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Original Articles

EVALUATION OF GASTROINTESTINAL COMPLICATIONS OF SULFUR MUSTARD POISONING IN IRANIAN COMBATANTS

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ABSTRACT

A total of 360 Iranian combatants who were exposed to mustard gas by the Iraqi forces in the war fronts were studied. Acute effects and gastrointestinal (GI) complications of sulfur mustard (SM) intoxication were studied separately in Iranian combatants admitted to Imam Reza Hospital from January 1984, to May 1988. In order to record the clinical and paraclinical findings, a special examination sheet and a questionnaire were designed. Routine laboratory tests such as CBC and ESR were performed for all patients and further investigation such as upper GI endoscopy were done as clinically indicated. Common GI symptoms were: nausea (47%), vomiting (42%), anorexia (40%), abdominal pain (35%), diarrhea (15%), melena (7%), and hematemesis (5%). Based on physical examination and endoscopy, acute esophagitis and gastritis were diagnosed. In the chronic phase 298 patients were observed two months to six years after exposure. Common GI symptoms were recorded as nausea (45%), anorexia (42%), abdominal pain (38%), hematochezia (12%), and hematemesis (5%). Based on upper GI series and endoscopy, gastritis (12%), duodenitis (8%), and duodenal ulcer (1%) were diagnosed. Other complications such as hepatomegaly and gastric carcinoma that were reported in the literature from the First World War experience, have not yet been observed in our patients. Only in one patient who was admitted for abdominal discomfort five years after SM poisoning, gastritis with intestinal metaplasia was observed on endoscopy and biopsy from the stomach.
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INTRODUCTION

The first large scale use of chemical warfare occurred on April 22, 1915 when the German forces unleashed clouds of chlorine on French and Canadian troops near Vapres, Belgium. The French and Canadian troops were without any protection. They suffered 20,000 casualties.[1]

For decades, bis 2-chlorethyl sulfide (mustard gas, sulfur mustard, Yperite) was regarded as the "king of chemical warfare agents." Despite the availability of highly toxic organophosphorus and other chemical warfare (CW) agents, this compound can not be omitted in any present-day appraisal of CW agents.[2]

Although SM, like other warfare chemicals, is usually absorbed through the respiratory system and skin, GI symptoms are relatively common in this poisoning as was

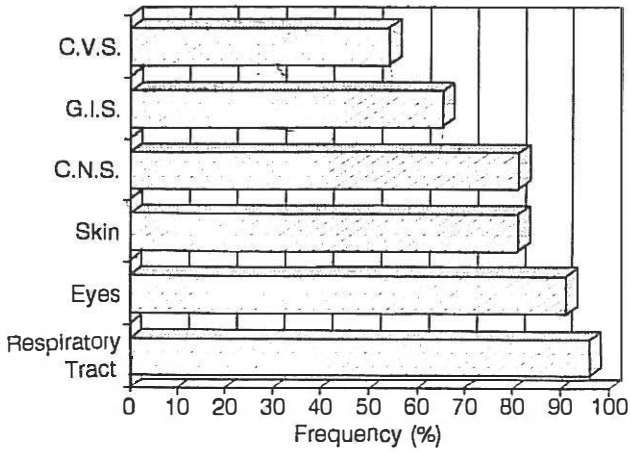

Fig. 1. Frequency of toxic effects of S.M. on body organs.

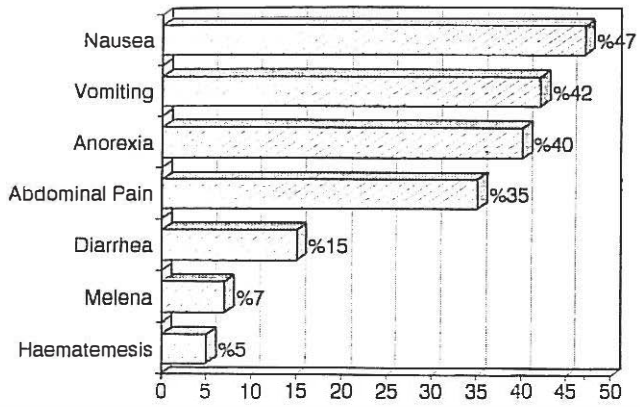

Fig. 2. Common G.I. symptoms in acute phase.

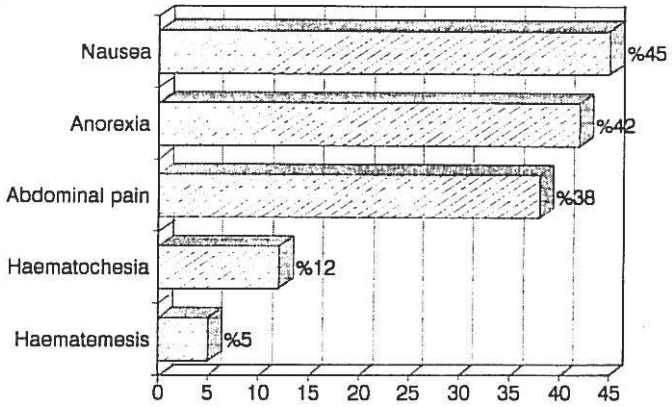

Fig. 3. Common G.I. symptoms in chronic phase.

previously reported[3] (Fig. 1). Some of these effects are due to direct toxic effects of the toxin on the upper GI tract and partly because of the cholinotoxic effects of SM. In the acute phase cholinergic effect of SM may cause clinical manifestations such as nausea, vomiting, and diarrhea.[4] In the chronic phase that will usually appear months or years later, complications such as hepatic involvement, hypochlorhydria, chronic gastritis, and even gastric carcinoma have been noticed.[5] The aim of this study is to investigate the acute and delayed toxic effects of SM on the GI tract in order to find out a better approach in the management of this severe wargas poisoning.

PATIENTS AND METHODS

A questionnaire and a special examination chart including GI symptoms and signs of SM poisoning were designed and completed by the trained medical staff for all combatants with chemical warfare exposure who were admitted to Imam Reza Hospital between January 1984, and May 1988. Diagnosis of SM poisoning was confirmed by toxicological analyses of urine and blister fluid by the method of Heyndricks et al. in the Toxicology Laboratory of Poisons Center.[6]

Clinical evaluation and records were performed during the first 24 hours after admission. Routine laboratory tests such as CBC and ESR were performed for all patients and further investigation such as upper GI series and endoscopy were performed as clinically indicated. Most of the patients who survived and were discharged 2 to 48 days after hospitalization, were then regularly followed up in a special C.W. clinic for the delayed toxic effects of SM poisoning. The GI complications on 360 patients were studied between May 1988, and June 1992. Clinical assessment, and when required, upper GI series, GI endoscopy, and pathological investigations were also performed on these patients. Further investigations were performed on the delayed toxic effects of SM on 289 poisoned combatants who were regularly checked up in the special clinic.

RESULTS

Patients were all male with the age range of 15-60 years (mean 24 years). In acute phase the symptoms were observed during the first week after exposure in 62% of the patients. The common GI symptoms were: nausea (47%), vomiting (42%), anorexia (40%), abdominal pain (35%), diarrhea (15%), melena (7%), and hematemesis (5%) (Fig. 2). Based on physical examination and endoscopy, acute esophagitis and gastritis were diagnosed in five patients who had ingested contaminated foods. Irritation effects such as erosion and blisters were seen in the pharynx, esophagus, and stomach. It was interesting to note that a patient who had taken a contaminated canned fruit, vomited later on his feet which were burned and blisters appeared.

In the chronic phase, two months to six years after exposure, common GI symptoms were recorded as nausea

(45%), anorexia (42%), abdominal pain (38%), hematochezia (12%), and hematemesis (5%) (Fig. 3). Based on upper GI series and endoscopy, gastritis (12%), duodenitis (8%), and duodenal ulcer (1%) were diagnosed.

Other complications such as hepatomegaly and gastric carcinoma that were reported in the literature from the First World War experience, has not yet been observed in our patients.

DISCUSSION

Sulfur mustard, or mustard gas, is an alkylating agent with a CL-CH2-CH2-S-CH2-CH2-CL formula. This dichloroethyl sulfide is a vesicant and similar to other alkylating agents, undergoes strong electrophilic chemical reactions through the formation of carbonium ion intermediates, or transition complexes with target molecules.[7,8] Although toxic effects of SM on respiratory system, eyes, skin, and neuropsychiatric system were more prominent, GI effects were seen in more than 50% of the patients as shown in Fig. 1.[3]

Toxic effects were divided into two groups: acute effects and chronic effects. Acute effects may be due to direct toxic effects of SM on the upper GI tract. Some of the acute toxic effects are due to cholinergic and cholinotoxic effects as indicated by Helm in 1986.[9]

In contrast to the cholinergic and cholinotoxic properties of mustard gases seen in animals, reports on cholinergic symptoms in SM casualties are rarely reported in the clinical literature.[3,4,10] On the other hand, varying neuropsychiatric disorders are described in clinical reports on SM casualties.[3,4,10-12] SM and also nitrogen mustard are lipophilic alkylating agents. They are rapidly absorbed by biological membranes. Their toxic actions, however, are due to some short living cycling hydrolysis products, i.e. cyclic sulfonium ions from the results of many studies with SM and nitrogen mustard or with the less short-living hydrolysis products of nitrogen mustard. It might be concluded that the specificity of mustard gas to cholinergic neurons originates from the close structural similarity of their intermediary products to choline.[9]

The symptoms recorded in this study were more common than the signs. This could be due to psychiatric disorders and exaggeration of the severity of intoxication by the patients.

Further investigation is required and the search for minor pathological changes in certain brain areas with high density of cholinergic neurons might be helpful to clarify the neurotoxic actions of mustard gas on the GI tract.

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