A Study of Pulmonary Functions of Spray Painters Working In Automobile Garage

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Abstract: Isocyanates are used in various industries including paints. Isocyanate induced asthma and extrinsic allergic alveolitis (Hypersensitivity pneumonitis) are known occupational hazards. Hypersensitivity pneumonitis is characterized by both restrictive (acute/subacute) and obstructive (chronic) pattern. Isocyanates are potent agents known to provoke immunological responses leading to a Hypersensitivity pneumonitis. This is a cross sectional study to observe the incidence of obstructive as well as restrictive pattern of disease. FVC, FEV₁, FEV₁/FVC, FEF₂⁰⁻⁵⁰, FEF₂⁻⁵⁰ and PEFR were evaluated in 50 male spray painters, aged 20 to 50 years exposed to spray paints for at least a year. FVC (p = 0.0009) and FEV₁ (p = 0.0006) were found to be significantly reduced in spray painters, but FEV₁/FVC ratio was statistically insignificant (p = 0.99) showing a restrictive pattern of disease. The changes in ventilatory pattern may be due to diffuse, predominantly mononuclear-inflammation of the lung parenchyma, particularly the terminal bronchioles, interstitium and alveoli.

Keywords: Isocyanates, restrictive pattern, spray painters

I. Introduction

Exposure to toxic or irritant substances at workplaces is a health risk and an increasing problem, concerning the affected persons on one side and the economic & financial sources of the industrialized world on the other side. In 2000 alone, according to the International Labour Organization, at least 160 million people became ill as a result of occupationally related hazards or injuries. Globally, occupational deaths, diseases and injuries account for an estimated loss of 4% of the gross domestic product [1,2]. Isocyanates and similar chemical compounds used in spray paints are known to be toxic. These are low-molecular-weight compounds characterized by highly reactive NCO groups & are one of the most commonly identified causes of respiratory impairments [3].

Isocyanates were first discovered in the 1850th but were not used industrially until World War II, when polyurethane foam was produced in Germany using Toluene diisocyanate (TDI). With technical advances, more widespread commercial production of polyurethane foam and other products using TDI, diphenyl diisocyanate (MDI) & hexamethylene diisocyanate (HDI) began in the 1950s. The first case of isocyanate asthma was reported in 1951 by Fuchs and Valade among TDI-exposed workers with subsequent studies documenting isocyanate asthma following exposure to MDI & HDI monomers & polymers, as well as less commonly used isocyanates. The isocyanate market has grown dramatically over the past 50 years both in production rates & variety of applications, reaching an estimated 10 million metric tons of polyurethanes (6 million tons of isocyanates) in the year 2002. Worldwide annual growth has been over 5% for MDI & 2% to 3% for TDI & is expected to continue. Several large new MDI production facilities have recently opened in China & other Asian countries with more planned for the future [4].

As of 2010, India is home to 40 million passenger vehicles. More than 3.7 million automotive vehicles were produced in India in 2010 (an increase of 33.9%), making the country the second fastest growing automobile market in the world. According to the Society of Indian Automobile Manufacturers, annual vehicle sales are projected to increase to 5 million by 2015 and more than 9 million by 2020. By 2050, the country is expected to top the world in car volumes with approximately 611 million vehicles on the nation's roads. Isocyanates are widely used in the manufacture of flexible and rigid foams, fibers, coatings such as paints and varnishes, and elastomers, and are increasingly used in the automobile industry, autobody repair, and building insulation materials. These low molecular weight compounds are one of the most commonly identified causes of occupational asthma [5]. Though isocyanate asthma is the major allergic disease induced after isocyanate exposure, a hypersensitivity pneumonitis type of reaction has also been reported in some workers [6,7]. Various studies have shown pulmonary functions impairment in automobile repair workers such as decrements of FEV₁ & FVC. Nearly 36.4% of the automobile garage workers had some form of pulmonary function impairment. Obstructive impairment was frequently observed in battery repair workers (58.33%) and spray painters (37.5%). It was more frequently observed in workers who had been working for a longer duration as compared to workers who had been working for...
small duration [8]. In case of occupational diseases, the affected workers are forced to abandon their jobs at least temporarily to recover or in the worst case scenario forever. Therefore, this becomes a major financial concern. Thus recognizing the early clinical and morphologic/pathologic sign becomes very important to avoid the exposure ending in a disease. This is especially important in the case of isocyanate-induced asthma, as the symptoms persist even after cessation of the exposure. For many substances dangerous and prescriptive limits have been implemented, but a lot of chemical substances are not only toxic or irritant, but could also lead to hypersensitivity reactions. The major problems are that:(i) these agents induce the hypersensitivity reactions at very low concentrations which technically are difficult to monitor and (ii) not all exposed workers are sensitive but develop the disease over time. Most of the studies have been carried out in Western population on spray painters. However, few studies have been done in the Indian population. In today’s industrialized era, India has the greatest potential for occupational health hazards. So it was thought that studies on Indian population were the need of the hour. This study was therefore undertaken to evaluate pulmonary function tests in spray painters working in automobile garages.

II. Objectives

To assess and compare the status of pulmonary function in control population and in spray painters and to study the correlation of pulmonary function impairment and duration of exposure in spray painters, if any.

III. Materials And Methods

The Institute Ethical Committee clearance was taken before start of the study. The present study was conducted in the Department of Physiology, Dr. D. Y. Patil Medical College, Pimpri, Pune. Fifty healthy adult males aged between 20-50 years working as spray painters at Pimpri-chinchwad area in Pune were selected. They constituted the study group (cases). Fifty healthy adult males aged 20-50 years who were not working in automobile garage were selected as a control group. Anthropometrical measurements were taken for predicted values of pulmonary function tests along with preliminary clinical examination to exclude any systemic disorder affecting respiratory system. Pulmonary function tests of these two groups were compared. Smokers, alcoholic and those with systemic illness which directly or indirectly affects the respiratory system were excluded from the study.

Age was calculated from date of birth of subjects and controls. A weighing scale was used to measure body weight with an accuracy of ±100 grams (0.1 kgs). Subjects were weighed without their shoes and with light summer clothing. Standing body height was measured without shoes with the use of height stand with shoulders in relaxed position and arms hanging freely. History taking, general examination and systemic examination of cardiovascular and respiratory system was done.

3.1 Pulmonary function tests

Pulmonary function test was carried out using RMS Helios 401 spirometer with built in computer program, using standard laboratory methods. The questionnaires were filled up and the relevant data, name, age, sex, height, weight, occupation, smoker or nonsmoker, lab temperature was entered into the computer. All the subjects were made familiar with the instrument and procedure for performing pulmonary function tests. All pulmonary function tests were done on the subjects comfortably seated in upright position. The subject was connected to the mouthpiece and was asked to breathe in order to familiarize himself with the equipment. During the tests the subject was adequately encouraged to perform at their optimum level and also a nose clip was applied during the entire manoeuvre.

To perform the FVC maneuver, the subject were instructed first to breathe in deeply to their full extent. The subjects then place the transducer to the mouth and expel the air from their lungs as quickly as possible, still with the transducer to the mouth. One single expiratory effort gives reading about many parameters. Out of those parameters following were selected for study.

(1) FVC: Forced vital capacity. The maximum volume of air forcibly expired from total lung capacity
(2) FEV₁: Volume of air expired at the end of first second of the FVC
(3) FEV₁/FVC: Ratio of forced expiratory volume of air expired at the end of first second of FVC to forced vital capacity expressed as a percentage
(4) FEF<sub>25-75</sub>: Forced expiratory flow during the middle half of the FVC (formerly called Maximum mid-expiratory flow rate or MMEF)
(5) FEF<sub>0.2-1.2</sub>: Forced expiratory flow between 0.2 to 1.2 liters of the FVC
(6) PEFR: Peak expiratory flow rate
(7) MVV: Maximum Voluntary Ventilation. Volume of air exhaled during maximum breathing efforts within a specified time period. Every test was repeated minimum 3 times and the best matching result were considered for analysis. All parameters were measured by the machine.
After giving rest of 10 minutes, the test to obtain maximum voluntary ventilation (MVV) was carried out. The subjects were instructed to breath as deep and rapid as possible through the mouthpiece for 15 seconds. Breathing should be as constant as possible. The built in mechanism of calculation in the Helios 401 spirometer gave MVV in liters per minutes. Three consecutive readings were taken by allowing rest for 10 minutes between each effort and best reading was selected and noted. The outcome of pulmonary function tests was presented as a mean ± SD for each of the parameter. The two groups were compared by applying student unpaired ‘t’ test and p value of less than 0.05 was considered as significant.

IV. Observations & Results

### TABLE 1: Anthropometry

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Controls Mean±SD n = 50</th>
<th>Cases Mean±SD n = 50</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28.23±6.383</td>
<td>28.96±8.2411</td>
<td>0.6168</td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>59.42±7.448</td>
<td>57.6±10.4627</td>
<td>0.3187</td>
</tr>
<tr>
<td>Height (cms)</td>
<td>158.56±10.76</td>
<td>155.56±6.7767</td>
<td>0.0985</td>
</tr>
</tbody>
</table>

### TABLE 2: Pulmonary Function Test Parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Mean ± SD n = 50</th>
<th>Cases Mean ± SD n = 50</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>3.297±0.5763</td>
<td>2.919±0.5358</td>
<td>0.0009**</td>
</tr>
<tr>
<td>FEV₁</td>
<td>3.057±0.6027</td>
<td>2.691±0.4084</td>
<td>0.0006**</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>92.38±7.8451</td>
<td>92.58±7.8451</td>
<td>0.9979</td>
</tr>
<tr>
<td>FEF₂₋₅₀</td>
<td>4.27±1.5245</td>
<td>3.88±1.3055</td>
<td>0.1362</td>
</tr>
<tr>
<td>PEF</td>
<td>6.769±1.6098</td>
<td>6.265±1.3844</td>
<td>0.1065</td>
</tr>
<tr>
<td>FEF₂₋₁₂</td>
<td>5.959±1.5834</td>
<td>5.554±1.2654</td>
<td>0.1609</td>
</tr>
<tr>
<td>MVV</td>
<td>120.5±27.698</td>
<td>106.34±21.2954</td>
<td>0.0047**</td>
</tr>
</tbody>
</table>

p* < 0.05
p** < 0.001
p*** < 0.0001

FIGURE 1: showing FVC (liters/second) & FEV1 (liters/second)
V. Discussion

The spray painters group showed a decreased level of FVC compared to control group. The difference in the two groups as expressed by the p value (p = 0.0009) was found to be statistically significant. The spray painters group showed a decreased level of FEV₁. The difference in the two groups as expressed by the p value (p = 0.0006) was found to be statistically significant. Ratio of forced expiratory volume of air expired at the end of 1st second to forced vital capacity (FEV₁/FVC) in the two groups was found to be statistically insignificant as expressed by the p value (p = 0.99).

According to American Thoracic Society recommendations, reduction in FVC without a reduction of the FEV₁/FVC ratio is a restrictive abnormality and the reduction of FEV₁/FVC ratio is interpreted as an obstructive abnormality [9]. The present study showed absolute decrease in FVC and FEV₁ without reduction of FEV₁/FVC ratio reflecting the restrictive pattern of disease as per the criteria given by American Thoracic Society. The difference was found to be statistically significant. However the ratio of FEV₁/FVC appeared to be unchanged. These results reflected the restrictive ventilatory pattern as observed in acute or subacute hypersensitivity pneumonitis (HP) in spray painters due to isocyanates. The changes in ventilatory pattern may be due to diffuse, predominantly mononuclear-inflammation of the lung parenchyma, particularly the terminal bronchioles, interstitium and alveoli. Similar results were found by Dahlqvist V et al, Baur X et al and Adam, W.G.F [7,10,11].

In this study 20% of the spray painters had shown deranged pulmonary function tests, 12% showed a restrictive pattern while 8% of the spray painters showed an obstructive pattern of disease. All spray painters that were part of this study were asymptomatic except for fever and myalgia. The predominant finding of this study has been the significant restrictive pattern of disease. Fever with bodyache and myalgia can be seen in hypersensitivity pneumonitis though a predominantly restrictive pattern is seen in acute HP and mixed pattern (both restrictive as well as obstructive pattern) is seen in chronic HP, occasionally obstructive pattern can also be seen in chronic HP. Very few subjects in this study gave history of breathlessness. Therefore isocyanate asthma seems to be an unlikely finding in these patients. It is more likely that they exhibit signs of isocyanate induced HP instead of isocyanate asthma. Another important observation in this study was that some spray painters in spite of 20 years exposure to isocyan ate showed neither a restrictive nor an obstructive pattern. This could indicate a lack of correlation between duration of exposure and the expression and progress of disease. There seems to be a possibility that it may depend on the genetic constitution of the subjects or other concurrent environmental factors. The exact cause for such an observation remains elusive and would require further studies. Hypersensitivity pneumonitis (HP), or extrinsic allergic alveolitis, is an allergic lung disease that occurs as the result of an immunologic inflammatory reaction to the inhalation of any of low molecular weight chemicals as isocyanates [12,13]. First described in Iceland in 1874 and termed heykatarr, hypersensitivity pneumonitis is caused by sensitization to repeated inhalation of organic antigens [14]. The disease is a diffuse, predominantly mononuclear inflammation of the lung parenchyma, particularly the terminal bronchioles, interstitium, and alveoli. The inflammation often organizes into granulomas and may progress to fibrosis. Thus, HP usually presents itself as an occupational respiratory disease.

In general, there appears to be a direct relationship between the intensity of antigen exposure and the development of HP. Intensity (concentration) and duration of exposure to the antigen, frequency of exposure, particle size, and antigen solubility may influence disease latency, prevalence, severity and course [15,16]. It is believed that acute HP usually results from intense intermittent exposure to inhaled antigens and that subacute HP results from a less intense but more persistent exposure. Chronic HP usually develops from acute or subacute forms of the disease. There may be an exposure threshold that has to be exceeded before acute and perhaps subacute forms of HP develop. The risk of HP is low under this exposure threshold and high beyond it, with a dose/effect relationship [16]. Concurrent environmental factors may influence the development of HP, for example, HP occurs more frequently in nonsmokers than in smokers (possibly by impairment of macrophage...
There are several other factors reported to play a major role in the pathogenesis of HP. These include surfactant proteins, extracellular matrix and free radical formation. Normal surfactant has been shown to inhibit the release of inflammatory cytokines by macrophages. However, surfactant from HP patients has been shown to have a higher content of surfactant protein A (SP-A) which stimulates inflammatory cytokine release, immunoglobulin production and mitogen induced proliferation [17]. In a study, surfactant proteins isolated from normal individuals and HP patients were added to alveolar macrophages and peripheral blood monocyte cell cultures [18]. It was demonstrated that surfactant proteins from control subjects inhibited alveolar macrophage induced lymphocyte proliferation in patients with HP, while surfactant from HP patients had a lower inhibitory effect on alveolar macrophage induced lymphocyte proliferation. This may indicate that changes in surfactant composition may lead to decreased suppressive activity of alveolar macrophages in patients with HP.

Several pulmonary function abnormalities may be demonstrable during an acute episode of HP. Pulmonary function tests typically reveal a restrictive pattern with a reduction in lung volumes and a decrease in diffusion capacity (DLCO). A decrease in airway compliance is also often seen with a shift in the pressure-volume curve down and to the right [19,20,21]. Hypoxemia is also observed on arterial blood gas analysis with an increase in the alveolar-arterial oxygen gradient. The hypoxemia and reduced DLCO reflect a filling of the alveolar space with fluid and inflammatory cells. Oxygen desaturation with exercise or with sleep may also be seen. Patients with subacute and chronic HP have a mixed restrictive and obstructive impairment, and occasionally patients with chronic HP may have only an obstructive disease. Patients with chronic HP also have a significant decrease in DLCO and exhibit hypoxemia. A number of patients (20-40%) display nonspecific airway hyper-reactivity and 5-10% have asthma. The bronchial hyper-reactivity seen in some individuals with HP may be secondary to the bronchiolitis found in these patients [22].

The present study also showed decreased FEF25-75, FEF2,12 and PEFR in spray painters as compared to control group but the difference was insignificant statistically. It has been found that some people show either an obstructive or restrictive pattern or both. Some of the subjects recruited in this study had an exposure of upto 15-20 yrs. Even after this period of exposure, a predominantly restrictive pattern was observed in these subjects as indicated by the decrease in FVC and FEV1. However the value of FEF25,75, FEF2,12 and PEFR are lower in these isocyanate exposed workers as compared to control population though not significant statistically. Whether this would indicate a developing or evolving obstructive pattern in these subjects remain to be identified. This would require further evaluation.

Maximum voluntary ventilation (MVV) in control group and spray painters group as expressed by the p value (p = 0.0047) was found to be statistically significant. MVV involves both inspiratory and expiratory phase of ventilation and it provides overall assessment of neuromuscular coordination as well as elastic and flow resistive properties of the respiratory system. The built in mechanism of calculation in the spirometer gives MVV in liters per minute. MVV can be viewed as measure of respiratory muscle strength. This test is effort dependent and therefore can be a poor predictor of true pulmonary strength and compliance. Statistically significant changes observed in the present study probably suggest that respiratory muscle strength was affected by exposure to isocyanates in spray painters for the duration, prescribed in the study.

Toluene diisocyanate (TDI) has been found to suppress the increase of intracellular cyclic adenosine monophosphate (cAMP) by the beta-agonist isoproterenol in peripheral blood lymphocytes indicative of a pharmacologic mechanism of action. Research data suggest that isocyanates may cause nonspecific inhibition of a variety of membrane receptors & enzyme systems. Both immunologic & nonimmunologic mechanisms appear to be involved. Although much research has been directed toward the mechanism of isocyanate-induced disease, the complete pathophysiology remains unknown [23]. 2,4-Toluene diisocyanate exerted a nonspecific inhibitory effect on the beta-adrenergic adenylate cyclase system of frog erythrocyte membrane preparation stimulated by the beta-agonist isoproterenol in vitro. This inhibition was dose-dependent, that is increase concentration of
toluene diisocyanate (TDI) produced progressively greater inhibition [24]. Exposure of workers to isocyanates may result in irritation and/or sensitization of the respiratory tract. An immunologic mechanism for sensitization has been presented. This investigation explored whether, as a possible mechanism for the irritation reaction, the toxic respiratory effect of isocyanates might be due to their ability to inhibit cholinesterase [25]. Thus, due to anticholinesterase activity of isocyanate, acetylcholine is not destroyed immediately. It rebinds to the same receptor, diffuse to act on neighbouring receptors and activate prejunctional fibres. So there is repetitive firing leading to twitching and fasciculations. Higher doses cause persistent depolarization of endplates resulting in blockade of neuromuscular junction leading to weakness and paralysis of respiratory muscles [26].

The spray painters studied in this study was included from various garages as per availability. They were not from a single garage. This study can be helpful to recognize the health hazards at an early stage and these spray painters can be isolated from spray painting and can be shifted to the other area of the garage where there is no exposure till recovery. However a country like India poverty remains an important issue. In India a single person earns bread and butter for a family of multiple members and because of population explosion, it is very difficult to leave the job and get another job for these persons. So in today’s era, to match the economic needs of an individual with mortality and morbidity associated with such exposure remains unsolved. The employees as well as employer are totally unaware of these occupational hazards. So they are not taking any preventive measures and so no preventive measures are in place. In fact they are even not aware of that it is hazardous they face. Even they are totally unaware that these occupational hazards can be prevented if certain preventive measures are taken early. In these patients what is also important is the psychological counseling of the employer and employee.

**VI. Conclusion**

This study showed a restrictive pattern in spray painters. However, this was a cross sectional study. Further longitudinal observation with immunological studies could help us in delineating the exact pathology and help us in identifying a suitable mode of treatment.

**References**