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CASE REPORT

Intestinal perforation associated with chlorine dioxide ingestion: an adult chronic consumer during COVID-19 pandemic

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Abstract

COVID-19 pandemic is one of the most devastating worldwide crises in recent years. During this pandemic, people have been exposed to products that have not been proven to be safe and effective against COVID-19. We present an adult chronic consumer of chlorine dioxide, in which a fatal outcome is described. This case demonstrates that for people searching products to protect themselves from COVID-19, unregulated access to industrial disinfectants represents a dangerous alternative. To date, there is no scientific evidence to uphold the use of chlorine dioxide or chlorine derivatives as preventive or therapeutic agents against COVID-19. Researchers and general population must take into consideration the fatal possible consequences of not following communications and warnings from health authorities and government institutions.

Keywords Chlorine dioxide · Ingestion · Perforation · SARS-CoV-2 · COVID-19

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the etiologic agent of COVID-19. In late December 2019, SARS-CoV-2 was discovered in Wuhan, China [1]. In the next few months, it spread at an exponential rate and came to be known as the COVID-19 pandemic, declared by the World Health Organization in March 2020. This resulted in a devastating impact on global healthcare and economic systems.

Several health authorities, including The Food and Drug Administration (FDA) and The Pan American Health Organization (PAHO) joined efforts to prevent the use of chlorine derivatives as treatment and/or preventive therapy against SARS-CoV-2. These products include chlorine dioxide or sodium chlorite, as well as the presentation "Miracle Mineral Solution (MMS)". Besides the lack of scientific evidence to support its use to treat COVID-19, they also lack sanitary authorization to be used in humans as medical treatment. Despite the attempts from health authorities to prevent its use, the effectiveness and safety of these products against COVID-19 as preventive and curative drugs is assured by the distributors and manufacturers [2].

Chlorine dioxide is a strong oxidizing agent. Because of its chemical properties, it is a very useful agent for antimicrobial applications, bleaching and water disinfection. Chlorine dioxide and sodium chlorite react rapidly upon direct contact with biological tissues. If ingested, may cause irritation of the gastrointestinal tract, with severe symptoms [3, 4].

During the COVID-19 pandemic, proponents of chlorine dioxide resurfaced, claiming that this product could be used to prevent and treat SARS-CoV-2 infections [5]. For this, it is crucial to demonstrate and recognize the importance of warnings issued by health authorities. To our knowledge, this is the first report of a patient with intestinal perforation associated to chlorine dioxide ingestion.

Case presentation

We present the case of a 65-year-old male patient, who sought medical care in our institution with a 1-week history of abdominal pain, nausea, vomiting, and melena on two

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occasions in the last 24 h. The patient denied chronic degenerative diseases. Surgical history of hemorrhoidectomy 28 years ago. Tobacco smoking history of 6 pack-year and denied having suffered COVID-19 disease. Also, the patient referred ingestion of chlorine dioxide in the last 9 months as a preventive therapy for coronavirus disease, with a gradual increase in the dose until reaching the consumption of 10 ml per day, diluted in 1 L of water and ingested in a period of 8 h. The exact chlorine dioxide solution concentration was unknown, although it was referred as high.

Physical examination at the time of admission revealed a bad general condition, with drowsiness, hypotension and tachycardia, and abdominal examination with data of peritoneal irritation, distention, and absent peristalsis. The patient was found to have a blood pressure of 75/40 mmHg, a pulse rate of 120 beats/min and a respiratory rate of 23 breaths/min, mildly pyrexial at 37.5 °C. The blood examination reported hemoglobin 12.2 g/dL, leukocytes 14.10 (10 *3 µL), platelets 241.9 (10 *3 µL), electrolyte imbalance with potassium 6.1 mEq/L and sodium 126 mEq/L, liver function tests in normal parameters.

Fig. 1 Abdominal CT demonstrates free intraperitoneal air and fluid secondary to hollow viscus rupture

Abdominopelvic computed tomography was performed, which revealed abundant free fluid in the abdominal cavity, peri-pancreatic space, in both paracolic gutters and pelvic hollow with densities of 10 HU. The presence of pneumoperitoneum secondary to hollow viscus rupture was also evident (Fig. 1).

Surgical approach was conducted with exploratory laparotomy, finding free fluid in the abdominal cavity (approximately 2.5 L), with jejunum perforation adjacent to the fixed loop. Intestinal resection was performed 80 cm from the jejunum with bowel loop closure; gastrostomy and jejunostomy were performed (Fig. 2). Pathological examination of the specimen revealed ulceration and denudation of the epithelium with severe changes due to tissue necrosis in the mucosa, in addition to acute and severe chronic inflammation with areas of transmural extension (Fig. 3). The clinical status of the patient was critical after surgery, with presence of septic shock, SOFA score 13 points (mortality > 95.2%), APACHE score 21 points (mortality of 30%), developing liver and kidney failure, as well as neurological deterioration requiring orotracheal intubation. Hemodiafiltration was indicated by the hemodialysis service, nevertheless, the patient was not in optimal clinical conditions. 48 h after the surgery, he presented cardiorespiratory arrest. Unfortunately, despite early cardiopulmonary resuscitation in the intensive care unit, and due to multiple organ failure and poor clinical condition, irreversible systemic deterioration led to the patient's death.

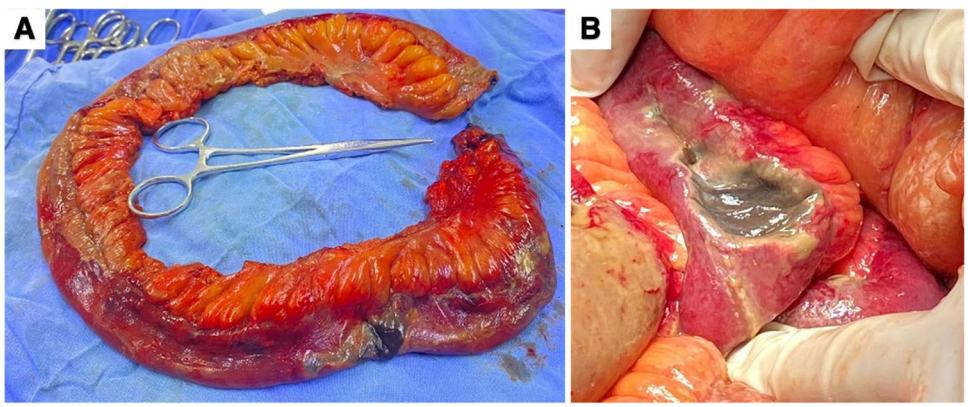

Fig. 2 Small bowel resected segment (jejunum) measuring 40.0 cm. Full thickness necrosis and perforation in the antimesenteric area is evident (**A**). Jejunal perforation with regular edges measuring 1.0 × 1.0 cm (**B**)

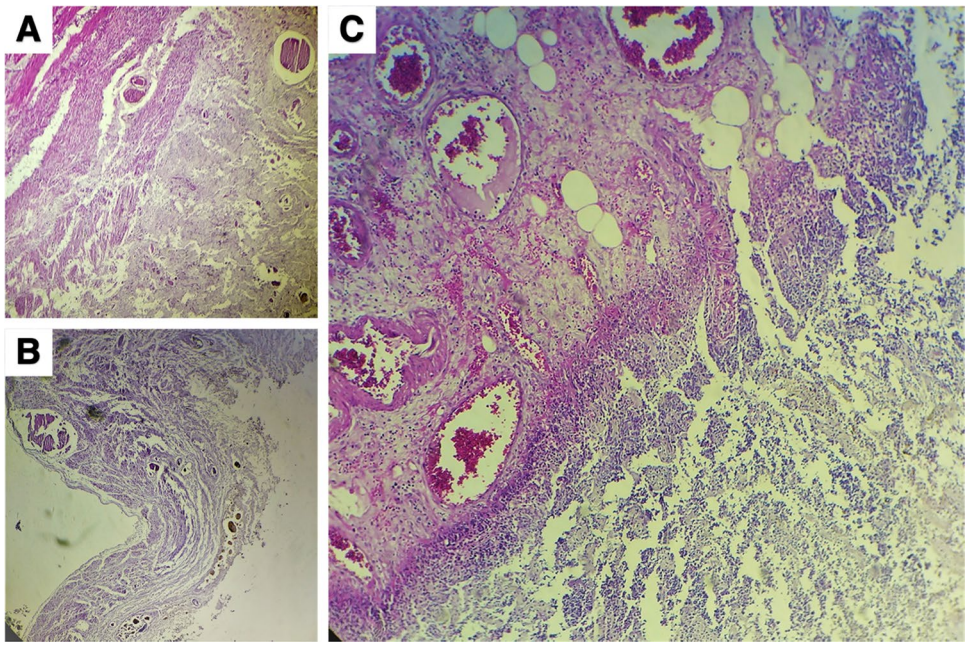

Fig. 3 Histopathological findings. Ulceration and denudation of the epithelium, with the presence of conserved epithelial cells. Serous layer with destruction of the parenchyma (**A**). Chronic inflammation of the serous layer with neutrophilic infiltrate. Inflammation and severe changes due to tissue necrosis in the mucosa are present (**B**). Muscle layers with chemical destruction and neutrophilic infiltration in the serous layer (**C**)

Discussion

Ingestion of corrosive substances can produce severe injury to the gastrointestinal tract. The extent and degree of tissue injury are dependent on such factors as the type of substance, morphological form of the agent, amount, intention, concentration, pre-ingestion condition of the tissues, and duration of contact. Oxidant agents, such as bleach, are among the corrosives commonly found. These agents can cause serious damage to the gastrointestinal tract, including perforation [6, 7].

Prior to the COVID-19 pandemic, chlorine derivatives products were already commercialized. Specifically, sodium chlorite under the name MMS (Miracle or Master Mineral Solution; Master Mineral Supplement). Distributors claimed that after mixing with an acid, it had antiviral and antibacterial effects, and was supposed to be a treatment for various unrelated diseases, such as autism spectrum disorder, cancer, flu, hepatitis and HIV/AIDS [8–10]. Several warnings and communications were published before and after the COVID-19 pandemic by government institutions and regulatory entities including USA, Canada and the UK, aiming to stop commercialization and demanded its withdrawal from the market [11–14].

Chlorine dioxide is a greenish–yellowish gas, and it is known to be highly effective at alkaline pH [15]. Although this compound is a gas, it is highly soluble in water [16]. Chlorine dioxide has many applications in numerous fields, such as water or wastewater treatment, bleaching, environmental and food disinfection, and sterilization of medical devices. The maximum concentration for chlorine dioxide in the drinking water has been set at 0.8 mg/L by The Environmental Protection Agency (EPA) [3, 17–20]. Conversely, exposure to higher concentrations might cause serious side effects. It is a respiratory irritant compound; hence, it may cause irritation of eyes, nose, throat and lungs [18]. Also, the ingestion of these products may cause irritation of the mouth, esophagus and stomach, with severe irritative digestive symptoms; nausea, vomiting and diarrhea, in addition to serious hematological (methemoglobinemia, hemolysis and disseminated intravascular coagulation), cardiovascular and kidney disorders, including renal failure [4, 21–23]. Therefore, the permitted amount of chlorine dioxide and chlorine levels per volume of water in drinking water is highly regulated [3]. It has been observed that the concentrations of these commercialized products exceed the maximum limits allowed in drinking water in countries where chlorine dioxide or sodium chlorite have been marketed as therapeutic agents [11].

It is necessary to understand the mechanism of action of oxidizing agents, such as chlorine dioxide and sodium chlorite. As mentioned previously, these substances serve as disinfectants due to their oxidizing properties. This means they can oxidize other compounds via an oxidation–reduction reaction [24]. Ultimately, chemical reactions will induce disruption of protein synthesis and outer membrane permeability due to rapid efflux of potassium ion, leading to the destruction of the transmembrane ionic gradient [25, 26]. This effect is not specific to a particular organism; human cells, like other microorganisms, are also affected [27].

No study has evaluated the clinical effects of chronic chlorine derivatives ingestion to date. Gradual and low increase in chlorine dioxide concentration may have lessened irritative symptoms until lesion of the mucosa

and ultimately, perforation of the gastrointestinal tract occurred. Additionally, chronic inflammation of the serous layer with neutrophilic infiltrate and tissue necrosis in the mucosa caused by chemical destruction was demonstrated by histological findings.

A recent data analysis of the American Association of Poison Control Centers (AAPCC) National Poison Data System (NPDS) identified 53 cases of chlorine dioxide associated exposure between January 1, 2000 and March 31, 2020 [28]. The main reasons for use were infectious disease (13.2%), accidental exposure (9.4%), supplement/cure all (9.4%) and detoxification (7.5%). Ingestion was the most common route of administration (83%). 62.3% cases were female, and the median age was 46 years. The most frequently reported related clinical effects were vomiting (49.1%), nausea (28.3%), abdominal pain (22.6%), and diarrhea (20.8%). The majority of exposures represent acute toxicity (84.9%), as most effects occurred the first 24 h of exposure (75.5%) (Table 1). It is likely to be a greater amount of exposures than are described in this report, as it is subject to limitations common to voluntary reporting systems. Because poison control centers primarily offer advice following acute exposure, the data rarely include late-onset clinical effects or long-term complications. Nevertheless, it grants a fair contrast in regarding the consumption of chlorine derivatives.

The first analysis that linked the geospatial dynamics of social media with public health interventions has been recently published. The study indicates that health misinformation on social media is associated with greater exposure to household cleaners, including bleaching agents [29]. Also, the access to concentrated formulations of chlorine derivatives has increased in recent years due to unsupported claims of efficacy in preventing and treating several medical conditions, now including COVID-19 [16, 30].

To date, there is no scientific evidence to uphold the use of chlorine dioxide or chlorine derivatives as preventive or therapeutic agents against COVID-19 [2]. This case demonstrates that for people searching cleaning products to protect themselves from COVID-19, unregulated access to industrial disinfectants represents a dangerous alternative. The use of products that have not been proven to be safe and effective against COVID-19 not only poses a potential health risk to those who use them, but also to the entire population. By generating a false sense of security due to the presumed but unproven beneficial effect, these products may also incur in the abandonment of prevention and control measures against COVID-19 that have proven to be effective, such as the use of masks, social distancing and hand hygiene. Furthermore, it is critical that public messaging steers clear of promoting these potentially lethal products as we continue to manage the COVID-19 pandemic. We urge consumers to avoid the use of chlorine dioxide derivatives and we expect to make health care providers aware of potential clinical sequelae associated with its administration.

Table 1 Data analysis of 53 patients associated to chlorine dioxide exposure

Purpose for use	Cases (%)
Infectious disease	13.2
Cure all/supplement	9.4
Accidental exposure	9.4
Detoxification	7.5
Toothache	3.8
Constipation	3.8
Sinus pain	1.9
Self-harm	1.9
Lymphoma	1.9
Autism	1.9
Not documented	45.3
Related clinical effects	
Vomiting	49.1
Nausea	28.3
Abdominal pain	22.6
Diarrhea	20.8
Oral or throat irritation, Cough, choke	17
Burns (any degree)	7.5
Ocular (irritation/pain/red eye/conjunctivitis)	5.7
Other	11.3
Chronicity	
Acute	84.9
Acute-on-chronic	1.9
Chronic	11.3
Unknown	1.9
Time to onset	
< 1 h	30.2
> 1 h to < 1 day	45.2
> 1 day to ≤ 1 week	9.4
2 months	1.9
Unknown	13.2
Gender	
Female	62.3
Male	37.7
Route of administration	
Oral ingestion	83
Other (inhalation, dermal, rectal, and ocular)	17

Modified from reference [28]

Conclusion

The ingestion of unregulated and unapproved products by health authorities, such as chlorine dioxide or chlorine derivatives, may have severe outcomes, including intestinal

perforation. It is of key importance to emphasize the necessity of following communications and warnings from health authorities and government institutions. Clinicians must consider this pathology in the differential diagnosis of patients exposed to chlorine derivatives and household cleaners.

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Data availability Data sharing was not applicable to this article, as no datasets were generated or analyzed during the current study.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Human rights All procedures followed have beenperformed in accordance with the ethical standards laid down in the1964 Declaration of Helsinki and its later amendments.

Informed consent Informed consent was obtained from the patient forbeing included in the study.

Consent for publication Written informed consent was obtained for publication of this case report and accompanying images. A copy of the consent form is available for review by the Editor of this journal.

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