust ventilation on the room roof)

2- Fix leakage of chlorine carrier pipes in the open area of the company with the shut down the production line and replacement connections

3- Emphasis on the use of filter masks by workers

4- Shutdown of chlorine production line in case of emergency repairs

To measure spirometric parameters, we used the Spirometer (Spirolab II, Via Del Maggiolino, 125, 00153, Rome, Italy). The parameters measured by the spirometer were FVC, FEV1, PEF, PEF (25-75%) and FEV1/FVC. Spirometry was performed by a trained technician under the supervision of a specialist physician based on the American Society of Thoracic Society (ATS). The mean percentage of the predicted value of each spirometric parameters was measured based on height, age, and gender. Before spirometry, essential instructions related to the method and maneuvers were thoroughly given to the workers and they were asked not to smoke and eat a heavy meal at least one hour before the test. For spirometry test, workers were requested to stand for 5 minutes, and then put special clips on their noses in a standing and comfortable position. For each worker, three acceptable maneuvers were performed and if the difference between the results of FVC (greater than 5%) was observed to obtain the best volume based on the predicted percent for lung function the test was repeated up to 8 times. In present study, the values of the predicted percent for lung function was the measured capacity by spirometry divided by the anticipated capacity (according to gender, age, height and race calculated by spirometry), and multiplied by 100. The chlorine gas in the workstation was measured using gas-gathering sampling pumps and gas chromatography and compared with Threshold Limit Value (TLV).

3. Statistical Analysis

Data were analyzed using Stata version 14. For descriptive analyzes mean, standard deviation (SD) and number (%) were applied. Then, multivariable linear regression model were used to determine the effective factors on mean difference of spirometric parameters before and after protective interventions. Finally, the β-adjusted coefficient regression with 95% confidence interval (CI) were estimated. Also P-Value <0.05 was considered as a significant level.
4. Ethics Statement

Before data collection, the aims of the research were explained to the workers, then informed consent was obtained. Also, this study was performed according to the principles expressed in the Declaration of Helsinki and was approved by the Deputy of Research and Ethics Committee of Semnan university of medical Sciences (Iran).

Results

The aim of this study was to assess the changes of spirometric parameters before and after of protective interventions among workers exposed to chlorine gas in Semnan chlorine production plant (Iran) during 2012 -2016. The total number of workers under study was 100. The results of descriptive analysis showed that the number of men and women were 97 (97%) and 3 (3%); respectively. The means of age, weight, height BMI and work experience were 34.82, 76.60, 173.54, 25.40 and 7.62; respectively. Also, 80% of workers have family history of respiratory diseases. After the implementation of intervention programs as well as 65% regularly had used the mask. Tables 1 shows demographic and occupational characteristics of population under study.

In 2012, the spirometric parameters were measured before protective interventions. Then, these parameters were measured and followed up for four consecutive years after interventions. Table 2 shows mean, standard deviation (S.D), minimum and maximum of each spirometric parameters by 2012-2016. Table 3 shows the results of Paired T-Test which the mean parameters before intervention (2012) are compared with the mean parameters four consecutive years after interventions (2013 – 2016). as can be seen, the results of this test indicated that the mean of all spirometric parameters (FVC, EFV1, FVC/ EFV1, PEF and PEF 25-75%) have significantly increased after protective interventions compared to before interventions (P-Value <0.05).

Kolmogorov – Smirnov test (K – S test) was applied to assess the normality of the mean difference in each of the spirometric parameters (FVC, EFV1, FVC/ EFV1, PEF and PEF 25-75%) before and after protective interventions which the results of this test showed that all of
them have a normal distribution (P-Values were > 0.05), then, we used the multivariable linear regression model to determine the effective factors on mean difference of spirometric parameters before and after protective interventions, because the mean difference in each of spirometric parameters before and after protective interventions as dependent variable was continuous variable with normal distribution. The multivariable linear regression model was used to determine the effective factors on mean difference of spirometric parameters before and after protective interventions (Table 4). As can be seen, the age ($\beta = -0.40$; %95 CI: -0.75 to -0.06), BMI ($\beta = 0.71$; %95 CI: 0.11 to 1.31) and type of mask ($\beta = -7.88$; %95 CI: -15.96 to -0.46) had significant effect on mean difference of FVC. As can be seen, $\beta$-age was -0.40 for FVC, this means that for every 1 unit increase in the mean of age, the FVC is reduced by an average of 0.40 units. Similarly, the age ($\beta = -0.35$; %95 CI: -0.70 to -0.01), BMI ($\beta = 0.80$; %95 CI: 0.20 to 1.41) and type of mask ($\beta = -8.88$; %95 CI: -16.98 to -0.79) had significant association with the mean difference of FEV1. Also, we saw which the type of mask ($\beta = -12.81$; %95 CI: -25.01 to -0.60) had significant effect on mean difference of PEF (Table 3).

**Discussion**

The aim of this study was to assess the changes of spirometric parameters before and after of protective interventions among workers exposed to chlorine gas in Semnan Chlorine Production Plant (Iran) during 2012-2016. The results of this study demonstrated that the mean of all spirometric parameters have significantly increased after protective interventions (P-Value <0.05). The multivariable linear regression model showed that age ($\beta = -0.40$), BMI ($\beta = 0.71$) and type of mask ($\beta = -7.88$) had significant effect on mean difference of FVC. Similarly, the age ($\beta = -0.35$), BMI ($\beta = 0.80$) and type of mask ($\beta = -8.88$) had significant association with the mean difference of FEV1. Also, the type of mask ($\beta = -12.81$) had significant effect on mean difference of PEF.

According to our knowledge, the present study is one of the first studies which has been investigated the trend of the spirometric parameters changes among workers exposed to chlorine gas before and after protective interventions with associated factors for five consecutive years. This study showed that the implementation of protective intervention measures significantly improved spirometric parameters in workers exposed to chlorine, and somehow these measures can be a way to prevent the permanent and irreversible damage to lung function of worker.
to the lack of interventional studies in this area, we were forced to compare the results with observational studies. However, in line with our results, the some studies have suggested that the number of spirometric parameters return to their normal levels after taking preventive measures in people with respiratory disorders caused by chlorine inhalation [13-15]. Therefore, design and implementation of the appropriate protective measures will slow down the process of pulmonary dysfunction and even make significant improvements in all spirometric parameters, hence, the importance of these protective interventions should not be neglected in workers exposed to chlorine gas in different industries.

The multivariable linear regression model showed that age, BMI and type of mask had significant effect on means difference of the FVC and FEV1. Also, the type of mask had significant effect on mean difference of PEF. The most studies have reported a negative relationship between BMI and weight with pulmonary function so that the spirometric parameters decreases with increasing BMI or weight [16-18]. However, in the present study, BMI had significant association and positive with FVC and FEV1 parameters. Perhaps one of the reasons for this inconsistency is the type of study, because of the most studies have been done in this regard are cross-sectional. In this study, there was no statistically significant association between the means of the spirometric parameters changes which was not consistent with some studies in this area [19-21]. However, the lack of statistically significant association was consistent with the results of several studies [22, 23]. According to the researchers of this study, the most important reason for these inconsistencies is the difference in the study type and sample size. Therefore, designing and conducting of the similar intervention studies is recommended in this field.

In our study, we was observed statistically significant relationship and negative between age and the means changes of FVC and FEV1, so that these parameters decreased with age increased. This finding seems reasonable. According to the results of various studies, lung capacity decreases with age increased, because the respiratory muscle strength decreases with age increased, then lung volume and capacity such as FVC and FEV1 are affected [24, 25]. Therefore, protective intervention measures should be given more attention especially in older workers.
Finally, we observed a statistically significant association between the type of masks and the means changes of the FVC, FEV1 and PEF so that these parameters were associated with a greater decrease when using inflatable and ordinary masks in comparison to filtered mask (N-95). Therefore, the type of mask is a factor important in the design and implementation of the protective intervention programs and should be considered.

The study had several strengths and limitations. Based on our knowledge, the present study is the first interventional study which has investigated the effect of protective interventions on lung function of the workers exposed to chlorine gas in industries of Iran. The second strength of this study is the follow up of workers' lung function and spirometric parameters for four consecutive years after intervention. Also, this study, like many other researches, has several limitations that should be considered when interpreting the results. The most important limitation of this study is the lack of control group and random allocation for comparison because this research was a quasi-experimental study. Secondly, the workers under study may be exposed to chlorine gas outside the factory in different ways which this issue has not been considered in our study.

In conclusion, this study showed that all spirometric parameters (FVC, FEV1, FVC/FEV1, PEF and PEF (25-75%)) had significantly increased in workers after protective interventions. Also, age, BMI and type of mask were the most important factors affecting spirometric parameters. Therefore, implementation of the protective interventions taking into account the above factors to prevent functional respiratory disorders of workers exposed to chlorine gas are suggested.

**Declarations**

**Ethics Approval**

This research was conducted according to the principles expressed in the Declaration of Helsinki and was approved by the Deputy of Research and Ethics Committee of Semnan University of Medical Sciences (Iran).

**Conflicts of interest**

The authors have no conflict of interest to declare.

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25.
| Variable                                      | Number | Mean | *S.D | Max  | Min  |
|-----------------------------------------------|--------|------|------|------|------|
| Age (year)                                    | 100    | 34.82| 7.44 | 65   | 25   |
| Weight (kg)                                   | 100    | 76.60| 12.55| 51   | 105  |
| Height (cm)                                   | 100    | 173.54| 7.42 | 192  | 152  |
| Body Mass Index (kg/m2)                       | 100    | 25.40| 3.68 | 35.63| 16.65|
| Work Experience (year)                        | 100    | 7.62 | 4.41 | 25   | 1    |

| Variable                              | Number (%) |
|----------------------------------------|-------------|
| Sex                                    | Female 3 (3) Male 97 (97) |
| Smoking                                | Yes 12 (12) No 88 (88) |
| Family History of Respiratory Diseases (FHRD) | Yes 17 (17) No 83 (83) |
| Exposed to Environmental Risk Factors (EERF) (Enzyme / Vapors / Solvents / Dust) | Yes 80 (80) No 20 (20) |
| Regular Use of Masks                   | Yes 65 (65) No 35 (35) |
| Type of Mask                           | Filtered Mask (N-95) 12 (12) Inflatable Mask 18 (18) Ordinary Mask 70 (70) |

*S.D : Standard Deviation
Table 2. Mean (S.D), Minimum and Maximum of Spirometric Parameters by Year 2012-2016

| Parameters | Intervention | Year | Number | Mean  | S.D  | Min | Max |
|------------|--------------|------|--------|-------|------|-----|-----|
| Before     | 2012         | 100  | 85.86  | 6.22  | 70   | 98  |
| Variable | Number | Before Intervention (2012) | Mean 2013-2016 | After Intervention (Mean 2013-2016) | Mean Difference (After – Before) | P-Value |
|----------|--------|---------------------------|-----------------|----------------------------------|----------------------------------|---------|
| FVC      | After 2013 | 100 | 100.99 | 11.35 | 64 | 132 |
|          | After 2014 | 100 | 99.74 | 1.57 | 72 | 140 |
|          | After 2015 | 100 | 88.57 | 11.24 | 66 | 116 |
| FEV1     | After 2015 | 100 | 9.16 | 11.52 | 64 | 129 |
|          | After 2016 | 100 | 96.24 | 16.15 | 60 | 182 |
|          | After 2013 | 100 | 72.19 | 4.83 | 63 | 87 |
|          | After 2014 | 100 | 82.65 | 6.72 | 62 | 95 |
|          | After 2015 | 100 | 84.19 | 6.63 | 63.30 | 95.70 |
|          | After 2016 | 100 | 84.43 | 7.48 | 66 | 115 |
| FEV1/FVC | Before 2012 | 100 | 82.73 | 9.49 | 60 | 105 |
|          | After 2013 | 100 | 103.77 | 16.15 | 67 | 143 |
|          | After 2014 | 100 | 103.68 | 17.73 | 57 | 168 |
|          | After 2015 | 100 | 98.77 | 16.04 | 68 | 146 |
|          | After 2016 | 100 | 108.30 | 23.12 | 63 | 199 |
| PEF      | Before 2012 | 100 | 62.98 | 9.52 | 46 | 85 |
|          | After 2013 | 100 | 86.53 | 22.28 | 44 | 157 |
|          | After 2014 | 100 | 85.97 | 27.42 | 45 | 172 |
|          | After 2015 | 100 | 86.98 | 24.96 | 39 | 159 |
|          | After 2016 | 100 | 93.74 | 27.41 | 36 | 186 |
| PEF (25-75 %) | Before 2013 | 100 | 80.21 | 11.84 | 63 | 127 |
|          | After 2014 | 100 | 96.66 | 11.35 | 64 | 132 |
|          | After 2015 | 100 | 88.57 | 11.24 | 66 | 116 |
|          | After 2016 | 100 | 97.65 | 12.59 | 69 | 143 |
|       |     |     |     |     |     |
|-------|-----|-----|-----|-----|-----|
| FVC   | 100 | 85.86 | 6.22 | 96.51 | 9.84 | +10.65 | <0.001 |
| FEV1  | 100 | 80.51 | 4.38 | 95.27 | 10.64 | +14.76 | <0.001 |
| FEV1/ FVC | 100 | 72.19 | 4.84 | 83.28 | 5.92 | +11.10 | <0.001 |
| PEF   | 100 | 82.73 | 9.49 | 103.63 | 15.56 | +20.90 | <0.001 |
| PEF (25-75 %) | 100 | 62.98 | 9.52 | 88.30 | 20.21 | +25.32 | <0.001 |
Table 4. The Effective Factors on Mean Difference of Spirometric Parameters Before and After Intervention by Multivariable Linear Regression Model

| Variable         | FVC β- Coefficient (CI 95%) | P.value | FEV1 β- Coefficient (CI 95%) | P.value | FEV1/FVC β- Coefficient (CI 95%) | P.value | PEF β- Coefficient (CI 95%) | P.value | PEF (25-75%) β- Coefficient (CI 95%) | P.value |
|------------------|-----------------------------|---------|-----------------------------|---------|---------------------------------|---------|-----------------------------|---------|-------------------------------------|---------|
| Age              | -0.40 (-0.75 to -0.060)     | 0.022   | -0.35 (-0.70 to -0.01)      | 0.043   | -0.03 (-0.28 to 0.21)          | 0.765   | -0.17 (-0.74 to 0.39)       | 0.549   | -0.34 (-1.08 to 0.40)             | 0.367   |
| BMI              | 0.71 (0.11 to 1.31)         | 0.022   | 0.80 (0.20 to 1.41)         | 0.010   | 0.16 (-0.27 to 0.59)          | 0.459   | 0.50 (-0.50 to 1.50)       | 0.325   | 0.91 (-0.40 to 2.21)              | 0.170   |
| Work Experience  | 0.11 (-0.47 to 0.69)        | 0.716   | -0.01 (-0.60 to 0.57)       | 0.962   | -0.06 (-0.48 to 36)           | 0.782   | -0.35 (-1.32 to 0.61)      | 0.472   | 0.06 (-1.20 to 1.32)              | 0.926   |
| Smoking          | 5.60 (-1.90 to 13.11)       | 0.141   | 6.50 (-1.02 to 14.03)       | 0.089   | 1.50 (-3.90 to 6.89)          | 0.583   | 10.72 (-1.72 to 23.16)     | 0.090   | 11.03 (-5.22 to 27.30)            | 0.181   |
| FHDR             | 1.14 (-4.66 to 6.96)        | 0.698   | -2.25 (-8.08 to 3.58)       | 0.455   | -3.77 (-7.96 to 0.40)          | 0.076   | -6.74 (-16.39 to 2.91)      | 0.169   | -8.19 (-20.80 to 4.41)            | 0.200   |
| EERF             | 2.23 (-3.27 to 7.74)        | 0.423   | 1.85 (-3.67 to 7.37)        | 0.507   | 0.71 (-3.24 to 4.67)          | 0.721   | -5.61 (-14.74 to 3.52)     | 0.226   | 0.45 (-11.48 to 12.39)            | 0.940   |
| Regular Use of Masks | 1.32 (-3.65 to 6.30)  | 0.599   | 0.97 (-4.01 to 5.97)        | 0.699   | -0.05 (-3.63 to 3.52)         | 0.977   | -4.39 (-12.65 to 3.86)     | 0.294   | 0.41 (-10.37 to 11.21)            | 0.939   |
|                  | Reference                    | -       | Reference                    | -       | Reference                      | -       | Reference                    | -       | Reference                          | -       |
| Type of Masks    | -7.88 (-15.96 to -0.46)     | 0.044   | -8.88 (-16.98 to -0.79)     | 0.032   | -0.19 (-6.01 to 5.61)         | 0.948   | -8.94 (-22.33 to 4.44)     | 0.188   | -7.70 (-25.20 to 9.80)            | 0.385   |
|                  | -6.41 (-13.78 to 0.95)      | 0.087   | -6.33 (-13.71 to 0.05)      | 0.092   | -0.11 (-5.40 to 5.18)         | 0.968   | -12.81 (-25.01 to -0.60)   | 0.040   | -5.57 (-21.52 to 10.38)           | 0.489   |

*:%95 Confidence Interval