EARLY CLINICAL, PULMONARY FUNCTION AND BLOOD GAS STUDIES IN VICTIMS OF BHOPAL TRAGEDY

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Abstract

Clinical, Pulmonary function and blood gas studies carricd out in 129 symptomatic toxic gas exposed individuals 1-3 months after exposure had revealed that pulmonary function measurements such as FVC, FEV_1 and FMF 25-75% were significantly lower in toxic gas exposed subjects and 57 subjects (44.2%) had ventilatory impairment. The predominant type of ventilatory defect was combined obstruction and restriction. Of these 57 subjects, 5 (9%) had severe respiratory impairment. With increasing severity of exposure, there was a tendency for a higher proportion of subjects to have increasing impairment in pulmonary function and this trend was significant statistically (P<0.001). Isolated small airway disease was present in 9 (7%) subjects. 20.3% of patients with normal physical findings and 19.1% with normal chest roentgenograms had abnormal pulmonary junction. Arterial hypoxemia and ventilatory abnormalities were predominant in severely exposed patients. Further studies are required to identify the subgroup o/patients with Reactive Airways Dysfunction Syndrome. Long term follow-up is essential to categorise the pulmonary syndromes due to toxic gas exposure.

Introduction

The leakage of toxic gas from the Union Carbide Factory at Bhopal on the night of 2-3 December, 1984 had resulted in the death of nearly 2500 people and morbidity in nearly 200000 people. The main organ involved was the lung and the patients were complaining of respiratory symptoms 1 to 3 months after exposure to the poisonous gas. The short term and long term effects of the toxic gas on human systems are not currently known and hence the Indian Council of Medical Research undertook this preliminary study to understand the effects of toxic gas on Respiratory system. This study was done during January - March, 1985.

Materials and Methods

Study Population

One hundred and fifty three patients exposed to toxic gas and presenting with respiratory symptoms were studied at the MIC clinic at Hamidia Hospital, Bhopal. Four categories of patients were observed at the time of initial screening. They were as follows:

a. Patients with respiratory symptoms such as dyspnoea at rest who required immediate hospitalisation. Pulmonary function tests could not be done in these patients because of their symptoms.

b. Patients exposed to toxic gas, not acutely ill, but presenting with respiratory symptoms such as cough and breathlessness on exertion. These patients did not have any apparent pre-existing cardio-respiratory disease prior to exposure. Pulmonary function tests were carried out in all these patients.

c. Patients with pre-existing cardio-respiratory diseases such as pulmonary tuberculosis, chronic bronchitis, bronchial asthma, bonchiectasis etc. Pulmonary functions were carried in thirteen of this category and numbers were not sufficient for reporting.

d. Patients exposed to toxic gas, but do not have any respiratory symptoms. Only a very few patients of this category attended the hospital for pulmonary function testing.

Pulmonary functions were mainly carried

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out in category b patients and this paper deals with pulmonary function abnormalities in these patients.

Clinical assessment and investigations of each patient included detailed history, physical examination and a full palte PA chest X-ray examination. Patients with pre-existing cardio-respiratory diseases were excluded from the study.

Pulmonary function studies:

The pulmonary function tests were done on the vitalograph. The tests were carried out in the sitting posture and a minimum of two consistent readings were obtained. All the values were expressed in BTPS and highest value obtained was used for analysis. The following pulmonary functions were carried out.

i.Forced Vital Capacity (FVC)
ii.Forced Expiratory Volume in 1 Sec (FEV_1)
iii.FEV_1/FVC %
iv.Forced Mid-Expiratory Flow 22-75% (FMF25-75%)
v.Spirometric response to inhaled bronchodilators: 31 patients. who had obstructive or obstructive cum restrictive ventilatory defect were given two 'puffs' of salbutamol from a inhaler and the spirometry was repeated 15 minutes later. The changes in FEV_1 and FVC were recorded and the sum of the percentage changes in FEV_1 and FVC was calculated. The results were reported as no response (<15%), significant response % and marked response (>30%)(Denison 1991).

Blood gas analysis:

Arterial blood gas analysis (pH, PO_2 and PCO_2) were done in 35 cases using the Instrumentation Laboratory Blood Gas Analyser. The arterial puncture was done in the lying down position with the patient breathing atmospheric air.

Classification of severity of exposure

a Severe Exposure:

If one of the members of the family died due to toxic gas exposure or the patient became unconscious after exposure or the patient had severe ophthalmic symptoms along with severe respiratory symptoms requiring immediate medical help with somebody's help, the patient was classified as having severe exposure.

b Moderate Exposure:

After exposure to toxic gas, if the patient developed respiratory symptoms and required immediate medical relief, the patient was classified as having moderate exposure.

c. Mild Exposure:

After exposure to toxic gas, if the patient developed respiratory symptoms and the patient did not seek immediate medical relief because of mild symptoms, the patient was classified as having mild exposure.

Classification of pulmonary function abnormalities:

As there were no facilities for measuring lung volumes and diffusion, classification of pulmonary function abnormalities into restrictive and combined obstructive cum restrictive types was difficult. However, the basis for classification of ventilatory defect into 3 types i.e obstructive, restrictive and combined obstructive and restrictive types (Miller et al 1956), using the predicted normal values of pulmonary function (Jain and Ramiah 1967 and 1969) was as follows:

a. Obstructive ventilatory defect:

When the ratio of measured FEV_1 to measured FVC was less than 75% and the ratio of measured FVC to predicated FVC was more than 75%, the patient was classified as having obstructive ventilatory defect.

b. Restrictive ventilatory defect:

When the ratio of measured FVC to predicted FVC was less than 75% and the ratio of measured FEV_1 to measured FVC was more than 75%, the patient was classified as having restrictive ventilatory defect.

c. Obstructive cum Restrictive ventilatory defect:

When the ratio of measured FEV_1 to measured FVC was less than 75% and also the ratio of measured FVC to predicted FVC was less than 75%, the patient was classified as having combined obstructive cum restrictive ventilatory defect.

The respiratory impairment was categorised by pulmonary function testing as follows (ATS, 1986):

a.Mildly impaired: FVC 60% to 79% of predicted or FEV_1 60% to 79% of predicted, or FEV_1/FVC x100 60% to 74%.

b.Moderately impaired: FVC 51% to 59% of predicted or FEV_1 41% to 59% of predicted of FEV_1/FVC x100 41% to 59%.

c.Severely impaired: FVC 50% or less of predicted or FEV_1 40% or less of predicted or FEV_1/FVC x100 40% or less.

In the presence of normal values of FVC, FEV_1 and FEV_1/FVC x100, a reduction in Forced Mid-Expiratory Flow 25-75% (FMF 25-75%) less than 75% of predicted is considered as evidence of small airway disease (McFadden et al 1972).

Analysis

Twenty four patients were excluded from analysis due to various reasons viz., old pulmonary tuberculosis (3), bronchial asthma and allergic rhinitis (2), chronic bronchitis (5), cyst in the lung (1), exposure to hydrochloric acid (1), Bronchiectasis (1), insufficient information (9) and normal subjects (2).

Data are presented as mean ± SD. Data were analysed by the students t tests. The trend chi square test was applied to see whether the level of exposure had any trend effect on pulmonary function.

Results

There were 90 males and 39 females in the study. The mean age of the males was 34 ± 11.5 years (range 12-70 years) and of females 30.9 ± 10.3 years (range 12-55 years), the mean height 1.65 ± 0.07 meters (males) and 1.54± 0.005 meters (females) and the mean weight 52.1 ± 12.0 Kg (males) and 46.0 ± 12.2 Kg (females). There were 14 patients with mild exposure, 49 with moderate exposure, and 66 with severe exposure. 32 males were smokers, 17 of them were smoking less than 5 cigarettes or bidis (sun cured tobacco packed 1oosely inside vegetable leaves) a day. Only five were smoking more than 10 cigarettes or bidis per day. Since there was no significant difference in pulmonary function between smokers and non-smokers, data were pooled for analysis. Fifty three patients (41.1%) were from low socio-economic status (less than 500 rupees a month), 42 (32.5%) middle (500-1500 rupees) and 34 (26.4%) high (more than 1500 rupees). All patients in this study were residents of areas within 2 kilometers of Union Carbide factory and most lived within 1 kilometer. There were 21 patients (16%) with dusty occupation such as labourers, painters, carpenters, masons, tailors, truck drivers etc and 81 (62.8%) were engaged in non-dusty occupations (Government employees, Engineers, Doctors, Business Executives, students etc). Twenty four females were house wifes and three did not have any occupation.

Clinical and X-ray findings:

Majority of the patients complained of breathlessness on exertion, 105 (81%) and cough, 95 (74%). A few, 42 (33%) had chest pain. The cough was not associatead with

expectoration. Usually cough was associated with breathlessness. A remarkable feature of the symptomatology was the absence of fever. Symptoms of the patients are given in Table 1. Auscultatory findings were normal in 79 (61%) patients. The abnormalities noticed on auscultation were rales in 27 (21%) patients, rhonchi in 8 (6%) and rhonchi and rales in 15 (12%). Fifty six (43%) patients had increased bronchovascular markings on X-ray chest. A substantial number of patients, 47(36%) had normal chest X-rays. Other abnormalities noticed in X-ray chest were reticular shadows in 22 patients (17%), pleural involvement in 3 (2%), raised diaphragm in 2 (15%) and cardiomegaly in one. All X-rays, were taken one month after the exposure of gas and hence none had X-ray findings suggestive of pulmonary oedema.

Table 1: Symptomatology.

Breathlessness on Exertion	105 (81%)
Cough	95 (74%)
Chest Pain	42 (33%)
Breathlessness at rest	5
Hoarseness of voice	4
Choking sensation	3
Fatiguability	3
Giddiness	3
Sore throat	2
Squeezing sensation in chest	2
Fever	2
Heaviness of chest	1
Loss of weight	1
Sleeplessness	1

Pulmonary function:

Pulmonary function results are shown in Tables 2 and 3. Pulmonary function measurements such as FVC, FEV_1 and FMF 25-75% were significantly lower in both males and females compared to the predicted normal values.

Pure obstructive ventilatory defect was observed in 13 patients (10.1%), restrictive defect in 16 (12.4%) and obstructive cum restrictive defect in 28 (21.7%).

T able 2: Pulmonary Function Results

		Males (n = 90)	Females (n = 39)
FVC	Predicted (L)	3.90 ± 0.40	2.64 ± 0.23
	Observed (L)	3.34* ± 0.90	2.19* ± 0.70
	% Predicted	85.6 ± 21.0	82.0 ± 24.0
FEV1	Predicted (L)	3.08 ± 0.45	2.11 ± 0.19
	Observed (L)	2.63* ± 0.94	1.79** ± 0.68
	% Predicted	84.1 ± 28.0	83.9 ± 29.5
FEV/FVC %		77.1 ± 11.8	80.2 ± 11.8
FMF 25 - 75 %	Predicted (L/min)	185.7 ± 54.7	158.8 ± 18.5
	Observed (L/min)	149.4* ± 90.0	118.7* ±67.4
	% Predicted	82.8 ± 43.4	74.2 ± 40.9

* $p < 0.001$ ** $p < 0.01$, as compared with predicted values.

Table 3: Pulmonary Function.

	Normal	Obstruction	Restriction	Obstruction + Restriction
Males (n = 90)	48 (53)	10 (11)	9 (10)	23 (26)
Females (n = 39)	24 (61.5)	3 (7.7)	7 (17.9)	5 (12.8)
Total (n = 129)	72 (55.8)	13 (10.1)	16 (12.4)	28 (21.7)

Figure.5 in Parenthesis are percentages

72 patients (55.8%) had normal ventilatory function. Thus a total of 57 patients (44.2%) had abnormal pulmonary function as a result of exposure to toxic gas. Of the 57 patients with ventilatory impairment, 20 (35%) had mild, 32 (56%) moderate and 5 (9%) severe impairment. Of the 72 patients with normal pulmonary function, 9 had isolated small airway disease as evidenced by lone reduction in FEF 25-75% and only one was a smoker. Thus 9 patients out of 129 (7%) had isolated small airway disease following toxic gas exposure.

Severitiy of exposure Vs pulmonary function:

Forty three of 66 patients (65.2%) with severe exposure had ventilatory defect whereas

none of the mildly exposed patients had ventilatory defect (Table 4). With increasing severity of exposure, there was a tendency for a higher proportion of patients to have increasing pulmonary function impairment and this trend was significant statistically (P < 0.001).

Table 4: Severity of exposure Vs Pulmonary function.

Severity of Exposure	Pulmonary function			
	Normal	Obstruction	Restriction	Obstruction + Restriction
Severe n = 66	23 (34.8)	9 (13.6)	11 (16.7)	23 (34.8)
Moderate n = 49	35 (71.4)	4 (8.2)	5 (10.2)	5 (10.2)
Mild n = 14	14 (100)	0	0	0

Figures in parenthesis are percentages.
Trend chi square test, p < 0.001.

Physical findings Vs pulmonary function:

It was observed that abnormal physical findings were associated with abnormal pulmonary function in 82% (41 of 50) of cases. It can further be observed that in 20.3% (16 of 79) cases with normal physical findings had abnormal pulmonary function (Table 5).

Table 5: Physical findings Vs Pulmonary function.

Physical findings	Pulmonary function			
	Normal	Obstruction	Restriction	Obstruction + Restriction
Rales n = 27	4 (14.8)	3 (11.1)	10 (37)	10 (37)
Rhonchi n = 8	4 (50)	1 (12.5)	0	3 (37.5)
Rales + Rhonchi n = 15	1 (6.7)	2 (13.3)	2 (13.3)	10 (66.7)
Normal n = 79	63 (79.7)	7 (8.9)	4 (5.1)	5 (6.3)

Figures in parenthesis are percentages.

X-ray findings Vs Pulmonary Function:

Though increased bronchovascular markings were the predominant chest x ray abnormalitiy, only 51.8% (29 of 56) of patients with increased bronchovascular markings had abnormal pulmonary function. This may be due to the subjective nature of this category. On the other hand, 77.3% (17 of 22) of patients with reticular shadows and all patients with pleural involvement had abnormal pulmonary function. In two patients with raised diaphragm, one had restrictive abnormality and the other had normal pulmonary function, but was associated with hypoxemia. Nine of 47 patients (19.1) with normal chest x rays had abnormal pulmonary function (Table 6).

Table 6: X-ray findings Vs Pulmonary function.

X ray findings	Pulmonary function			
	Normal	Obstruction	Restriction	Obstruction + Restriction
Reticular n = 22	5 (22.7)	2 (9.1)	5 (22.7)	10 (45.5)
Pleura n = 3	0	0	2 (66.7)	1 (33.3)
Raised diaphragm n = 2	1 (50)	0	1 (50)	0
Cardio-megaly n = 1	0	0	0	1
↑ BV markings n = 5	27 (48.2)	9 (16.1)	7 (12.5)	13 (23.2)
Normal n = 47	38 (80.9)	2 (4.2)	3 (6.4)	4 (8.5)

Figures in parenthesis are percentages.

Response to Bronchodialators:

None of the patients (n:31) assessed had any previous episodes of bronchial asthma. However, one patient had a history of atopy and another had a family history of bronchial asthma. 13 (41%) out of 31 patients had shown reversibility to bronchodialators and 9 (29%) had marked reversibility suggesting the possibility of Reactive Airways Dysfunction Syndrome (Brooks et al, 1985).

Blood gas results:

Arterial oxygen tensions were done in 35 patients. Severe hypoxemia (<60 mm Hg) was observed in 3 patients (9%) and two of these subjects could not perform pulmonary function.

Moderate (61-70 mm Hg) hypoxemia was present in 7 cases (20%) and mild (71-85 mm Hg) in 14 cases (40%).

Table 7: Severity of exposure Vs PaO_2

	<60mmHg	61-70mmHg	71-85mmHg	>85mmHg
Severe n=29)	3 (10.3)	7 (24.1)	13 (44.8)	6(20.7)
Moderate (n=5)	0	0	1	4 (80)
Mild (n=1)	0	0	0	1
Total (n=35)	3 (8.6)	7 (20)	14 (40)	11 (13.4)

Figures in parenthesis are percentages.

23 of 29 (793%) severely exposed patients had hypoxemia. All 3 patients who had PO_2 of less than 60 mm Hg had severe exposure. Only one patient with moderate exposure had hypoxemia. All other moderately exposed (n:4) and mildly exposed (ml) patients had normal PO_2 (Table 7). All patients (n:10) with combined obstruction and restriction had hypoxemia (Table 8). 7 patients (21%) with hypoxemia had normal pulmonary function. Hypocapnia (i.e. arterial CO_2 tension less than 35 mm Hg) was observed in 12 cases (34%). None had hypercapnia (i.e. CO_2 tension more than 46 mm Hg).

Table 8: Pulmonary function Vs PaO_2

Arterial O_2 tension	Pulmonary function			
	Normal	Obstruction	Restriction	Obstruction + Restriction
<60mmHg n=1	0	0	0	1
61-70mmHg n=7	2 (28.6)	1 (14)	1 (14)	3(42.9)
71-85mmHg n=14	5 (35.7)	1 (7.1)	2 (14.3)	6 (42.9)
>85mmHg n=11	7 (63.6)	3 (27.3)	1 (9.1)	0

Figures in parenthesis are percentages.

Discussion

Pulmonary function tests carried out 1-3 months after exposure to toxic gas had revealed that there was significant reduction in pulmonary function in individuals attending the hospital with respiratory symptoms and 44.2% of them had ventilatory impairment. The predominant type of ventilatory defect was combined obstruction and restriction. Majority of patients with abnormal physical findings had abnormal pulmonary function. Abnormal pulmonary function were noticed mainly in severely and moderately exposed patients, and all patients who had mild exposure had normal pulmonary function. However, the observations that 20.3% of patients with normal physical findings and 19.1% of patients with normal chest X-rays had abnormal pulmonary function suggest that complete evaluation including pulmonary function testing are essential in all patients, even if physical findings and chest X-rays are normal. Arterial blood gas analysis in 35 patients had shown that 3 patients were in respiratory failure (pO_2<60 mm Hg); and hypoxemia was observed mainly in patients with severe exposure and with severe pulmonary function impairment as evidenced by combined obstruction and restriction.

The absence of fever and the findings that cough was associated with breathlessness and not with expectoration suggest that the respiratory symptoms in these patients may not be due to bacterial or viral infections. This is further supported by the absence of radiographic evidence of pneumonia or bronchopneumonia in these subjects. The fact that only 16% of patients in this study were engaged in dusty occupation and that only five subjects were heavy smokers point to the probability that the respiratory symptoms and ventilator-y impairment in most of the patients are not due to occupational/environmenta1 exposures or smoking. The development of respiratory symptoms and the persistence of ventilatory impairment in a substantial number of subjects. following toxic gas exposure, and the fact that these subjects had no pre-existing lung disease prior to exposure and were residing in the vicinity of Union Carbide factory at the time of exposure suggest the possibility that the respiratory morbidity in these subjects might have resulted from inhalation of the toxic gas.

Previously it had been reported that the commonest lung function abnormality in toxic gas exposed subjects was airflow limitation with or without reduction in lung volume (Bhargawa

et al 1987). However, Kamat et al (1987) found a predominant restrictive lung disease between the seventh and 55th days after exposure. Two months after exposure, Rastogi et al (Rastogi et al 1988) observed that 39% of 783 patients had ventilatory impairment, a finding similar to the present study.

Eventhough 44.2% of patients attending the hospital with symptoms had ventilatory abnormalities, a thorough follow-up of these patients at 1/2 yearly or yearly intervals will only answer the question whether the ventilatory abnormalities are reversible or not. Even individuals with normal ventilatory function should be followed up to observe any progressive abnormalities developing on a long term basis. Clinical and Pulmonary function studies had shown that 2 types of clinical syndromes were induced by toxic gas inhalation. The first was due to high-dose exposure of toxic gas, resulting in pulmonary oedema and high mortality immediately after the exposure (Misra et al 1987). The second syndrome was characterised by dyspnoea on exertion, cough and pulmonary function abnormalities of obstruction and restriction in subacute stage as demonstrated in our subjects. This may lead to chronic lung disease. The finding of reversibility to bronchodilators in a substantial number of subjects without previous history of bronchial asthma and atopy suggests the possibility of a third syndrome resulting in Reactive Airways Dysfunction Syndrome (Brooks et at 1985). Immunological investigations coupled with pulmonary function studies and bronchoalveolar lavage may help in identifying the pulmonary syndromes caused by toxic gas exposure.

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References

1. Denison DM. Physiology. In: Clark T.J.H.: Clinical investigation of Respiratory Disease. London Chapman and Hall, 1981; 33-94.

2. Miller WF, Wu N and Johnson RL Convenient method of evaluating pulmonary ventilatory function with a single breath test. Anesthesiology 1956; 17: 480-493.

3. Jain SK and Ramiah TJ. Spirometric studies in healthy women 15-40 years age. Ind. Journ. Chest Disease 1967; 9:1-12.

4. Jain SK and Ramiah TJ. Normal standards of pulmonary function tests for healthy Indian men 15-40 years old. Comparison of different regression equations (prediction formulae). Indian J. Med. Res. 1969; 57: 1543-1466.

5. Evaluation of impairment/disability secondary to respiratory disorders A statement of the American Thoracic Society. Am.Rev.Respir.Dis. 1986;133:1205-1209.

6. McFadden ER, Linden A. A reduction in maximum mid-expiratory flow rate. A spirometric manifestation of small airway disease. Am. J. Med. 1972; 52: 775-731.

7. Brooks SM, Weiss MA and Bernstein IL. Reactive airways dysfunction Syndrome (RADS). Persistent Asthma Syndrome after high level irritant exposures. Chest 1985; 88: 376-384.

8. Bhargawa DK, Verma A, Batni G, Misra NP, Tiwari UC, Vijayan VK and Jain SK. Early observations on lung function studies in symptomatic gas exposed population of Bhopal. Indian J. Med. Res. 1987; 86(Suppl): 1-10.

9. Kamat SR, Patil MH, Kohhatkar VP, Dave AA and Mahasur M. Sequential respiratory changes in those exposed to the gas leak at Bhopal. Indian J. Med. Res. 1987; 86(Suppl): 20-38.

10. Rastogi SK, Gupta BN, Husain T, Kumar A, Chandra S, Ray PK. Effects of exposure to toxic gas on the population of Bhopal II: Respiratory impairment. Indian J. Exp. Biol. 1988; 26: 161-164.

11. Misra NP, Pathak R, Gaur KJBS, Jain SC, Yesikar SS, Manoria PC, Sharma KN, Tripathy BM, Asthana BS, Trivedi HH, Sharma VK, Mehrotra Y, Verma A, Bhargava DK and Batni G. Clinical profile of gas leak victims in acute phase after Bhopal episode. Indian J. Med. Res. 1987; 86 (Suppl): 11-19.