Irritant gases

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Abstract

Acute inhalation injury can result from the use of household cleaning agents (e.g. chlorine, ammonia), industrial or combustion gases (e.g. sulfur dioxide, nitrogen oxides) or bioterrorism. The severity of the injury is to a great extent determined by the circumstances of exposure. If exposure was in a confined or badly ventilated room, the intoxication is generally more severe. Concentration rather than duration of exposure is the more important determinant for tissue injury. Two types of responses to acute inhalational exposure to irritant gases can be discerned, depending on the water solubility of the compound. More water-soluble toxic gases (e.g. ammonia, chlorine, sulfur dioxide) affect the upper part of the respiratory tract. Following exposure to these gases, clinical symptoms appear instantly and consist of lacrimation, nasal discharge, bronchospasm, increased mucus production and cyanosis. Patients with chronic bronchitis or asthma are usually more susceptible. The less soluble gases (e.g. nitrogen dioxide) tend to produce effects in the peripheral airways and alveoli. Clinical symptoms can be absent during the first hours after exposure. Generally, bronchospasm is not a prominent symptom. Consequently, physical examination of the patient immediately after exposure may not provide information regarding the full extent of the clinical severity of intoxication.

Keywords Acute lung injury; acute respiratory distress syndrome; ammonia; chlorine; cold burns; corrosive agent; nitrogen dioxide; nitrogen oxides; poisoning; sulfur dioxide

Introduction

Acute pulmonary exposure to irritant gases occurs regularly. It is therefore important for physicians to be prepared for these kinds of toxic exposures in order to organize adequate medical aid. The severity of the symptoms after irritant gas exposure depends on the concentration of the intoxicating substance, the duration of exposure, the toxicity of the substance, its water solubility, the respiratory minute ventilation and the individual susceptibility of the victim.

Concentration rather than duration of exposure is the important determinant for tissue injury. During exercise, the respiratory minute ventilation increases considerably and thus the amount of toxic substance inhaled is increased. More water-soluble toxic gases affect the upper and more central airways. The less soluble gases tend to produce effects in the peripheral airways and alveoli.

In order to assess the severity of exposure, it is also important to know: (1) the colour and smell of the irritant gas, whether the gas is heavier than air, the landscape (irritant gases heavier than air can accumulate in lower situated areas) and weather conditions (temperature, rain, wind, daylight, fog might be relevant for the spreading and disintegration of the gas), and whether exposure took place in a confined space; (2) whether the victim was wearing protective clothing and/or a gas mask with an adequate filter; and (3) the victim's medical history.

Mechanisms of toxicity

Two types of responses to acute inhalational exposure to irritant gases can be discerned.

Compounds causing **type I inhalational injury** (chlorine, ammonia, sulfur dioxide[1–5]) dissolve easily in water and therefore also in the mucus of the upper airways, because mucus predominately consists of water. The process causing symptoms occurs usually at the site where the substance encounters the mucosal membranes of the airways. After being dissolved, molecules react with elements of the cell walls. The process involved is mostly of an inorganic chemical nature, such as oxidation, reduction or pH change. After cessation of the initial exposure, the process stops. Damage to the mucous membranes can also result in the release of mediators causing an inflammatory cascade that alters vascular permeability and acts as a set of chemotactic factors. The vascular permeability can lead to an influx of plasma that can decrease airway calibre and consequently increase airway resistance. Patients with pre-existing pulmonary diseases, such as chronic bronchitis or asthma, are usually more susceptible, with increased bronchospasm and excessive mucus production.

Compounds causing **type II inhalational injury** (e.g. nitrogen dioxide[1,2,6,7]) dissolve poorly in water and therefore penetrate deeper into the lung. Consequently, the process causing symptoms is usually situated much lower in the respiratory tract, i.e. in the alveoli and terminal bronchioles. The ciliated cells of the bronchioles and the alveolar type I cells are especially susceptible to injury. Following the alveolar damage, an influx of plasma and inflammatory cells occurs, causing acute lung injury (ALI)/acute respiratory distress syndrome (ARDS), which is characterized by stiff, non-compliant lungs, non-hydrostatic pulmonary oedema and hypoxaemia. The clinical findings are dyspnoea, tachypnoea, hypoxaemia and decreased lung compliance. The diffuse pulmonary infiltrates on chest radiography represent the consequences of diffuse alveolar damage, which is a non-specific response of the lung to various forms of lung injury. The full development of ALI/ARDS takes time because the formation of toxic reactive intermediates continues after cessation of the exposure. Furthermore, mucus retention, as a result of greater mucus production and damaged ciliary cells, contributes to the sensitivity to infections.

Clinical features

Type I inhalational injury

The symptoms appear instantly on exposure and consist of pain in the upper airways while breathing, nasal discharge and

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lacrimation. In more severe cases, bronchospasm, bronchial oedema, glottal oedema and increased mucus production may be present. Although pulmonary oedema can be observed, it will never be the sole phenomenon.[1–3,5,8–10]

These features in combination with blood gas analysis will give the most relevant information about the severity of the exposure. Initially, the chest X-ray is less valuable in assessing severity.

Type II inhalational injury

Symptoms can be absent during the first hours after exposure. Consequently, physical examination of the patient immediately after exposure may not provide information regarding the full extent of the clinical severity of the intoxication. Rarely, minor effects in the upper airways or nausea can be present. Generally, bronchospasm is not a prominent symptom. After several hours, depending on the concentration and the duration of exposure, ALI/ARDS may become clinically manifest.[1,2,6,11,12]

The chest X-ray in combination with blood gas analysis will give the most relevant information about the severity of the intoxication.

Management

Type I inhalational injury

Early inspection of the upper airways is important because the mucosal membranes can be very oedematous in severe cases, precluding oral endotracheal intubation; tracheostomy or coniotomy (emergency airway puncture) may be necessary. If there is no mucosal irritation of the eyes or nose, it can be concluded that the exposure was not severe and that the individual is not at risk of delayed pulmonary oedema; there is no need to admit such patients to hospital for observation.[1,2]

Type II inhalational injury

As symptoms are usually absent during the first few hours after exposure, the patient should be kept under observation until more information is obtained regarding the severity of exposure, or until clinical effects can no longer reasonably be expected. If, 6 hours after exposure, the patient has normal arterial blood gases and the chest X-ray is normal, there is little likelihood that life-threatening lung damage will develop. Patients can then be discharged with instructions that if increased dyspnoea occurs after discharge, they must undergo medical observation again.[1,2]

Inhalational injury

There is no specific treatment for airway injury caused by exposure to compounds causing type I or type II airway injury.[1,2] However, *early* administration of corticosteroids may be beneficial (later administration offers no benefit[13]) for some physiological parameters such as airway resistance and arterial oxygenation tension. The optimal duration of treatment has not been assessed but seems to be only a few hours. Corticosteroids do not reduce mortality, and can increase morbidity.[6,13–15] Adequate supportive therapy such as supplemental oxygen, bronchodilators and mechanical ventilation should be given. Use of prophylactic systemic antibiotics is not recommended because of the increased risk of infection with resistant organisms. When intubation is required, the largest practicable tube should be introduced to allow adequate bronchial toilet. Obstruction is often caused by increased mucus production and bronchospasm.

In the last few decades, mechanical ventilation has dramatically improved the outcome of severely poisoned patients with life-threatening lung injury. Nevertheless, mechanical ventilation can be difficult in ALI/ARDS. In this situation, veno-venous extracorporeal membrane oxygenation (VV-ECMO) can be considered. VV-ECMO is used for patients with severe ARDS to secure adequate oxygenation of the organs while protecting the lungs from harmful ventilation pressures or a prolonged high inspiratory oxygen fraction. ECMO is considered a good salvage therapy.[16]

Ammonia

Ammonia (Table 1) is one of the most extensively used industrial chemicals. It is lighter than air. Ammonia is highly soluble in water and is easily absorbed through mucous membranes. Most individuals can identify its odour at a concentration of 35 mg/m^3 (1 mg/m^3 is about 1.42 parts per million). Occupational atmospheric exposure is usually regulated to a limit of 18–40 mg/m^3.

Features and management

Airways: at concentrations of >50 mg/m^3, ammonia vapour is irritant to the upper respiratory tract. Exposure to concentrations >1000 mg/m^3 can lead to severe respiratory distress within minutes. Concentrations of >1500 mg/m^3 are immediately life-threatening.[17,18] See above for the mechanisms of toxicity, clinical features and management of a type I inhalational injury.

Eyes and skin: exposure of the skin and eyes to concentrated ammonia water (liquid ammonia) can cause corrosive damage;[3,19,20] evaporation of ammonia can cause extreme cooling when spilled on the skin or eyes, and cold burns may result.

Eyes and skin exposed to ammonia water should immediately be thoroughly irrigated with water; irrigation should be continued for at least 15–30 minutes. Delay increases ocular and skin damage. Eye irrigation is facilitated by the use of a topical anaesthetic.

Fluorescein staining of the cornea is required to show the extent of epithelial loss, and slit-lamp examination is mandatory. Moderate to severe eye injury should be assessed by an ophthalmologist, who can prescribe a mydriatic–cycloplegic drug to reduce the risk of synechial formation in the presence of iritis. Topical antibiotics can prevent secondary infection of the eye. Topical corticosteroids can retard re-epithelialization and cause thinning of the corneal stroma.

Properties of ammonia at room temperature and atmospheric pressure

- Gaseous
- Colourless
- Corrosive
- Alkaline
- Inflammable
- Sharp, pungent odour

Table 1

Healing is often accompanied by scarring. Conjunctival damage can lead to adhesion of the eyelids to the eyeball. Loss of conjunctival cells, which produce tears, results in a poor tear film that increases the risk of eye infections and further damage to the eye. Corneal grafting is less successful in these patients.[19]

Gastrointestinal tract: ingestion of ammonia water induces severe caustic lesions of the mucous membranes of the oropharynx, oesophagus and stomach. Oesophageal or gastric perforation can occur, causing mediastinitis and peritonitis, respectively. Neutralizing agents should not be administered after ingestion of ammonia water because the resultant exothermic reaction can worsen the injury. Induction of vomiting and gastric lavage are contraindicated. Systemic corticosteroids do not improve the outcome in patients with severe oesophageal lesions.[21–24]

Following severe exposure, oesophagoscopy should be performed as soon as possible to introduce a nasogastric tube, which is necessary to prevent complete obstruction of the oesophagus. If oesophagoscopy is delayed in severe cases, the mucous membranes become very swollen, increasing the risk of perforation after oesophagoscopy. In less severe cases, the optimum time for oesophagoscopy is about 12–24 hours after the injury; after this time, the risk of perforation of the oesophageal wall during oesophagoscopy is increased.

Healing of oesophageal lesions is often accompanied by strictures. A further oesophagoscopy after about 3 weeks is indicated in all patients in whom the results of initial oesophagoscopy are abnormal.

Chlorine

Chlorine is a greenish-yellow, corrosive gas with a distinctive odour at room temperature and normal atmospheric pressure. Chlorine is heavier than air. Most individuals can identify the odour at a concentration of about 1 mg/m^3 in air (1 part per million is about 3 mg/m^3).[9]

Features and management

Exposure to concentrations >90–150 mg/m^3 for a protracted period of time can lead to severe respiratory distress. Concentrations of chlorine of >1200 mg/m^3 are immediately life-threatening.[4,9] See above for the mechanisms of toxicity, features and management of a type I inhalational injury.

At concentrations >15 mg/m^3, chlorine is irritant to the eyes and upper respiratory tract.

Sulfur dioxide

Sulfur dioxide is a colourless and irritating gas, is heavier than air, is soluble in water and has a pungent odour. It can be identified at concentrations >0.8–2.6 mg/m^3. Sulfur dioxide is used as an insecticide, fungicide and disinfectant in breweries and food industries, and to bleach textiles and sugar. It is an important combusting product of fossil fuels and can therefore be found in smog.

On contact with body fluids, sulfurous acid, H^+, bisulfite and sulfur trioxide are formed; sulfurous acid especially is responsible for the toxic effects.

Nitrogen oxides

- Nitrous oxide – N_2O
- Nitric oxide, nitrogen monoxide – NO
- Nitrogen dioxide – NO_2
- Nitrogen trioxide – NO_3
- Nitrogen tetroxide – N_2O_4 (dimer of NO_2)
- Dinitrogen trioxide – N_2O_3
- Dinitrogen pentoxide – N_2O_5
- NO_x – a collective name for NO, NO_2 and N_2O_4

Table 2

Features and management

Healthy subjects develop bronchospasm following short-term exposures at rest of 13.3 mg/m^3, while asthmatic subjects do so at much lower concentrations (2.66 mg/m^3 at rest and 0.66–1.6 mg/m^3 during exercise[25–27]). Exposure to concentrations >300 mg/m^3 causes life-threatening features within minutes. Occupational exposure is usually regulated to a limit of 5–13 mg/m^3. See above for the mechanisms of toxicity, features and management of a type I inhalational injury. Liquid sulfur dioxide is corrosive, and evaporation can cause extreme cooling when spilled on the skin or eyes; cold burns may result.

Nitrogen and nitrogen oxides

Nitrogen is a colourless, odourless gas. NO_2 is heavier than air. It is the most toxic nitrogen oxide and causes hypoxic asphyxia by displacing oxygen. Of the nitrogen oxides (Table 2), NO and NO_2 occur naturally. In ambient air, NO is oxidized to NO_2. NO_2 exists principally as N_2O_4; at higher temperatures, more NO_2 than N_2O_4 is present.

Features and management

Exposure to NO_2 concentrations of 45–100 mg/m^3 (1 mg/m^3 is about 0.5 parts per million) for short periods causes only mild respiratory effects. Exposure to 100 mg/m^3 for longer than 1 hour can induce pulmonary oedema. Even brief exposure to >500 mg/m^3 can cause life-threatening pulmonary damage.[6,28] See above for the mechanisms of toxicity, features and management of a type II inhalational injury. Spillage of liquid nitrogen on the eyes or skin causes extreme cooling, leading to cold burns. ◆

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