

Systemic Review

Health effects of sodium hypochlorite: review of published case reports

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Abstract

Sodium hypochlorite is widely used as the main component of cleaners and has an excellent bleaching and sterilizing effect in living and medical environments. In addition to bleaching, it is used for wastewater treatment and for sterilization in food factories, and also for disinfectants during the COVID-19 pandemic. This study analyzed reports of the health effects of sodium hypochlorite and classified them by toxicity along the exposure pathway. Most case reports described the health effects of acute high-concentration exposure, with a common case being dental exposure, mainly during treatment.

Keywords: sodium hypochlorite, toxicity, exposure pathway

Introduction

Sodium hypochlorite (NaClO) is a chlorine-based compound with a molecular weight of 74.44; it is a white solid at room temperature and light yellow or green in aqueous solution. Sodium hypochlorite is widely used as the main component of cleaners with excellent bleaching and sterilizing effect. It is also used for wastewater treatment and sterilization in food factories, and for oxidizing various organic chemicals and refining petrochemicals.

During the COVID-19 pandemic, the most recommended disinfectants are 70% ethanol and chlorinated disinfectants such as sodium hypochlorite and calcium hypochlorite. To prepare 0.1% chlorine suitable for disinfection of surfaces, one cup of sodium hypochlorite bleach containing 5% active chlorine should be mixed with 49 cups of water [1,2]. As study that investigated the pattern of disinfectant use during the outbreak of COVID-19 reported that 74.2% of participants used a wrong proportion of sodium hypochlorite to make this disinfectant at home and approximately 42% experienced at least one side effect on their hands, feet, eyes, respiratory or gastrointestinal systems after sequential uses of disinfectants [3]. The Ministry of Food and Drug Safety of Korea urged consumers to take special care, saying that disinfectants for food and utensils are misused to prevent COVID-19 infection [4,5]. A report of conditions used at 227 food services assessed the efficacy of various sanitizers including sodium hypochlorite (100 ppm and 200 ppm) under various conditions found that it is necessary to provide useful and practical information, for instance how to sanitize objects properly in food services [6]. With the appearance of the new coronavirus, interest in sanitizing has increased. This study reviewed cases of health effects of sodium hypochlorite exposure and classified them according to the exposure pathway and reviewed case progress.

Methods

An internet search used the search engines PubMed and Google Scholar. The keywords used for the search were "sodium hypochlorite" and "hypochlorite", both in combination with "toxicity". Review articles which were published from January 2000 to June 2021 and articles published between January 2019 and June 2021 were collected. After deleting duplicate articles, all full-length papers and English-langue papers were included. 1,194 articles were obtained. They were classified into three categories by two researchers. Category 1 included health effects, toxicity, side effects, and cytotoxicity of sodium hypochlorite in laboratory animals. Dentistry-related papers were classified into category 2. Papers on complex compounds and papers not related to health effects were classified into category 3. After classification, a new researcher collected classifications and reclassified inconsistent items, and papers corresponding to category 1 were used for further

analysis. And the papers which were related document by retracing the references in the searched literature and review articles were finally included.

Health effects by exposure route

Ingestion

It is the most common route of exposure, and ingestion of sodium hypochlorite (less than 6% hypochlorite) causes nausea, vomiting, and burning sensation in the mouth [7]. Serious toxicity occurs when sodium hypochlorite is ingested in large amounts (5 mL/kg in children, 150-200 mL in adults) or at concentrations more than 6% [8,9]. Redness, edema, and ulceration may occur in the oral cavity, nasopharynx, and esophagus, and in severe cases gastric perforation may occur. Complications may include coughing, shortness of breath, aspiration pneumonia, and upper airway edema. In severe cases, pulmonary edema may occur, and tachycardia, hypotension, and convulsions have also been reported. Systemically, metabolic acidosis, hypernatremia, and hyperchloremia appear [4,10,11].

A study of corrosive substance intake cases between 01/07/2017 and 01/07/2019 in emergency department of training and research hospital reported that sodium hypochlorite was the most frequent caustic substance ingested, with 51.6% accidental intake and 41.6% suicidal intake. In such cases, endoscopy should be performed as soon as possible, whereas the use of neutralizing treatment is controversial because of the risk of causing thermal injury [12].

A 16-year-old girl who attempted suicide by ingesting 100 mL of 4.5% sodium hypochlorite bleach was transferred to an emergency department after gastric lavage. She presented with dyspnea and drowsiness. Endoscopy 10 days later showed severe esophageal stenosis, and she was diagnosed with esophageal perforation and mediastinitis by radiology 16 days after ingesting bleach. The patient received nonsurgical intensive management with antibiotics, fluids, proton pump inhibitors, and chest tube insertion and gastrostomy for nutritional support. Two months after NaOCl ingestion, she underwent definitive corrective surgery that involved esophagectomy and reconstruction with a colonic interposition graft and was discharged after a good recovery [13].

A unique case of diffuse alveolar hemorrhage (DAH) following the ingestion and intravenous injection of bleach has been reported. A 42-year-old woman presented after injecting 12 mL of sodium hypochlorite bleach intravenously in her arms and legs during a suicide attempt. She also ingested one-half cup of bleach. She complained of painful swelling in her extremities at the sites of injection and noted nausea, diarrhea, and abdominal fullness. Three days later, she returned with a gradual onset of dyspnea, chest pain, fever, and cough with clear sputum production progressing to respiratory distress. Noncontrast chest computed tomography demonstrated a diffuse interstitial “crazy paving” pattern with bilateral ground-glass opacities. The patient was given high-dose intravenous steroids for DAH. Her oxygenation improved significantly in the next three days, and she was discharged on a steroid taper with a complete resolution of symptoms. In this case, it was hypothesized that injury resulted from direct damage to alveolar capillaries by sodium hypochlorite delivered intravenously [14].

A 66-year-old female ingested an unknown quantity of regular Clorox bleach (5.25% sodium hypochlorite, pH = 11.4). She was vomiting spontaneously and had slurred speech and oral mucosal discoloration. On hospital arrival, the patient had hypernatremia (169 mEq Na/L), hyperchloremia (143 mEq Cl/L), and metabolic acidosis (5 mmol total CO₂/L) in laboratory studies and bilateral pneumothoraxes and pneumoperitoneum were found by radiology. Vital signs deteriorated rapidly, with cardiorespiratory arrest that resulted in death. Autopsy revealed esophageal and gastric mucosal erosions, perforation at the gastroesophageal junction, and extensive necrosis of adjacent soft tissue [15].

In a suicide attempt case using 750 ml of 13.3% sodium hypochlorite and flunitrazepam 24 mg, a 32-year-old woman presented with coma, dyspnea, vomiting, superficial burns in the mouth, and metabolic acidosis. An X-ray showed pneumoperitoneum due to a gastric perforation and opacities in the left lower lobe. At 65 h after bleach ingestion, she died of multiple organ failure, refractory hypoxemia, and disseminated intravascular coagulation [9]. A 55-year-old female actively ingested a 3.5-L bottle of Clorox bleach (6% sodium hypochlorite) without any information on the ingested amount which resulted in total gastrectomy [16].

Dental exposure

Sodium hypochlorite (typically 1–5% solutions) is used extensively by dentists for cleaning root canals during endodontic therapy because of its antimicrobial and tissue-dissolving properties [17]. Several cases have been reported of the adverse effects of accidental exposure of intraoral areas to sodium hypochlorite solution.

The case of Sodium hypochlorite and chlorhexidine extrusion through the apical foramen result in acute pain, swelling, and mucosal fenestration. Immediate and copious irrigation with saline or water for 15 min, ice pack compression for 24 h, followed by warm compress for 24 h are the suggested strategies to reduce damage caused by hypochlorite injuries. Analgesics to manage pain, antibiotics to prevent secondary infection, and steroid therapy for severe injuries are considered (with referral as required [18,19]. A 1.5% sodium hypochlorite solution was inadvertently injected into the buccal mucosa of a 56-year-old female during routine root canal treatment. Soft tissue necrosis, labial ptosis, and paresthesia occurred shortly after the injection. Tissues healed with scarring, and lip paresthesia persisted for 3 years [20].

In some cases, exposure to sodium hypochlorite solution during dental treatment can cause serious complications. Accidental sodium hypochlorite injection into the infraorbital tissue during a dental procedure caused acute kidney injury secondary to renal tubular injury, causing mild acute tubular necrosis [21]. Another case report described a hypochlorite accident that occurred in a healthy 42-year-old female who was undergoing routine root canal therapy for the lower right central incisor (tooth #41) with 3% sodium hypochlorite (for a total of 12 cc). After approximately 1 h of irrigation, the patient complained of severe pain and burning in the lip, and then swelling progressed over the next 8 h to involve the sublingual and submental fascial spaces with elevation of the tongue and resultant upper airway obstruction. The patient was intubated and remained on mechanical ventilation for 3 days. She recovered without any skin necrosis or nerve deficits [22]. Therefore, although sodium hypochlorite is generally a safe root canal irrigation solution, it may lead to life-threatening complications due to negligence or inexperienced handling. Careful injection without pressure, the use of proper rubber dam isolation, and the use of the endodontic needle are necessary to avoid such complications. Early recognition and management of the untoward effects of sodium hypochlorite are vital for the patient's safety.

Dermal exposure

Sodium hypochlorite is a known irritant and there are some reports that it can also cause allergic contact dermatitis of type IV hypersensitivity. The degree of damage depends on exposure time: short exposures cause only temporary damage, but long exposures cause skin irritation, damage, and irritability. At high concentrations, chemical damage such as burning pain, redness, edema, watering, or necrosis can also occur [23,24].

Allergic contact dermatitis caused by hypochlorite is a delayed-type hypersensitivity (type IV) reaction, in most cases caused by accidental occupational or home exposure; other immediate urticarial reactions have also been reported. A rare case of work-related type I hypersensitivity to sodium hypochlorite was reported. A 22-year-old theater cleaner wore personal protective gear while cleaning with a 0.1% sodium hypochlorite solution spray. He had recurrent urticarial rash and a positive prick test reaction to this chemical and was subsequently removed from further exposure with no further recurrences of the urticarial rash [25].

A 70-year-old female was wiping the stool mass with YUHANROX®. YUHANROX® (>4% sodium hypochlorite) is a domestic bleach widely used in Korea. The wiped skin area developed edema, an erythematous lesion developed on the second day, and it caused necrosis of the subcutaneous tissue layer and exposure of the muscle layer, and she was diagnosed with a third-degree burn equivalent to 5% of the body surface area. Complete epithelization was achieved after 3 split-thickness skin grafting procedures, but a severe scar formed [26].

Inhalation exposure

Inhalation of hypochlorite causes irritation, nausea, vomiting, dizziness, breathing distress, headache, and cough. At high concentrations, hypochlorite may cause upper respiratory tract edema and pulmonary edema [27]. Long-term use of hypochlorite increases neutrophil levels and causes lower airway symptoms. Chlorine gas derived from chemical reactions between sodium hypochlorite and other substances accounts for most of the aspiration exposure and can cause upper respiratory tract symptoms and serious hypoxemia, pneumonia, bronchitis, pulmonary edema, and acute respiratory distress syndrome [28,29]. The mechanism of the respiratory effects of low-dose chlorine gas exposure involves an immune response with increases in innate lymphoid cells and monocyte-derived macrophages, and acute or chronic exposure to low doses of chlorine gas worsens lung function, induces oxidative stress and mucus production, and increases inflammation in healthy mice [30,31].

Chemical pneumonitis caused by chlorine gas inhalation, generated as a secondary product by the chemical reaction between sodium hypochlorite and red diesel, has been reported in a child. A 9-year-old boy developed shortness of breath and chest pain after playing with friends at a building site, where they produced a bonfire using sodium hypochlorite and a red diesel barrel. Supportive care, including airway intubation, recovered after six weeks without any ongoing pulmonary symptoms [32].

One report described organizing pneumonia confirmed by transbronchial lung biopsy after exposure to sodium hypochlorite for a long period of time. A 77-year-old male was admitted to a hospital with nonproductive cough, myalgias, fever, and progressive weight loss after prolonged exposure. The patient was treated with antibiotics and oral prednisolone. The clinical condition of the patient improved starting from one week after the onset of prednisolone treatment. The proposed mechanism was that hypochlorite could release chlorine that damaged moist tissues by reacting with water to form hydrochloric and hypochlorous acids [33].

Several cases related to worksite exposure to sodium hypochlorite have been reported. Cases of work-related asthma caused by exposure to cleaning products have been reported in California, Massachusetts, Michigan, New Jersey, and New York, 12.4% of occupational asthma was associated with cleaning products, and occupations with a high frequency of the disease were health carers, building cleaners, and registered nurses. It was suggested that continued and more effective prevention efforts are needed to reduce the unnecessary use of disinfectants in both health care and non-health care setting, identify safer products, and implement safer work processes [34]. Home care aides may be exposed to volatile

organic compounds and chlorine during bathroom cleaning and spraying in small, poorly ventilated spaces typical of bathrooms. This occupational exposure leads to the development of adverse respiratory symptoms [35]. Nurses exposed to hypochlorite bleach, hydrogen peroxide, or both in combination with exposure to aldehydes as disinfectants had a high risk of chronic obstructive lung disease caused by injury of the airway epithelium and oxidative stress [36]. According to a survey of the use of disinfectants during the COVID-19 outbreak, 4.8% of people use sodium hypochlorite bleach because of low cost and easy availability, and 57.3% of people widely use sodium hypochlorite for surface disinfection. The survey reported that improper preparation, the use of disinfectants in unconventional concentrations, storage in unsafe places, excessive use of these materials, receiving instructions for their use from unreliable sources, and improper disposal of empty containers are the most important mistakes made by the participants and misuse of these substances had adverse effects on 41.4% of the participants such as lung irritation, shortness of breath, cough, and sneezing [3].

There was an extraordinary case of mass inhalational exposure: 25 soldiers were exposed to chlorine gas because of mixing sodium hypochlorite with hydrochloric acid during cleaning activities. The main symptoms were coughing and dyspnea; forced expiratory volume in 1 s (FEV1) and FEV1/forced volume capacity (FVC) ratio were found to be normal in all patients, but FVC and peak expiratory flow were below the normal range (80%) in 9 patients (36%) in a pulmonary function test. All patients received warmed humidified oxygen combined with nebulized salbutamol. Inhaled budesonide and nebulized sodium bicarbonate were administered additionally for 19 patients (76%). No mortality was observed. The results suggest that inhaled steroids combined with nebulized sodium bicarbonate could be a safe and effective treatment for the symptomatic patients [37]. Another mass inhalation exposure of two groups of 36 patients each (72 in total) to chloramine gas produced from mixing common household cleaning agents containing sodium hypochlorite and ammonia was reported. All patients were soldiers exposed during a "cleaning party" in their barracks. Nebulized sodium bicarbonate solution has been suggested for treatment of chlorine gas inhalation, but no report of its successful use for treatment of chloramine gas inhalation injury exists. In this case, 22 patients were treated with a nebulized solution of 3.75% sodium bicarbonate, but this treatment resulted in no significant statistical or clinical difference in the outcome in comparison to the treatment without nebulized sodium bicarbonate [38].

Systemic acute allergic contact dermatitis through inhalation has been reported in a wastewater treatment worker, and professional exposure substances were sodium hypochlorite, hydrogen peroxide, ferric chloride, and other chemicals [39].

The chlorine-based disinfectants can enter the sewer system or stormwater drains in the form of surface runoff, eventually leading to severe contamination of surface water and disinfection by-products (DBP) forming potentially harmful organochlorine compounds by reacting with natural organic matter, and the majority of DBP also act as potential human health hazards [40,41]. Lou reported increasing concentration of DBP in the air during the COVID-19 pandemic that the median concentration of all DBPs was 34.1 $\mu\text{g}/\text{m}^3$, 2.8 $\mu\text{g}/\text{m}^3$, and 1.0 $\mu\text{g}/\text{m}^3$ for hypochlorite spray doses of 100-200 mg/m^3 , 3-20 mg/m^3 , and 0 mg/m^3 , respectively and a hazard index value for children was 0.5 (1 being the threshold for non-cancerous risks) indicating that this group may face inhalation-related risks [42].

Ocular exposure

The reported symptoms following eye exposure to hypochlorite are generally mild to moderate and include conjunctival edema, conjunctivitis, lacrimation, impaired vision, foreign body sensation, photophobia, corneal abrasions, and superficial punctate keratopathy. Additionally, chemical burn of the eye induced by 3.5% sodium hypochlorite was reported in an endodontist; the exposure occurred during antibacterial irrigation for root canal infection [43]. In another case, a 5.25% sodium hypochlorite solution was accidentally splashed in patient's eyes during endodontic therapy. As a measure against chemical trauma of the eye by sodium hypochlorite solution in this case, ocular irrigation was performed immediately with a continuous stream of normal saline from a 1-l bag attached to an intravenous line with a 16-gauge Teflon catheter placement sleeve affixed to the distal end of the line. Additionally, immediate evaluation, treatment, and consultation by an ophthalmologist were arranged [44].

Intravenous exposure

Intravenous exposures typically occur accidentally in intravenous drug users or intentionally as self-harm attempts. A case of DAH following the ingestion and intravenous injection 12 ml of sodium hypochlorite in her arms and legs during a suicide attempt was reported in a 42-year-old woman [14]. A 30-year-old man was intentionally infused with 20 mL of 5% sodium hypochlorite in 500 mL normal saline. Clinical symptoms were local pain and edema with no laboratory abnormalities. Doppler sonography revealed thrombosis in superficial (antecubital and basilic) veins, and pain and edema were relieved after 3 days by limb elevation, warm compress, and ibuprofen [45].

Kidneys are vulnerable to the effects of massive hemolysis induced by oxidative stress due to sodium hypochlorite. An 18-year-old female was reported who presented with black urine after parenteral self-administration of Clorox® Lemon Fresh Bleach ($\leq 5\%$ sodium hypochlorite and $\leq 1\%$ sodium hydroxide, 100 mL) intended for treatment of purported chronic Lyme disease. Laboratory studies demonstrated acute kidney injury, intravascular hemolysis, and mild

myocardial injury. She required hemodialysis after becoming anuric. The patient received seven hemodialysis treatments before recovering sufficient renal function [46]. The pathophysiologic mechanism may be that NaOCl is converted to HOCl upon contact with plasma, which generates superoxide radicals causing oxidative cell death, hemolysis, and rhabdomyolysis. Hemolysis can also occur due to rapid protein degradation by this hypertonic and strongly alkaline solution. Massive hemolysis leads to excessive hemoglobin breakdown, overwhelming haptoglobin stores and causing generation of heme-free proteins. These heme breakdown products cause kidney injury by direct toxicity, reduced kidney blood flow, pigment cast formation, and subsequent tubular obstruction [47].

Conclusions

Health effects of sodium hypochlorite exposure and treatment progress were reviewed according to the exposure path. Except intentional exposures such as the attempts of suicide, exposures to high concentrations of hypochlorite were mostly accidental, but reports of the health impact of long-term occupational or environmental exposure to low concentrations were rare. To prevent the health effects of disinfectants, it is recommended to wear protective equipment such as masks, gloves, waterproof aprons, and goggles [48]. Hypochlorite is rarely accumulated in vivo [49,50], but many disinfectants containing sodium hypochlorite are constantly being used throughout the COVID-19 pandemic period (since late 2019), and the opportunities for exposure of certain occupations as well as the public have increased significantly in comparison to the pre-pandemic levels. Therefore, continuous monitoring about health effects of disinfectants such as sodium hypochlorite will be recommended to account for the possibility of exposure to public health as well as personal exposure as usage increase.

Conflict of interest

The authors declare no conflict of interest.

CRedit author statement

ISC: Conceptualization, Writing-Original draft preparation; HSR: Investigation, Validation; SY: Methodology, Project administration; JCH: Investigation, Resources.

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