EFFECTS OF TOXIC GAS INHALATION ON RESPIRATORY SYSTEM IN BHOPAL GAS VICTIMS

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INTRODUCTION

Toxic gas leak at about mid-night from Union Carbide pesticide plant affected majority of the citizens of Bhopal, on 3rd December, 1984. Since it was a comparatively cold and humid night the gas formed almost an aerosol and settled on the adjoining area in the shape of a mushroom; engulfing the population in the affected area and then gradually spreading to the neighboring area after reaching the ground level. It resulted in immediate death of approximately 2500 victims and a large number of those who survived developed irreparable damage to lungs and other systems which has crippled them for their life. The present report summarizes the effects of toxic gas inhalation on respiratory system including clinical, radiological and physiological abnormality, which was studied in depth, soon after the disaster.

MATERIAL AND METHODS

Selected cohort of severely affected individuals, as well as a control population is being followed for studying the long term effects of toxic gas inhalation. 978 patients were admitted in Medical College Hospital,[1] out of which 458 (46.8%) were males and 520 (53.2%) were females. Age and sex distribution of 544 victims admitted on first day is shown in Table I.

OBSERVATIONS

Of 978 victims analysed 733 hailed from areas within 1 km. of Union Carbide Factory, 127 were within 1–2 Km. and rest 117 were from areas situated more than 2 Kms. from factory. Thus all of them were exposed to gas in a sufficient concentration. All the hospitalized patients had respiratory complaints. They described that toxic gas had a curious odour, unfamiliar smell that they had never experienced. Soon after inhalation they developed an extreme degree of irritation in nose and throat, almost resulting in a sense of suffocation. They found it extremely difficult to breathe and some of them died in the same state almost instantaneously.

Main respiratory symptoms noted in a series of 544 patients were breathlessness, cough with scanty expectoration, presence of pink froth, irritation in throat and a choking sensation, pain in chest, haemoptysis and hoarseness of voice. Symptoms are illustrated in Table II.

Most of the victims had tachycardia, pulse rate above 100/mt. and almost all of them were afebrile (except 2%), which is remarkable, as with so much of pulmonary congestion to oedema in most of the cases, they did not develop frank infection, which possibly is due to lethal action of the toxic gas on the microbials. Almost all of them had tachypnoea. Ronchi and crepitations were present in 452 (83.08%) cases, pleural rub was recorded in 7 cases. When compared with radiological picture physical signs appeared to be much less.

Symptoms and physical signs decreased with passage of time but a few victims developed paroxysmal dyspnea of considerable severity. Dyspnea was of considerable severity soon after the episode but with passage of time both the severity and frequency of episode of dyspnea decreased.

At the end of three months and six months follow up respiratory symptoms mainly cough and pain in chest had decreased, clinical score had gone down; but breathlessness persisted in all patients almost with the same severity.

Radiological Abnormalities

There were X-Ray abnormalities in almost all cases. Most of them had diffuse non-homogenous opacities, mostly in mid and lower zones; in some of the severely exposed cases almost whole of the lung fields were opacified with ground-glass like appearance. The opacities in lungs started decreasing at the end of first week and there was considerable radiological clearing by the end of second week.

X-Rays of 500 patients who were symptomatic were taken sequentially to study the changes with the passage of time.

Various types of radiological lesions observed were:

1. Interstitial lesions.
2. Combined interstitial and alveolar lesions.
3. Destructive lesions.
4. Parenchymal opacities:linear, punctate, nodular—micro and macro-nodular, and reticular, alone or in combination.
5. Evidence of pre-existing lung disease was detected in few X-Rays, along with fresh changes due to toxic gas inhalation.

Interstitial lesions:

In 207 victims out of 500 interstitial pulmonary lesion was detected leading to pulmonary oedema of various grades, most of them having involvement of both mid and lower zones and in some whole of the lung was opacified. It appears that inhalation of toxic gas caused exudation of large amount of fluid in the interstitium not capable of being drained by lymphatic channels. This resulted in an increas-

Table I
Showing Age and Sex Distribution of Victims Studied

Age Group	Male	Female
Under 15 years	45	42
Between 15–30 years	100	154
Between 31–45 years	66	60
Between 46–60 years	43	16
Above 60 years	10	8

Table II
Showing Symptoms of the Victims in Early Phase

SYMPTOMS (n=544)	No.of patients	Percentage
Breathlessness	538	98.89
Cough	516	94.84
Presence of pink froth	283	52.00
Irritation in throat/choking	250	45.95
Pain in chest	136	25.00
Expectoration	87	15.99
Haemoptysis	66	12.60
Hoarseness of voice	11	2.00

ing streaky shadows developing and miliary shadows developing in the interstitium of the lung.

Alveolar lesions:

Alveolar pulmonary oedema was seen in 203 out of 500 victims whose serial X-Rays were analysed. 184 cases had bilateral involvement. In 94 cases all the six zones were effected, in 90 there was involvement of lower zones only. 19 victims had unilateral involvement only. Confluent fluffy shadows indicated alveolar lesions. Alveolar lesions could have resulted from higher dose of toxic gas than was inhaled by those patients who has only interstitial lesions, where exudation took place only in interstitial spaces. With increased amount of exudate it poured into alveolar spaces, resulting in alveolar oedema as well.

Destructive lesions:

In 40 victims lesions such as surgical emphysema, pneumomediastinum and pneumothorax were seen, in addition to alveolar lesions. These abnormalities indicate that a higher

dose of the toxic gas led to break down of lung tissue resulting in leaking of air into soft tissues and mediastinum. A few cases had pleural effusion obliterating costophrenic sinus, which tended to disappear with passage of time, resulting from inflammation of underlying pulmonary tissue.

Pre-existing lesions:

Evidence of pulmonary tuberculosis and emphysema was found in 36 cases. Evidence of chronic obstructive airway disease was found in many X-Rays, mostly in smokers. All of them had evidence of lesions resulting from inhalation of toxic gas, described above, besides evidence of pre-existing disease. In many cases hyperinflation was observed due to air-trapping resulting from involvement of airways limiting airflow following inhalation of toxic gas.

In another study of radiological changes in 113 victims,[2] X-rays were taken soon after disaster and after three months. 2 victims showed normal picture. Emphysema was seen in 15%, pleural scars in 21%, consolidation in 4%. In lung parenchyma interstitial deposits were seen in almost all cases, 82% had linear and 37% punctate deposits. These deposits tended to clear with the passage of time. 36% had infiltrates in 2 zones, 40% in 3–4 zones and 24% in more than 4 zones. Evaluation of X-Rays taken three months later 38% showed some improvement, while some deterioration was seen in 16%.

Some victims developed episodes of paroxysmal dyspnea following toxic gas inhalation. Radiological studies of these subjects showed evidence of air-trapping indicated by hyperinflation in upper zones with evidence of infiltrates in lower zones mostly on right side, perhaps because right bronchus is direct continuation of trachea. A few of these subjects showed evidence of hypersensitivity pneumonitis and evidence of patchy consolidation in others.

Pulmonary Functions

Pulmonary functions were estimated in the victims to observe the abnormality that the toxic gas inhalation produced, immediately after the episode and are being followed in a longitudinal fashion to find out the long term changes in the victims with a control group.

224 gas exposed victims were studied,[3] soon after the episode. For the purpose of analysis of results they were divided into four groups on the basis of FVC and FEV_1 values, as shown in Table III.

All the victims showed involvement of peripheral (small) airways thus it appears that main brunt of the toxic gas inhalation was borne by the small airways. Almost half of the gas victims showed normal pulmonary functions as far as FVC and FEV_1 values are concerned, rest were almost equally distributed amongst those having obstructive (24), restrictive (38) and combined (36) abnormality.

Blood Gases

Arterial blood gases and pH were studied in the gas victims after the acute episode. PCO-2 values were slightly on the hypocapnoeic side, indicating that these victims were hyperventilating. There was slight hypoxaemia in a few subjects but most of them had a value above 70 m.m., only 7 out of 46 had values of PO-2 below 70 m.m. and only 2 out of these 7 had values below 60 m.m. All of them had normal pH.

COHb was studied in 70 cases, it was raised in 94.3%; in 11.4% it was higher than 6%.[4] Repeat study after 3 months showed that COHb values had returned to within normal limits in almost all cases. MetHb. was estimated in 111 subjects, and in 83% it was raised hut declined to almost within normal range after 3 months.

Table III

Showing Distribution of Victims as per Pulmonary Function Abnormality (n=224)

Group	Pulmonary function abnormality	No.of cases
I.Normal	Normal FVC and FEV-1	126
II.Combined	Reduced FVC and FEV-1	36
III.Obstructive	FVC normal FEV-1 reduced	24
IV.Restrictive	FVC reduced FEV-1 normal	38

Oxygen uptake studies revealed that oxygen uptake had improved after 3 months, which was low initially but the improvement was not significant. Values of VO_2 being 1122.6 ± 280.4 initially and 1157.0 ± 402.6 after 3 months.

In an attempt to correlate pulmonary functions with clinical status of the gas victims, it was found that initial FVC and FEV_1 before bronchodilator and FEV_1 after bronchodilator were inversely proportional to symptoms score ($r=0.76$ for FVC and -0.79 and -0.85 in FEV_1 before and after bronchodilator therapy). There was no correlation of pulmonary functions with oxygen uptake at rest; and of pulmonary function and radiological abnormalities.

Flow Volume Loop Studies

There were four types of flow volume loops:

1. Doming: inability to sustain peak flow indicating fixed central obstruction.
2. Hesitation: poor starting flow with fluctuations due to incoordination of inspiration.
3. Saw tooth: incoordination of inspiratory movement indicating variable intra or extra-thoracic central obstruction.
4. Concavity: indicating small airway obstruction.

No correlation was found between these patterns and the initial severity of symptoms. Changes did not seem to improve significantly at the end of 3 months period. Bronchodilator therapy produced an improvement only upto 15% in small percentage of cases but most of them did not respond to bronchodilators, suggesting irreversible airway obstruction.

Bronchoalveolar Lavage:

Bronchoalveolar lavage was carried out in 12 subjects soon after the episode. 4 out 8 victims who were studied in first 4 weeks showed swelling of tracheo-bronchial mucosa and distortion of lumen. There was patchy congestion in 3, ulceration in 2, and suspected lymphoid hyperplastic follicles in 3 cases. B.A.L. showed a rise in total cell count indicating continuing inflammatory status even after 4 weeks of the acute episode. Mean cell count of 344 m./c.mm. (normal upto 150 m./c.mm.). In nine samples neutrophils were raised (more than 3%; total mean 14 ± 25%, range 1 to 93), in two macrophages were raised (above 94%), while in five they were lower than normal. In one case there were eosinophilia (14%). In another case there was 11% lymphocytosis.

Lung Histo-Pathology

Lung biopsies were performed in 3 patients by open biopsy technique and adequate tissue could be obtained.

Histology showed pleural fibrosis with focal mesothelial proliferation thickened inter-alveolar septa, mono-nuclear infiltration in bronchial and peri-bronchial tissues, with patchy evidence of peri-bronchial and peri-vascular fibrosis, with destruction of bronchial wall and epithelium. No desquamation was seen. Muscular arteries and arterioles showed intimal hyaline thickening in one case suggestive of hypersensitivity. In another patient who had a severe exposure to gas besides changes described, the bronchioles were full of inflammatory exudate obliterating the lumen completely with round cell infiltration around, a typical picture of Bronchiolitis Obliterans; which seems to be a feature of toxic gas inhalation.

DISCUSSION

Methyl iso-cyanate is highly irritant to respiratory mucosa and can produce irreversible damage, as has been proved by experimental studies, data which was not available at the time of the episode, which was a main handicap in dealing with the patients; as well as lack of its toxicological data and availability of antidote, presented enormous problem in the management of the patients. Toxicity to human beings was reported in a study from U.K. due to accidental release of TDI in 35 fireman, toxicity of phenyl isocyanate, hexyl isocyanate and hexyl di-isocyanate has also been reported, but there was no documented study on MIC at the time of acute episode. Toxicity and pulmonary irritation described in these studies is very close to observed effects in gas victims in lungs. Exposure to TDI has led to development of hypersensitivity 'isocyanate asthma'. A few patients in our series had paroxysmal dyspnea following gas exposure perhaps due to sensitisation with single large exposure to the gas (R.A.D.S.).

All victims who had a severe exposure to the gas developed pulmonary infiltrates and many of them developed pulmonary oedema, which cleared with the passage of time, leaving evidence of either radiological or functional pulmonary abnormality. All the subjects were symptomatic. Patients who were managed with high dose steroids (Methyl prednisolone 1 gm I.V. repeated after 12–24 hrs., if necessary) showed much better response than those who did not receive it.

Although after the acute episode there was slight improvement in the condition of the victims but most of them continued to be symptomatic, many showed radiological shadows, and had abnormal pulmonary functions, indicating continuing inflammatory process, supported by histopathological finding. A long term follow up of a cobort is being conducted to study the ill-effects of toxic gas inhalation.

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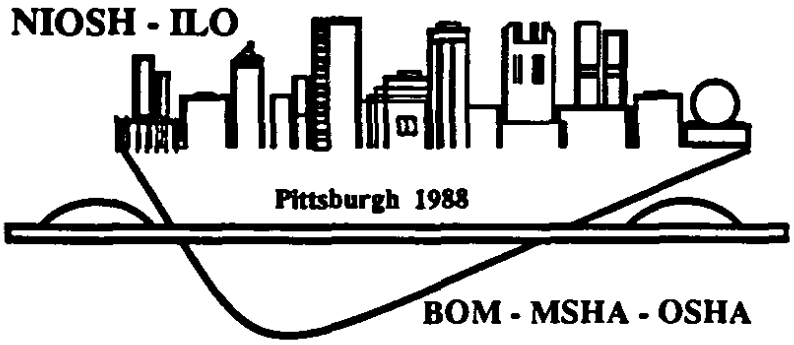

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