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ACUTE MAMMALIAN TOXICITY OF O-CHLOROBENZYLIDENE MALONONITRILE(CS)

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ABSTRACT: *Acute inhalation intoxication of CS (O-chlorobenzylidene malononitrile) occurred among the 192 animals in confined animal cages of farm as the result of prolonged exposure. A total of 8 animals (3 silver foxes, 3 fitches and 2 minks) died in 15 hours after the exposure. Distinct evidences of pulmonary atelectasis were observed as with hepatorenal damages. The lethal toxicity of CS was considered to be due to early severe lung damages leading to asphyxia, accompanying acute toxic hepatitis and nephritis.*

Key words: *CS(o-chlorobenzylidene malononitrile) toxicity, Atelectasis, Asphyxia Necrosis, Hemorrhage*

INTRODUCTION

Ortho-chlorobenzylidene malononitrile commonly referred to as CS, has rapidly replaced the old sensory irritant materials (Shmunes *et al.*, 1973; Gaskins *et al.*, 1972). The use of CS in smoke form by police authorities for temporary incapacitating agents in uncontrolled demonstrations may bring about a possible health hazard. Nothing has been reported concerning cutaneous and inhalation hazards related to its use. The study reported in this paper was undertaken to characterize the acute inhalation toxicity of CS generated in the form of a pyrotechnic smoke.

MATERIALS AND METHODS

Animals and History

A total of 8 animals (3 silver foxes, 3 fitches and 2 minks) from 192 animals died in 15 hours after continuous exposure (about 2 hours) to pyrotechnically generated CS via the upper respiratory tract. The animals were held in confined racks of individual cages during the exposure to the gas contaminated at an animal farm, Jeonju, Chonbuk. Mostly death occurred either during or immediately following the episodes of lacrimation, nasal discharge, convulsion, limb muscle spasm, painful dyspnea, and lethargy.

Necropsies

All dead animals were submitted to post mortem examination approximately 1 to 6 hours after death. The tissue samples were taken after macroscopic observation.

Histopathologic Examinations

The tissues removed from lung, liver, kidney, adrenal gland stomach, intestine, gonad spleen, and lymph node were fixed in 10% neutral formalin, and 7 μm sections were stained with hematoxyline and eosin (H&E).

RESULTS

Gross Findings

The gross findings were essentially similar in the three species. Most of organs demonstrated congestion and edema especially in upper repiratory tract, liver, kidney, spleen, intestinal tract and mesentery, conjunctiva, and adrenal gland.

The varying degree of diffuse atelectasis was apparent in most cases with marginal ectasia, and multiple petechiae were also found frequently in pale pinkish white lungs. Excessive amounts of foamy fluid oozed out from the cut surfaces of bonchi and bronchioles.

There were a number of yellowish brown mottles on the surfaces of fragile hepatic parenchyma. Small intestines contained bloody fluid mixed with digested food stuff. Heart chambers were dilated as evidenced by rounded apex and the right side to result

Fig. 1. Ballooning degeneration and necrosis of bronchiolar epithelial cells observed. Note tortuous basal lamina with collapsed alveoli and electron dense materials visualized by eletron microscopy. ×2,000.

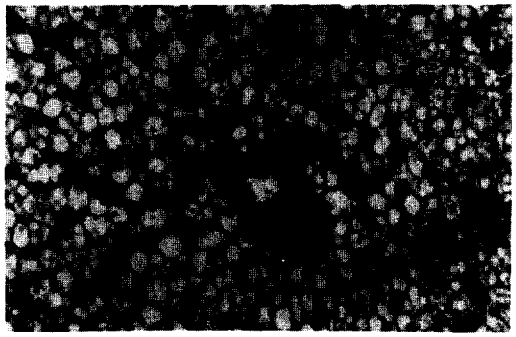

Fig. 2. Diffuse severe fatty changes and necrosis observed in hepatic parenchyma accompanied by congestion. H&E. ×200.

Fig. 3. Note extensive coagulative necrosis of re nal tubules and petechae. H&E × 100.

in thinning of the wall in most cases. Most venous vessels contained increased amount of dark red blood with incomplete blood clotting.

Microscopic Findings

On microsicopic observation it was found that most parenchymotous organs included adrenal gland were severely congested and edematous, and many internal organs showed patchy hemorrhage of variable size.

The lungs demostrated moderate to marked congestion of alveolar capillaries and intra-pulmonary veins, intra-alveolar hemorrhages, and excessive secretions in the bronchioles and intrapulmonary bronchi. Most alveoli and alveolar ducts were collapsed beyond occluded brochioles. There were severe ballooning degeneration and necrotic foci of epithelial cells in some brochioles with occasionlal areas of acute inflammatory cell infiltration in the tracheas, bronchi, and brochioles. In electron microscopy the compound-like particles were found in the epilthelial cells (Fig. 1).

The livers revealed marked congestion and multiple hemorrhages accompanying diffuse fatty changes and acute necrosis of the hepatic cells (Fig. 2). More extensive coagulation necrosis was scattered throughout the renal parenchyma with massive extravasation of red blood cells (Fig. 3). Splenic red pulp showed moderate congestion with variable amounts of hemosiderin and a number of plasma cells were found in the increased reaction centers. The only obvious findings observed in the gastrointestinal tracts were mild congestion and increased goblet cells in addition to progressed postmortem changes. Extensive congestion and a few petechiae were observed among large vacuolated cortical cells and the medulla of the adrenal glands.

DISCUSSION

Short-term acute inhalation toxicity studies in silver foxes, fitches, and minks indicate that CS is a severly toxic material. The gross signs of intoxication produced by this material are lacrimation, convulsion, spasm, dyspnea, and lethargy (Punte *et al.*, 1962). The toxic signs exhibited by the three species during exposure to the CS gas were mostly the same. The findings of pulmonary cogestion, hemorrhages, edema,

and atelectasis are consistent with the death due to asphyxia following lung damages for the CS exposure.

The other characteristic pathological findings were those of fatty changes and necrosis of hepatic cells, coagulation necrosis of renal tubules, and occasionally dispersed congestion and hemorrhages of internal organs including adrenal glands. The nature of the lesions and the facts that they they were consistent with severe lung damages accompanying dyspnea, suggest that these hepatorenal pathologic changes were due to hypoxic hypoxia secondary to lung damages which preceded cardiovascular collapse (Brimblecome *et al.*, 1977).

The lethal toxicity of CS is by lung damages leading to asphyxia and shock or by delayed brochopneumonia secondary to respiratory tract damages. However, that CS can be absorbed across the respiratory mucosa is indicated by the finding of 2-chlorobenzyl malononitrile and 2-chlorobenzaldehyde, two metabolites of CS, in blood from animals exposed to CS (Ballantyne *et al.*, 1972; Park *et al.*, 1972; Ballantyne *et al.*, 1977).

Although exactly how CS causes acute intoxication of the animals is not pricisely known (Jones *et al.*, 1970; Leadbeater *et al.*, 1973), this report warrants funther study to evaluate an exact mode of toxic action of CS.

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