ORIGINAL ARTICLE

EFFECT OF DURATION OF EXPOSURE ON AIRWAYS OF TANNERY WORKERS DEPENDING UPON HISTAMINE INHALATION CHALLENGE

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Background: Occupational asthma has a prevalence of about 9–15% in adult onset asthma. Leather production in tanneries increases the atmospheric concentration of pollutants such as chromium, oxides of Nitrogen and Sulphur, particulate matter, volatile organic chemicals and Hydrogen disulphide, which may be linked to airway disorders. **Methods:** One-hundred-fifty male asymptomatic tannery workers of age 18 to 40 years were selected by convenient sampling and divided into three groups according to duration of exposure. The protocol of histamine inhalation challenge (HIC) has been standardized by American Academy of Allergy and Immunology. According to protocol HIC was not given to subjects with FEV_1 less than 80%. Those who had decrease in FEV_1 more than 20% before 8 µmol dose of HDP, were labelled as HIC positive and those who did not show any dip in FEV_1 up to 8 µmol HDP, were labelled as HIC negative. **Results:** Group 1 with shortest exposure had lowest number of compromised airways and highest number of HIC negative subjects (p<0.01). Group 3 with longest exposure had highest number of compromised airways and lowest number of HIC negative subjects (p<0.01). **Conclusion:** Bronchial hyper-responsiveness with deranged PFT's increases significantly with increase in duration of exposure (p<0.01). This study confirms the diagnostic value of HIC.

Keywords: Bronchial hyper-responsiveness, pulmonary function tests, Histamine Inhalation Challenge, HIC, Histamine diphosphate

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INTRODUCTION

Asthma is a chronic inflammatory disease of airways characterized by hyper responsiveness to a variety of stimuli like inhaled histamine and methacholine.[1] Occupational asthma (OA) has a prevalence of about 9–15% in adult onset asthma.[2] The prevalence of OA in tannery workers based upon history and clinical examination is 10.8%.[3] The respiratory diseases (16.7%) are mainly responsible for a higher morbidity among the exposed workers.[4]

The protocol of inhalation has been standardized on behalf of American Academy of Allergy and Immunology. PD_{20} is defined as the dose of histamine diphosphate (HDP) in micromole which when inhaled by the subject produces a 20% decrease in baseline forced expiratory volume in first second (FEV_1).[5] Bronchial hyperresponsiveness (BHR) is considered as a risk factor for the development of asthma and chronic obstructive pulmonary disease (COPD).[6]

The increased atmospheric concentration of pollutants such as chromium, oxides of Nitrogen (NOX), oxides of Sulphur (SOX), particulate matter (PM10), volatile organic chemicals (VOC) and Hydrogen disulphide may be linked to the increased prevalence of allergic diseases, bronchial asthma and enhanced airway response to inhaled allergens.[7] Chromium salt has potential to bind with skin proteins of tannery workers to produce complex antigens which lead to increased level of IgE antibodies and hypersensitivity. This may be the preliminary condition to the development of bronchial asthma.[8]

Tannery workers are potentially exposed to harmful agents rendering them vulnerable to health problems of respiratory tract and skin.[9] The process of preparation of leather from hide is multistage and stepwise procedure. There is growing concern over dangerous and harmful aspects of chemicals used in the leather industry and the disposal of waste from the tanneries.[10]

This study aimed to observe the effect of duration of exposure to tannery pollution on airways and bronchial hyperresponsiveness with the help of histamine inhalation challenge (HIC) test.

MATERIAL AND METHODS

It was a community-based, cross-sectional, comparative study. Subjects were selected from the tanneries located in suburban regions of Lahore. According to Lahore Association of Tanneries, there are 133 recognized tanneries in Lahore suburban areas having 4,300 workers. Using WHO sample size calculator, with 95% confidence interval and 5% chance of error was 138. One hundred and fifty male asymptomatic tannery workers of age 18–40 years were selected by convenient sampling technique from tanneries and were divided

into groups of 50 each. Group 1 had 0.5–1 year duration of exposure; Group 2, had 1–2 year; and Group 3 had 2–5 year exposure to tannery process.

As per protocol, 5 different concentration solutions of histamine diphosphate were prepared by serial dilutions in 5 concentrations (Table-1). Six handheld nebulizers were used to administer saline or histamine. The subject used to take two inhalations of each dose. The FEV_1 was recorded with the help of software installed spirometer after 1–3 minutes of each dose and followed immediately by the next dose. The challenge was stopped when FEV_1 dropped by more than 20% from the post saline value or if the maximum cumulative dose of 8 µmole was achieved.[11]

Table-1: Concentration and dose of histamine

Conc. in molar solution mole/L	Conc. (µmol/ml)	Output per squeeze (ml)	Puffs	Dose of histamine (µmol/ml)	Cumulative output dose (µmol/ml)
0.0625	0.0000625	0.00025	2	0.5	0.5
0.125	0.000125	0.00025	2	1	1.5
0.25	0.00025	0.00033	2	1.5	3
0.5	0.0005	0.0005	2	2	5
1	0.001	0.00066	2	3	8

RESULTS

Correlation of frequency distribution with duration of exposure was determined by Pearson's Correlation coefficient and $p<0.05$ was considered as statistically significant. In Group 1, with duration of exposure from six months to one year the HIC negative subjects are high in number, while HIC positive and with compromised airways (FEV_1 <80%) subjects are less in number. It has correlation coefficient, $r= 0.85$ ($p<0.01$). Group 3 with exposure of 2–5 year has highest number of subjects with compromised airways and lowest number of HIC negative subjects with correlation coefficient, $r= -0.87$ ($p<0.01$).

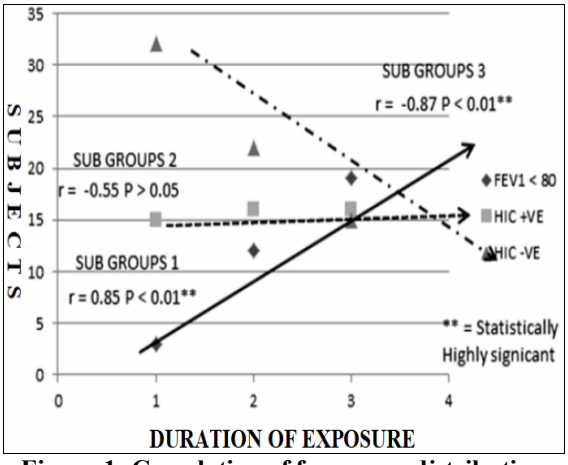

Figure-1: Correlation of frequency distribution with duration of exposure and HIC status measured in PD_{20}

Table-2: Frequency distribution of study population in three groups according to duration of exposure, airway sensitivity

Duration of Exposure	Baseline Airway Sensitivity FEV_1 Status			Airway Sensitivity after Histamine Challenge HIC Status		
	<80%	>80%	Percentage	HIC+	HIC-	Percentage
0.5–1 Year (n=50)	3	-	6%	-	-	-
	-	47	94%	15		30
					32	64
1–2 Year (n=50)	12	-	24%	-	-	-
		38	76%	16	-	32
					22	44
2–5 Year (n=50)	19	-	38%	-	-	-
		31	62%	16	-	32
					15	30

HIC Histamine inhalation challenge
HIC+ Hyperresponsive to inhaled histamine (PD_{20} <8 µmole)
HIC- Non-responsive to inhaled histamine (PD_{20} >8 µmole)

DISCUSSION

This study emphasizes the precise prevention of occupational asthma in tannery workers under the umbrella of histamine inhalation challenge. The lung function tests, measurement of hyper responsiveness and calculation of PD_{20} of the tannery workers may help us to find out the frequency of occupational asthma in this group of workers. Although non-specific bronchial reactivity to inhaled histamine was established by Cockcroft[5] but some factors which might influence the response had not been taken in account. These factors were nebulizer output, method of inspiration and proper reporting with the help of software installed spirometer. These factors were kept in mind while planning this study and Histamine Inhalation Challenge was given to every subject with FEV_1 >80% to measure BHR and PD_{20}.

This study helped to determine the role of HIC test in case of occupational asthma in tannery workers. In this study, PD_{20} of every HIC positive subject was measured and level of BHR was determined to choose the line of treatment. Tannery workers have high number of HIC positive subjects with FEV_1> 80% (31%) and deranged PFT's with FEV_1<80% (23%) by using sophisticated HIC test.

One hundred and fifty asymptomatic individuals participated in the study and their baseline PFT's, BHR and PD_{20} were recorded. The number of subjects with deranged PFT's and FEV_1 <80% increased with duration of exposure (6%, 24% and 32%). In this study, the percentage of hypersensitive subjects identified by HIC test in all groups according to duration of exposure was almost same (30%, 32% and 32%) whereas the percentage of HIC negative subjects was decreasing with increase in duration of exposure (64%, 44%, and 30%). It showed that duration of exposure has significant impact on frequency distribution of compromised airways.

There had been few studies carried out to establish the link between duration of exposure and bronchial hyper responsiveness in tannery workers. Our findings are also supported by Chandrasekaran *et al*[12] and according to their study, PFT's values correlate negatively with the duration of exposure to tannery hazards. They considered FEV_1 as early marker of allergy. In another study by Ortega *et al*[13] it was suggested that clinical history had poor specificity to establish linkages between workplace exposures and asthma. Thus, use of clinical history alone was expected to result in substantial under diagnosis of OA. They recommended that monitoring of bronchial asthma should be more precise to measure the disease process. This had been suggested that only brief medical history questionnaire and examination were inadequate and an objective protocol was needed to determine active asthma or airway hyperesponsivness in tannery workers.

CONCLUSION

Hyperresponsiveness with deranged PFT's increases with increase in duration of exposure to tannery hazards and early intervention measures at this level may save many workers from the adverse health effects. This study confirms the diagnostic and prognostic values of HIC test and PD_{20}.

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