



The Management and Prevention of Sodium Hypochlorite Accidents: A Scoping Review

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Abstract

Sodium hypochlorite (NaOCl) accidents are a serious iatrogenic complication in endodontic treatment that may cause severe tissue damage, life-threatening conditions, long-term sequelae, and medico-legal consequences. This scoping review aimed to provide a comprehensive overview of the management and prevention of NaOCl accidents. A systematic search of major databases, including PubMed/Medline, Web of Science, Scopus, Cochrane, Google Scholar, ScienceDirect, LILACS, and Crossref, was conducted using relevant MeSH terms and keywords. After screening and eligibility assessment, 262 articles comprising case reports, case series, original studies, and review articles were included. The findings indicate that although many patients experience complete recovery, the clinical course and outcomes of NaOCl accidents remain unpredictable. Some cases may result in incomplete recovery, persistent symptoms, or permanent adverse effects. Therefore, prompt recognition and immediate intervention are essential. Initial management should focus on minimizing tissue damage through rapid detection, aspiration and/or dilution of the extruded irrigant, symptom control, and appropriate referral when necessary. Because clinical manifestations often worsen during the early stages, careful monitoring, detailed documentation, and regular follow-up are critical throughout the progression and recovery phases. Extended management may be required for patients with short- or long-term complications. The review also emphasizes that prevention remains the most effective strategy. Clinicians should adopt preventive measures related to patient assessment, tooth selection, irrigant characteristics, and irrigation techniques before and during intracanal irrigation. Adherence to safe irrigation protocols can substantially reduce the risk of NaOCl extrusion and associated complications. In conclusion, NaOCl accidents represent potentially serious events that require immediate and structured management. Given their unpredictable nature and possible long-term consequences, clinicians must be prepared to respond promptly and monitor patients closely. Future efforts should focus on standardized reporting of NaOCl accidents and high-quality clinical research to strengthen the evidence base and improve protocols for their prevention and management.

Keywords: Accident; Prevention; Root Canal Irrigants; Root Canal Therapy; Sodium Hypochlorite

Introduction

Sodium hypochlorite (NaOCl) solution is one of the most widely used irrigants in endodontics due to its broad antibacterial properties with action on biofilm and ability to dissolve necrotic tissues and organic matter. However, the main concern with NaOCl is its cytotoxicity to the surrounding living tissues. NaOCl is commonly employed with a concentration ranging from 0.5-6%. Although NaOCl at concentrations higher than 6% can provide greater tissue dissolution and endodontic disinfection, accordingly

its cytotoxicity also increases proportionately and/or significantly. Cytotoxicity of NaOCl becomes a cause for clinical concern when it comes in contact with the orofacial tissues [1-4].

Extrusion of NaOCl beyond the confines of the root canal into the surrounding periapical or periradicular tissues and/or tissue spaces during irrigation, with resultant tissue damage and clinical manifestations, is known as a NaOCl accident. NaOCl accident is a serious iatrogenic mishap [5, 6]. Due to the highly cytotoxic nature of NaOCl, it can lead to extensive tissue destruction, life-threatening situations, and devastating consequences

[7-11]. Therefore, it also has malpractice and medico-legal implications [12, 13]. Although a clinical study reported NaOCl extrusion/accident with a rate less than 1%, it should be noted that this study was carried out by controlling most of the predisposing factors that are generally attributed to the occurrence of NaOCl accidents [14, 15]. On the other hand, NaOCl accidents, being an iatrogenic event, mostly occur in the presence of one or more of these predisposing or contributing factors [15]. Moreover, it is stated that many practitioners would have experienced it at least once in their career [16, 17].

The mechanism of NaOCl accidents mainly involves extrusion of NaOCl through the portals of exit, such as apical foramen and root defects (e.g., fracture or perforation), into the surrounding tissues or spaces in the presence of 1 or more predisposing factors and operator-related causes [15, 18]. When NaOCl is extruded into periapical tissues under high pressure exceeding tissue back pressure, it gets infused into intraosseous blood circulation and enters the facial vasculature. Consequently, NaOCl damages the vasculature, permeates into the surrounding facial tissues, and exerts its cytotoxic effects. This leads to NaOCl accidents with classic manifestations comprising sudden acute pain, swelling, ecchymosis, and bleeding from the root canal [6, 19]. However, NaOCl extrusion into buccal or infraorbital tissue through apical bony fenestration or into gingival and/or periodontal tissues via cervical or subgingival perforation may not involve the vascular pathway, and NaOCl can directly come in contact with the surrounding tissues, leading to NaOCl accidents with less classic manifestations [19]. A positive correlation was reported between the occurrence of NaOCl accidents involving a non-vascular pathway and the presence of apical bony fenestration [20]. Extrusion of NaOCl into the maxillary sinus also mostly leads to less classic or non-classic manifestations due to the presence of a drainage pathway. The salient features of NaOCl accidents can manifest with or without soft and/or hard tissue, airway, neurological, ophthalmological, or systemic complications depending on the severity and extent of involvement [6, 15, 19].

Although a NaOCl accident could be relatively less common compared to many other iatrogenic mishaps, it can have significant bearing on both patient and clinician. From the patient's perspective, a NaOCl accident as a totally unexpected outcome during a routine endodontic procedure can be traumatic, with concerns related to facial or aesthetic effect/s and can lead to immense physical, emotional, and social distress. This can also hugely influence the psychological perception and behaviour towards further or future dental or endodontic treatment. From a clinician's perspective, the risk of medico-legal repercussions can be a major concern. Hence, prevention of NaOCl accidents is the best strategy. However, at times, a NaOCl accident can occur despite following appropriate

guidelines or protocol and taking adequate precautionary measures [21-23]. Moreover, under such circumstances, improper management of a NaOCl accident, which is an iatrogenic event by itself, further increases the clinician's risk of drawing medico-legal liability [24-28].

Hence, apart from having a thorough understanding of the mechanism and clinical details of NaOCl accidents [6, 19], it is very important for clinicians to have an in-depth knowledge of the management of NaOCl accidents to handle them in the best possible manner when such an unfortunate iatrogenic incident occurs and to avert or minimize its consequences. It is equally important to comprehensively know and apply all the measures to prevent NaOCl accidents. Therefore, the purpose of this article is to provide a scoping review on the management and prevention of NaOCl accidents.

Material and Methods

The review was conducted after carrying out an extensive literature search. The literature search was conducted by employing both electronic and manual methods. The electronic search was conducted in PubMed/Medline, Web of Science, Google Scholar, Cochrane, Scopus, LILACS, ScienceDirect, and Crossref databases. The electronic search was done up to May 2026 without applying any language restrictions. It was done using specific Medical Subject Heading (MeSH) terms and key search terms, which included sodium hypochlorite, irrigant, irrigation, rinse, root canal, apical, periapical, tissue, accidental, inadvertent, extrusion, extravasation, injection, iatrogenic, error, mishap, accident, adverse effect, complication, management, prevention, dentistry, and endodontics. The search line included these MeSH and key terms along with Boolean operators "AND" and "OR" to find articles on NaOCl accident or extrusion and irrigant-related mishaps. Various categories or types of articles, such as case reports, case series, original studies, and systematic and critical reviews, available as full text were included for this review. A manual method of search was also conducted by screening the references of the included articles. Duplicate articles and articles available only as abstracts were excluded from this review.

Results

A total of 262 articles in the form of reported cases/case series, original studies, and systematic and critical reviews were included for the review. The included articles were reviewed, and relevant details were extracted, compiled, analysed, interpreted, and discussed in depth under the sections of management and prevention of NaOCl accidents.

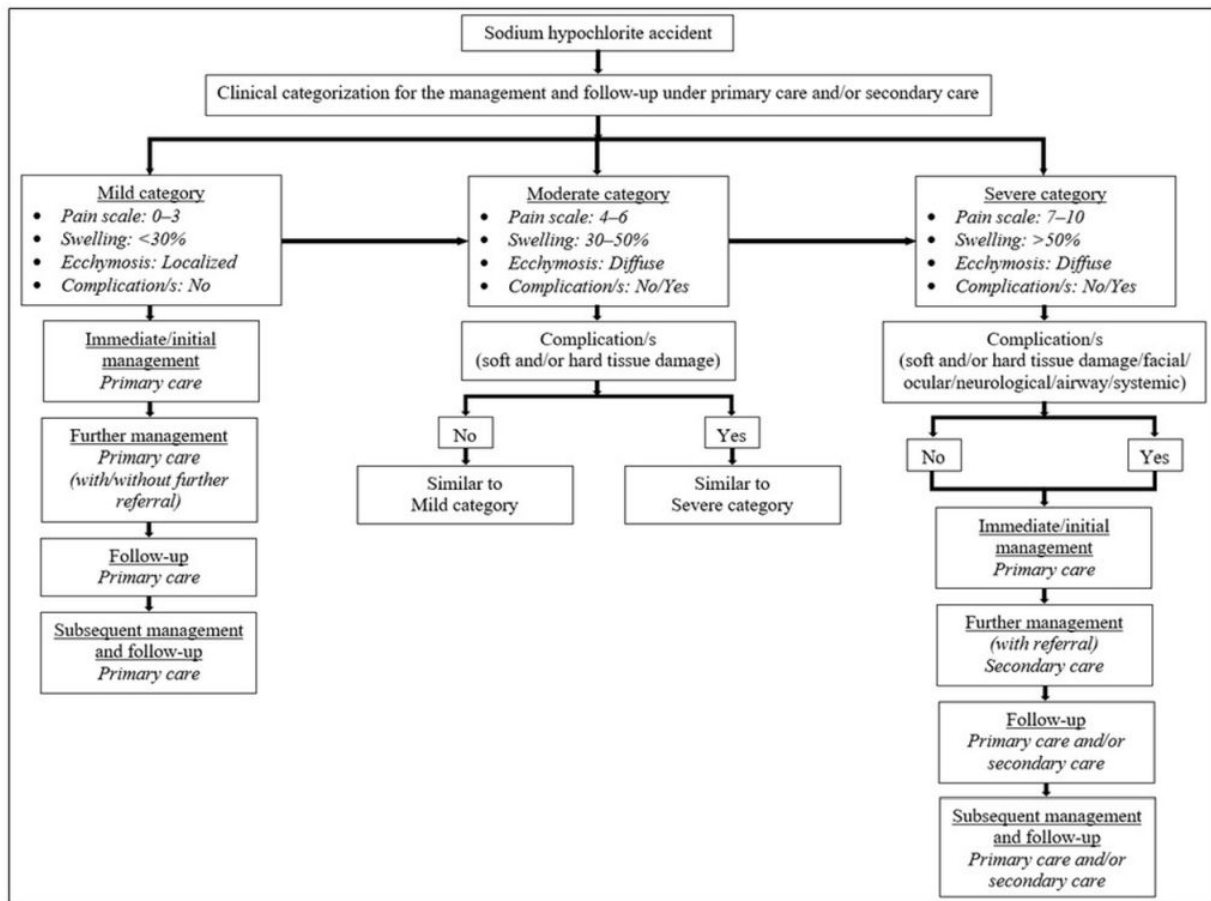


Figure 1. The clinical categorization of sodium hypochlorite accidents for decision-making towards its management under primary care and/or secondary care

Discussion

A recent systematic review reported that NaOCl is an effective and valuable irrigant but is associated with significant risks. Considering those risks, it highlighted the importance of management and preventive or safety measures [29]. Hence, having a detailed review on the management and prevention of NaOCl accidents is clinically relevant and beneficial. Because clinical or in vivo studies on NaOCl irrigation and its extrusion are limited, and conducting such studies is also associated with many challenges [17, 30], the source of clinical evidence for this review mainly included reported cases/case series [5-8, 10, 11, 21-28, 31-137] with a few original articles based on survey, retrospective, in vivo, or clinical observational studies [12-14, 16, 20, 138] and a few systematic and critical reviews [9, 17, 29, 129, 139, 140] about NaOCl accidents or extrusion. Similarly, apart from these articles, additional articles comprising case reports/case series [141-149], original studies [150-258], and systematic and critical reviews [259-270] related to NaOCl irrigant, alternative or other irrigants, and irrigation procedures,

that are deemed relevant or applicable under the scope of management and/or prevention of NaOCl accident or extrusion, were also reviewed to obtain the clinical evidence.

Management of NaOCl Accidents

NaOCl accidents can be categorized into mild, moderate, and severe based on their extent, severity, and any tissue damage and/or complication (Fig. 1). They involve management under primary and/or secondary care. Primary care management refers to treatment under the same setup where the patient is being endodontically treated and a NaOCl accident occurs. Whereas management under secondary care involves patient referral to a medical, dental, or concerned specialist or specialty clinic and/or admission to an oral and maxillofacial surgery unit, emergency unit, or hospital (*i.e.*, for outpatient or inpatient-based management). The decision to manage under primary and/or secondary care (Fig. 1) must be based on the category of NaOCl accident, course of symptomatology, presence of tissue damage or complication, and patient's clinical response or improvement [7, 8, 10, 17, 19, 64, 69, 112, 113, 271]. The course and duration of symptomatology of NaOCl accidents are

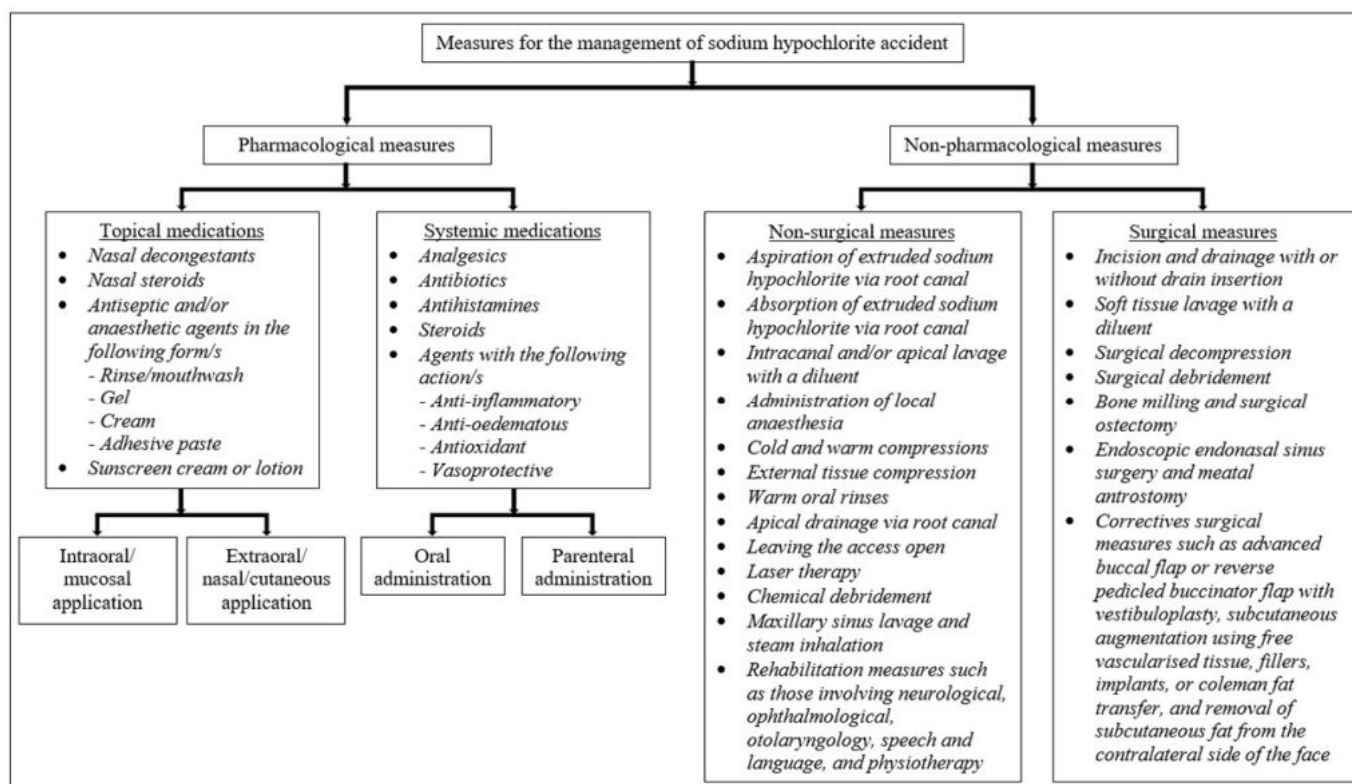


Figure 2. The categorization of various measures which can be applied on a case-to-case basis for the management of sodium hypochlorite accidents

unpredictable and varies on a case-to-case basis. The course of symptomatology can manifest as mild, moderate, or severe category from the initial stage itself and/or progress rapidly or gradually to the next category in the order of increasing extent of involvement or show further worsening if it's already severe, particularly with any failure or delay to immediately detect and carry out measures to remove and/or dilute extruded NaOCl. Hence, as time progresses, the course of symptomatology of NaOCl accident can change with more clinical manifestations and/or increase in their extent or severity. In case of a rapidly progressing or worsening NaOCl accident, the clinical distinction of categories may not be clearly evident, and it can be difficult to objectively assess the transition or overlap of categories. Among the cases reported, approximately 55-60% cases manifested as moderate-severe NaOCl accidents, 40-45% cases had not immediately detected and/or addressed the extruded NaOCl, and 65-70% cases had worsening symptomatology [5-8, 10, 11, 21-28, 31-137].

Since there is no antidote for NaOCl, management of NaOCl accidents is mostly symptomatic, palliative, and protective [5, 32, 40, 42, 76]. As universal or standard guidelines are lacking [14, 90, 111, 125], the most appropriate management strategy for NaOCl accident is to follow a recommended treatment protocol with additional empirical measures on a case-to-case basis [9, 22, 32]. Management of NaOCl accident can be broadly considered

under initial, progression, and recovery and/or extended recovery phases. It can involve pharmacological and/or non-pharmacological measures. The latter can be categorized into non-surgical and surgical measures (Fig. 2).

Initial Phase Management

It consists of initial treatment and procedures, including documentation, which must be carried out within the first 24 hours following a NaOCl accident. Irrespective of the category of NaOCl accident at the onset, it must preferably be initiated or carried out under primary care itself to avoid any delay because the time factor influences the extent and outcome of NaOCl accident [15, 22]. This also helps quickly limit the cytotoxic effects of NaOCl, control the progress or severity of NaOCl accident, and facilitate satisfactory outcome/s. Initial phase management mainly includes the following.

Quickly Detecting NaOCl Accident and Rendering Initial Treatment

Acute pain and/or burning sensation during intracanal irrigation indicates NaOCl extrusion. Failure to immediately recognize it and intervene at this juncture leads to a full-blown NaOCl accident with classic features [14, 19], though this is less likely or appreciable in the case of NaOCl extrusion into the maxillary sinus that mostly presents with non-classic features such as metallic or chlorine taste, dysgeusia, and epistaxis or nasal bleeding [19, 137]. However, regardless of

classic or non-classic presentation, it is crucial to quickly detect and render initial treatment to remove and/or dilute extruded NaOCl to control the overall progress and outcome of NaOCl accidents. Among the cases where extruded NaOCl was immediately addressed, although the symptomatology progressed or a couple of cases needed hospitalization [8, 46, 56], except for a few cases with unsatisfactory outcomes [22, 25, 46, 62, 69, 73, 95, 114, 122], nearly 82% of cases had an uneventful recovery with satisfactory outcome/s. In comparison, when cases where extruded NaOCl was not quickly managed are considered, apart from the worsening in the extent and/or severity of NaOCl accident, a greater number of cases needed hospitalization [10, 26, 34, 36, 41, 47, 55, 66, 67, 130, 136], especially when the patient was medically or immunocompromised [10, 41, 55, 66, 113, 130]. Additionally, the percentage of recovery with satisfactory outcome/s was relatively lower (approximately 68%), and the number of cases with adverse outcome/s was also greater [11, 24, 26, 32, 34, 35, 43, 47, 58, 59, 64, 78, 83, 92, 119, 123]. It must also be noted that failure to timely detect a NaOCl accident can draw attention towards negligence under medico-legal proceedings [27, 272].

Following quick detection, initial treatment for NaOCl accident comprises the following.

Applying Immediate Measures

The clinician must remain calm and composed and stop further treatment [50, 273]. In most of the cases, further irrigation and endodontic treatment were stopped. However, in around 20% of cases where further irrigation or dental or endodontic procedure was carried out, with or without initial detection and management of NaOCl accident, there was worsening of manifestations [6, 10, 11, 25, 32, 33, 36, 41, 44, 49, 60, 66, 67, 76, 80, 88, 92, 101, 104, 117, 123, 132, 136]. But stopping irrigation or treatment and rendering symptomatic measures without addressing the extruded NaOCl might still not be effective in controlling the symptomatology or outcome of a NaOCl accident [38, 43, 55, 58, 61, 62, 81, 92].

Patient's position must be adjusted by elevating the reclined dental chair to bring the patient to an upright posture so that the head is positioned above the level of the heart to relieve some pressure from the facial area to reduce swelling and/or nasal bleeding, though only a few cases have reported on this measure and the evidence regarding its beneficial effect is lacking [5, 27, 54, 68, 99]. Although it assisted in reducing nasal bleeding [54], it was not effective in controlling swelling because the extent of swelling increased either immediately or gradually despite adjusting chair position or the patient following an upright sleeping posture [5, 27, 62, 68, 99]. In case of NaOCl extrusion into the maxillary sinus, a reclined position is suggested to facilitate drainage of NaOCl and reduce the severity of manifestations, though clinical evidence is lacking in this regard too [5, 6, 15, 37, 68, 78].

It must be borne in mind that a rubber dam can be a hindrance to monitor the extent or severity and progress of manifestations, verbally communicate with the patient regarding symptoms, reassure and calm the patient, facilitate breathing in case of any respiratory complications or anxiety, effectively deliver local anaesthetic (LA) for immediate pain control, and thoroughly examine and assess the patient to categorize NaOCl accident for treatment planning. Hence, as the priority shifts towards treating NaOCl accident as an emergency, the rubber dam must be removed as early as possible, either before or after initiating emergency treatment [5, 6, 8, 14, 45, 54, 63, 71, 77, 94, 102, 122, 133, 135].

Although the step of brisk clinical examination and assessment and informing the patient about the incident of a NaOCl accident and its consequences can be carried out at this point [50, 56, 122, 128, 131, 273, 274], it can consume the initial valuable time, which is more crucial to rapidly control the cytotoxic effects of extruded NaOCl and its associated symptomatology. Hence, this step can be performed following the emergency treatment [6, 135].

Applying Emergency Treatment

Aspirating and/or Diluting the Extruded NaOCl

It must be borne in mind that the cytotoxic effect of NaOCl is time-dependent and it increases with passing time [195]. Hence, the extent or severity of tissue damage following NaOCl accident depends on how soon the amount and/or concentration of extruded NaOCl is addressed. When the extruded NaOCl is not addressed, the extent or severity of tissue damage increases until extruded NaOCl is diluted and/or cleared off by the body's inflammatory process, biological fluids, and defence mechanisms, including vascular and lymphatic systems, which may take up to several days to weeks. Therefore, immediate negative aspiration and/or dilution of extruded NaOCl is an important emergency step in the management of NaOCl accidents.

Negative aspiration is advocated to remove as much extruded NaOCl as possible through the root canal [6, 9, 14, 22, 56, 69, 112, 129, 274]. Root canal irrigation with a diluent is recommended to dilute the concentration of the extruded NaOCl, neutralize the highly alkaline pH of NaOCl, which is responsible for its deeper penetration into surrounding tissues, and wash out any remaining NaOCl in the canal [6, 9, 14, 22, 69, 125, 271, 272, 274]. However, dilution and neutralization of the extruded NaOCl do not occur unless the diluent is also forcibly extruded, which can increase the pressure in the affected area and the tendency to further spread NaOCl deeper into tissues [9, 56]. This concern can be reduced to some extent by employing a negative pressure-based irrigation system to deliver the diluent or by applying a high-volume evacuator to the access opening during the dilution



Figure 3. A) Immediate negative aspiration of extruded sodium hypochlorite through the root canal to control the extent of sodium hypochlorite accident; B) Allowing bleeding through the root canal by leaving the access open to facilitate drainage of extruded sodium hypochlorite

step [54, 275]. It must also be noted that irrigating only with a diluent can hinder bleeding and/or NaOCl drainage through the canal. Hence, performing negative aspiration along with dilution must be considered.

Negative aspiration can be performed using a suction system or high-volume aspirator, or an irrigation syringe and needle (Fig. 3A) [9, 14, 22, 69, 77, 115, 121]. Evacuating extruded NaOCl and any residual NaOCl in the canal by absorbing with paper points and microtips has also been suggested [9]. However, this can be time-consuming and less effective compared to negative aspiration [9]. Although the same NaOCl irrigation syringe can be employed for aspiration [69], it is safer to use another empty syringe for this purpose [56]. Hence, it sounds practical to always keep an empty syringe ready during NaOCl irrigation as a precautionary measure. If a suction apparatus or aspirator is employed, the tip can be secured to the access opening and stabilised with modelling wax or impression compound for an effective, longer, or uninterrupted aspiration, particularly during the patient monitoring period [77]. Gentle facial massage on the affected area may further aid in this aspiration or evacuation process [56, 77]. However, vigorous rubbing should be avoided as it may lead to further penetration of NaOCl in the tissues [56].

For root canal irrigation with a diluent [39, 73, 273], saline has been the most commonly employed solution. Saline was used in nearly 88% of cases, which reported a dilution step, though use of sterile or distilled water [14, 37, 114, 276], local anaesthetic (LA) [22, 135], and chlorhexidine (CHX) [9, 25, 69] solutions have also been reported or recommended. It must be noted that CHX can form a precipitate when it interacts with NaOCl in the canal and/or in the periapical tissues [9, 276, 277]. Since this precipitate could also be tissue toxic, it can add to the periapical damage already caused by the extruded NaOCl [277]. Moreover, CHX itself has also been reported to cause tissue damage upon periapical extrusion due to its cytotoxic effect [109, 147]. Similarly, although LA as a diluent can provide an analgesic effect too [22], interaction between extruded NaOCl and LA, particularly lignocaine-based one, can also lead to

formation of a carcinogenic precipitate (2,6-xylidine) [278]. Hence, saline or distilled water is safer as a diluent. As a part of precautionary measure, it also sounds appropriate to always keep, along with an empty syringe, a labelled irrigation syringe fully loaded with saline or distilled water to be readily available during NaOCl irrigation. Before dilution, the canal must be dried with aspiration or paper points to remove any residual NaOCl to prevent its further extrusion under the irrigation pressure of a diluent [86]. Use of an air syringe is not recommended for canal drying to prevent air emphysema [36]. In case of extrusion of a larger volume of NaOCl into the surrounding buccal tissues or tissue spaces, apart from root canal lavage, soft tissue lavage can also be performed by inserting 2 needle hubs into the soft tissues and injecting a diluent such as saline through 1 needle to dilute and neutralize the extruded NaOCl and facilitate its drainage or aspiration through the other needle [149].

Controlling Pain and/or Burning Sensation

Sudden acute pain with or without burning sensation is a salient feature of NaOCl accident, and can manifest despite preoperative LA [6, 8, 19, 32, 33, 44, 45, 48, 63, 75, 79, 80, 85, 89, 102, 121, 124, 128, 133]. Hence, immediate pain control is important to reduce patient distress. If the patient is not anesthetized, LA must be delivered immediately [25, 27, 40, 57, 62, 112]. In case the patient is already anaesthetized, LA must be delivered again, particularly if a NaOCl accident occurs when the anaesthetic effect is wearing off [23, 33, 69, 97, 111, 128, 133]. Despite LA, pain can persist, albeit with a reduced intensity [23, 83], and when LA effect starts to wear off, pain can resurface with the same or increased intensity. Hence, analgesics must be prescribed or administered as soon as possible as a progressive pain control measure [75]. In case of extreme pain, parenteral administration of analgesics must be considered [69]. Similarly, emergency measures such as steroid administration and extraoral cold compression also help to relieve or soothe pain and/or burning sensation [5, 89, 100, 133].

At times, NaOCl accident can manifest with minimal or less pain [36, 37, 49, 63, 72, 76, 103, 114, 117, 137] when NaOCl extrudes into maxillary sinus or gingival tissues via cervical or subgingival perforation or root fracture, LA is already given for endodontic therapy, patient is under general anaesthesia (GA), or patient has a high pain threshold [19, 36, 37, 66, 72, 76, 103, 107, 109–111, 117, 123, 137, 279]. Under such circumstances, although immediate LA may not seem needed, delivering LA can still be beneficial because pain can manifest as the extent or severity of the NaOCl accident increases and/or tissue damage starts, and medications may take time to exert their therapeutic effect.

A nerve or regional block, particularly with a long-acting LA such as bupivacaine, is preferable for effective pain control [9, 57, 64, 128, 273, 280]. In case of NaOCl accident involving the anterior or labial region and a long-acting LA administration, precautions must be taken to prevent any lip biting due to prolonged numbness and risk of additional traumatic tissue damage [281]. Infiltration technique is generally contraindicated as it can further increase pressure in the affected area, particularly in the presence of swelling, and can provide a pathway for further extension of manifestations or infection [9, 44, 99].

Although an LA containing a vasoconstrictor is preferable [133] a vasoconstrictor might increase tissue necrosis by causing local ischemia. Moreover, a vasoconstrictor can increase the duration of contact of extruded NaOCl with tissues by delaying the absorption and/or clearing of NaOCl from the affected area [9]. This could also matter, particularly with infiltration anaesthesia, in case of NaOCl extrusion into gingival tissues via cervical or subgingival perforation or root fracture, where the risk of gingival necrosis is a major concern. Invasive procedures like cortical or bony trephination cannot be recommended for immediate pain control, as this can further traumatize tissues or aggravate the tissue damage [33].

Controlling Swelling and/or Haematoma Including Ecchymosis

Swelling and/or haematoma, including ecchymosis, are other salient features of NaOCl accidents [19]. They mostly manifest immediately, though their manifestation could be slow or gradual in some cases [6, 49, 56, 103, 104]. Immediate extra-oral cold compression over the affected area, at least for the first 24 hours, is recommended to control them by reducing blood flow through vasoconstriction [6, 9, 125, 271, 273, 274]. Hence, it is advisable to keep an ice pack readily available during NaOCl irrigation. However, in NaOCl accident cases with rapid tissue necrosis as the main manifestation [49, 103, 108, 119, 122, 127] the potential for cold compression-induced vasoconstriction to become counterproductive by further compromising the vascular supply and increasing the extent of tissue necrosis cannot be ruled out.

Immediate external compression over the involved area is another measure to control swelling and/or haematoma by means of exerting gentle external pressure and/or facilitating intracanal drainage [77]. However, its application is mostly anecdotal, with limited clinical evidence regarding effectiveness [77, 99]. Additionally, excessive compression pressure can be more distressing to the patient [99].

Alternatively, immediate local or parenteral steroid administration is an effective pharmacological measure to minimize swelling and/or pain because of its potent anti-inflammatory effect [133]. Hence, it is suitable for cases with

severe or rapidly extending swelling [8, 272]. However, it can be risky if the patient is immunocompromised [275, 282].

Incision and drainage (I&D) of buccal tissue spaces with or without drain insertion is a surgical/invasive measure to minimize swelling and/or haematoma [7, 67, 73, 93]. It allows immediate drainage of inflammatory exudate and mediators, including any extruded NaOCl. However, it can be traumatic and/or provide a pathway for secondary infection in the presence of tissue damage or compromised medical status [73]. Therefore, it must be considered only when conservative measures fail, and swelling is rapidly progressing with a threat of Ludwig's angina or involving adjacent vital structures [7].

Controlling Further Spread of Extruded NaOCl and Inflammation

Since initial phase measures cannot control the body's intense inflammatory reaction to the extruded NaOCl, and oral medications need time to start their action, immediate local, intraligamentary, intramuscular (IM), or intravenous (IV) administration of a potent anti-inflammatory agent such as steroids is suggested to control inflammation and minimize further spread of extruded NaOCl by the fluid phase of the inflammatory response [8, 35, 56, 133, 282]. Additionally, anti-inflammatory action helps to control swelling and pain. The parenteral route is preferable over local injection as the latter can further increase tissue pressure and/or lead to cross-interaction between steroid and any LA agent delivered for pain control. Local injection of steroid must be delayed by 10-15 minutes to avoid cross-interaction with LA agent [282]. Steroid administration must be avoided if the patient is immunosuppressed [275, 282].

Allowing and/or Encouraging Bleeding or Exudation or Drainage from the Root Canal

Following a NaOCl accident, bleeding from the canal would be profuse, prompting measures to stop it. Measures such as intracanal deposition of LA 2% lidocaine with 1:100,000 epinephrine for haemostasis and parenteral administration of medications such as carbazochrome sodium sulfonate and tranexamic acid to reinforce blood vessels and facilitate vascular resistance have been reported to stop or control canal bleeding [9, 76, 99]. However, it is recommended to allow and/or encourage bleeding from the canal to facilitate drainage of extruded NaOCl and reduce interstitial tissue pressure (Fig. 3B) [9, 56, 112, 125, 129]. Hence, gentle facial massage, continued aspiration and irrigation with a diluent, and drying the canal with paper points during patient monitoring are beneficial to further facilitate intracanal bleeding, and if canal bleeding continues, discharging the patient by leaving the tooth open will complement this step [5, 8, 44, 72, 77, 90, 128, 133, 265]. It must be noted that when LA containing epinephrine is employed as an intracanal diluent or

irrigant, it can dilute extruded NaOCl and provide analgesia [22, 135]. But its haemostatic effect can become counterproductive, with a potential to interrupt canal bleeding and affect drainage of extruded NaOCl. It would be clinically interesting to know whether apical trephination can have any role in further facilitating canal drainage in case of NaOCl extrusion/accident, but without ignoring its potential to add more trauma or irritation to the tissue damage in the affected periapical area.

A clinical observational study by Özdemir *et al.* [14] has shown that the prompt application of an emergency treatment protocol involving immediate detection, aspiration, dilution, and canal drainage is effective in facilitating faster resolution of symptomatology and controlling the extent or severity of NaOCl extrusion/accident.

Contrary to the need for promoting bleeding via root canal, any epistaxis or nasal bleeding in case of NaOCl extrusion into the maxillary sinus must be controlled by pinching the nose with the fingers and applying an ice pack to the bridge of the nose and cheek area [54, 136]. If this measure proves ineffective, then nasal packing and/or systemic or IV administration of tranexamic acid can help to achieve haemostasis [137].

Leaving Tooth or Access Open

Leaving tooth open allows canal drainage and venting of apical and/or interstitial tissue pressure and assists in controlling the extent or progress of NaOCl accident. On the contrary, it can serve as a pathway for microbial contamination of the canal and secondary infection in case of tissue necrosis [36, 62, 112]. In this context, by considering NaOCl accident as an emergency and its management as a priority, the risk and benefit of leaving the tooth open must be carefully weighed.

Many cases have reported closing the access opening in the same visit following a NaOCl accident [37, 38, 44, 45, 48, 49, 54-57, 67, 68, 72, 92, 94, 112, 135, 190] either without [37, 48, 54, 57, 68, 190] or with an intracanal medicament such as calcium hydroxide [Ca(OH)₂] [49, 56, 67, 92, 94, 112, 135], iodine potassium iodide (IKI) [44], and corticosteroid-antibiotic mixture [38, 45]. Although Ca(OH)₂ dressing is said to neutralize residual NaOCl and reduce inflammation [136], clinical evidence is lacking in this regard. However, even when no intracanal medication or obturation was done, some cases needed access reopening within sometime in the same visit due to aggravated symptomatology. Upon reopening, copious drainage was seen [44, 48]. Such a risk is high, particularly when a NaOCl accident is not diagnosed and/or managed in the initial stage itself, and the access is closed [9, 38, 44, 48, 49, 55, 67, 134]. Moreover, as NaOCl accidents mostly tend to show initial worsening of symptomatology, any root canal dressing [9, 38, 44, 45, 63, 67, 92,

94] or obturation [6, 9, 33, 40, 41, 66, 136] procedure carried out in the same visit only exacerbates the clinical situation. Additionally, any extrusion of intracanal medicament such as Ca(OH)₂ [92] or over-obturation can further complicate the iatrogenic incident. Hence, it is preferable to leave the involved tooth open [40, 63, 89, 133, 271].

Although a clinical study reported that NaOCl accident/extrusion subjects with immediate application of an emergency treatment protocol of quick detection, aspiration, dilution, and canal drainage had uneventful recovery within a shorter period despite closing the access with intracanal medication or obturation and coronal sealing in the same visit [14], the available evidence to support access closure, even when canal bleeding or drainage is not seen [36, 67] or has ceased [68, 72] or symptomatology is mild [37, 49, 72, 82] is limited due to lack of such similar studies. Hence, it is advisable to leave access open for the first 24 hours following a NaOCl accident [27, 40, 44, 75, 90, 122, 128, 133]. If no sign of drainage is seen, access can be closed, preferably without any intracanal medication [133]. Only if drainage persists, leaving the tooth open for the next 24 hours or until it ceases must be considered before deciding to close the access [32, 44]. The access must preferably be closed with a temporary cement which is easier to remove if a need for emergency drainage arises.

Carrying out Patient Assessment

After immediately applying emergency treatment on a priority basis, depending on the patient's condition, a brisk clinical assessment, including monitoring of vital signs, intraoral and extraoral examinations, and any radiographic investigations, particularly 3-dimensional imaging, must be carried out to know the cause/etiology, confirm the category of NaOCl accident, see for initial signs of any complications, and for decision making towards continuing the patient monitoring and further treatment under primary or secondary care [8, 26, 28, 45, 59, 66, 68, 86, 94, 99, 100, 107, 112, 114, 122, 130-133, 135]. Stress relaxation measures can be considered if the patient is anxious to allow assessment and/or investigations [101, 104, 117].

Patient Monitoring, Reassurance, and Any Emergency Referral

The course of symptomatology of NaOCl accident is unpredictable, with a tendency for worsening or complication/s after the patient is discharged from the primary care, particularly when it is not detected quickly and/or emergency treatment is not applied effectively. Therefore, the patient must be closely observed, including monitoring of vital signs, for the next few hours before discharge [8, 23, 27, 77]. During this period, the patient must be constantly counselled and reassured [27, 42, 67, 77, 85, 106, 112, 125]. Oral tranquilizers or sedatives or nitrous

oxide sedation can assist in calming an anxious or agitated patient [5, 9, 104, 279]. Further patient management must be based on the following 2 clinical situations.

A Patient with No Sign of Worsening or Complication or Emergency

In case of mild or moderate category of NaOCl accident with no severe worsening or complication or emergency during monitoring, the patient can be discharged from the primary care by applying any additional or adjunctive measure/s, administering or prescribing medications, explaining the incident, giving instructions, scheduling follow-up, and documenting the incident as explained subsequently. However, as the potential to worsen or develop complication/s after the patient's discharge cannot be ruled out, it is always a safer practice to refer the patient to secondary care or an oral and maxillofacial surgeon [58, 61, 62, 75, 82, 108, 112, 114, 125, 133, 137]. It must be noted that despite quick detection and/or management of a NaOCl accident, any failure to refer the patient appropriately can amount to negligence with medico-legal implications [272].

A Patient with Signs of Worsening or Complication or Emergency

In case of moderate or severe category of NaOCl accident with signs of further worsening or complication or emergency during patient monitoring, the patient must be immediately referred to secondary care, especially if the patient is medically or immunocompromised. In such cases, any further surgical or invasive procedures such as cortical trephination or extraction of the involved tooth under primary care, even at the insistence of the patient, for immediate relief must be avoided, as this can further worsen the patient's condition [11, 33, 36, 88, 91]. Although an open wound or socket following extraction may facilitate bleeding and drainage of extruded NaOCl, extraction adds more trauma to the tissues that are already affected by a NaOCl accident. In moderate to severe or extremely severe cases, where immediate or quick referral to secondary care is a priority, initial measures such as cold compression, patient monitoring, assessment, and investigations, prescribing or administering medications, and patient follow-up could be rendered under secondary care itself [8, 41, 59, 66, 70, 74, 88, 90, 98, 100, 108, 113, 119, 122, 130, 132-134, 137].

Oral or facial, maxillary sinus, ophthalmological, and neurological-related complications need referral to the respective specialists of stomatology [57, 62, 79, 108, 136], oral and maxillofacial surgery [11, 28, 45, 62, 66, 119, 136], ear, nose, and throat (ENT) [62, 82] or otorhinolaryngology [26, 37, 43, 71, 78, 113, 118, 123, 137], ophthalmology [66, 112, 116, 123] and neurology sections [26, 83].

Emergency referral to secondary care on an outpatient basis facilitates patient monitoring, assessment and investigations, and administration of medications [57, 58, 61, 100, 108, 137]. However,

in case of airway or systemic complications, in-patient admission under secondary care is crucial for a detailed patient examination and assessment, medical, laboratory, and advanced radiologic investigations [8, 26, 41, 55, 59, 85, 90, 119, 132, 136, 273] airway management by fiberoptic nasal-tracheal or oral endotracheal intubation [7, 8], surgical drainage [67] or decompression of the submandibular, sublingual, and submental spaces [7, 41, 59], parenteral delivery of opioid, nonsteroidal anti-inflammatory (NSAID), steroid, and antibiotic medications to effectively control pain, inflammation, and infection, nasal saline irrigation of the maxillary sinus, ocular measures such as flushing of eye/s with sterile saline and applying topical medications, medical supportive measures such as controlled and continuous facial tissue cooling therapy, oxygen administration, sedation, blood transfusion, and parenteral nutrition, patient monitoring in the intensive care unit, and multidisciplinary treatment on a case-by-case basis [7, 8, 10, 17, 26, 34, 35, 41, 55, 59, 60, 66, 67, 70, 85, 90, 92, 98, 99, 112, 113, 116, 119, 130, 132-134, 136, 271]. When referring the patient, sharing detailed information on the incident of the NaOCl accident with the concerned specialist or secondary care is important [90, 112, 122]. Following patient recovery under secondary care, subsequent management or follow-up can be resumed or continued under primary care [45, 53, 55, 59, 67, 83, 92, 98, 108, 113, 122, 133].

Applying Additional or Adjunctive Measure/s

Initiating the application of low-level laser therapy (LLLT), preferably immediately or within the first 24 hours in the initial phase of NaOCl accident, can assist in controlling the extent or severity of intraoral and extraoral manifestations, including pain, swelling, and ecchymosis from the early stage itself without any further concerns of tissue necrosis or damage, hasten the resolution of manifestations, and reduce the recovery time needed [102, 113, 135, 216]. LLLT can preferably be applied during the patient monitoring or observation period. It can be more advantageous when the patient is aged or medically compromised with reduced healing or recovery ability [113]. It can also minimize or reduce the need for medication/s in the management of NaOCl accidents, which is beneficial particularly in cases with contraindications to such medication/s due to underlying medical or drug history.

The beneficial effects of laser therapy could be attributed to its ability to regress edema, inhibit inflammation, and reduce pain [108]. As part of the initial treatment protocol for NaOCl accidents, laser can be applied both locally and remotely to achieve its beneficial effects through the action of tissue and systemic photobiomodulation, respectively. Locally, laser can be applied both intraorally and extraorally. Intraoral laser application involves the affected oral soft tissues and the apical

area in relation to the involved tooth. Extraoral laser application involves the facial tissues over the affected area and the areas having facial, auricular, and cervical lymph node drainage pathways on the affected side. Upon local laser application, tissue photobiomodulation occurs through a cellular mechanism involving absorption of laser energy by tissue cells, mitochondrial stimulation, and biochemical changes within the cells, which improve metabolic activity and regulate inflammation at the tissue level. It also leads to stimulation of local lymph nodes to facilitate better lymphatic drainage from the affected area. On the other hand, remote laser application for systemic photobiomodulation involves a vascular mechanism by employing the intravascular laser irradiation of blood (ILIB) technique. With the ILIB technique, laser energy is delivered into systemic vasculature either by invasive (intravenous catheterization via radial vein) or non-invasive mode (transdermal or transcutaneous irradiation over radial artery) [108, 135, 267]. In case of the latter mode, the technique is also referred to as vascular photobiomodulation [267]. Irrespective of the mode of delivery, systemic photobiomodulation increases red blood cell function and oxygen transportation and improves blood circulatory and cellular metabolic activity in the affected tissues. It also leads to an immunomodulatory effect. Thus, it enhances tissue perfusion, hastens clearance of tissue irritants, free radicals, and inflammatory mediators, boosts immunity, and complements tissue photobiomodulation to amplify anti-inflammatory, anti-oedematous, antioxidant, and analgesic effects exerted by local laser application [135, 267]. Since systemic photobiomodulation can be performed via any accessible blood vasculature [267] and considering a blood vessel such as the sublingual artery with its advantages of rapid absorption across the sublingual mucosa and proximity to the site of NaOCl accidents compared to other vasculature, it would be interesting to see the scope of employing a transmucosal and/or transcutaneous approach of vascular photobiomodulation involving the sublingual artery during local laser therapy that is being applied for tissue photobiomodulation in the management of NaOCl accidents.

Overall, LLLT as a non-pharmacological option in the management of NaOCl accidents can be a useful adjunctive measure to effectively control manifestations in the beginning stage itself and hasten the recovery process. Although the number of case reports with the application of LLLT from the initial stage in the management of NaOCl accidents is only a few, they have reported its beneficial effects as an additional measure in ensuring full and faster recovery with uneventful or satisfactory outcomes [84, 102, 113, 135]. However, there is a lack of standardization in reporting the specifications or parameters employed for LLLT application, as only a couple of case reports have reported such

details [84, 108, 135, 267]. Considering these aspects, LLLT has the potential to be recommended as part of an initial treatment protocol for NaOCl accidents [102, 135, 267], but this needs more clinical validation due to the limited level of evidence currently available, and a greater emphasis is required on reporting guidelines or standardization in reporting the specifications or parameters of LLLT application for NaOCl accidents.

Prescribing and/or Administering Medications

Medications are important to control the extent of symptomatology during initial and progression phases of NaOCl accident. They must be selected on a case-to-case basis by considering the patient's medical and drug history [129, 282]. Depending on the facilities and expertise available, they can be administered via oral, parenteral, or both routes. In the case of both routes, administering the initial/loading dose via the parenteral route assists in achieving a faster onset of action, and the oral route can be considered for the sustenance/maintenance dose. Parenteral route of administration is preferable in severe cases to quickly control the extent of symptomatology [7, 8, 26, 35, 41, 59, 66, 67, 69, 75, 90, 92, 113, 116, 130, 134].

Analgesics are recommended for effective pain control. World Health Organization (WHO) pain ladder can be useful for selecting the analgesics [64, 283]. Among the cases where analgesics were employed, approximately 80% of cases have reported NSAIDs such as ibuprofen, ketorolac, and diclofenac sodium either alone or combined with other NSAIDs or analgesics, though NSAIDs, including aspirin, have a risk of increasing interstitial haemorrhage in the soft tissue during the acute phase of NaOCl accident [59, 273]. Although currently not widely recommended, use of cyclooxygenase-2 inhibitor (COX-2) selective NSAIDs such as nimesulide has also been reported [88, 101, 102]. On the other hand, a few cases have employed acetaminophen (*i.e.*, paracetamol) either alone [5, 44, 59, 69, 133, 134] or in combination with narcotics such as codeine [33, 68, 81, 83, 85] for pain relief. For cases with extreme pain, narcotics [41, 42] or opioids [22, 33, 94] can be considered. Moreover, analgesic administration via the sublingual route is an option for quicker onset of action [124]. Parenteral administration [41, 67, 69, 106, 118, 134] or a continuous analgesia infusion pump [41, 130] provides effective and sustained analgesic effect.

Antibiotics have been used in NaOCl accident cases with prophylactic or therapeutic objectives. Prophylactic antibiotic therapy is suggested considering the potential for extrusion of root canal microorganisms and debris, as well as extruded NaOCl [7, 41, 52, 59] and the ability of extruded NaOCl to cause extensive tissue necrosis with dead space [7, 41, 52, 59] and reduce neutrophil activity [35, 90]. It is strongly advocated for cases with a medical or immunocompromised status [9, 10, 34, 40, 46, 55, 56,

73, 113, 130, 143, 271] or sinusitis following NaOCl extrusion into the maxillary sinus [26, 37, 71, 72, 136, 137]. When tissue necrosis is present, antibiotics are crucial to prevent and/or treat secondary infection or control spread of infection or osteomyelitis [5, 8, 10, 26, 27, 32, 34, 43, 45, 88, 101, 108, 111, 119-121, 123, 124, 134]. Among cases with antibiotics used, nearly 75% reported amoxicillin, including penicillin, either alone or combined with clavulanic acid or other antibiotics. Some cases have employed other antibiotic/s belonging to the cephalosporin [26, 33, 36, 68, 86, 89, 100, 101, 123], metronidazole [7, 8, 34, 67, 77, 122, 123, 136], macrolide [9, 22, 44, 54, 74, 87, 137], lincosamide [26, 68, 87, 113, 134], quinolone or fluoroquinolone [27, 43, 77, 113], ampicillin with beta-lactamase inhibitor [66, 107, 130], tetracycline [5, 9, 45], and chloramphenicol [35] category.

Steroids are beneficial due to their anti-inflammatory effect [273] which helps to limit the extension of swelling. It becomes more relevant in case the step of immediate parenteral administration of steroid is not done. However, the benefits of steroids must be carefully weighed against their potential for increased risk of secondary infection, especially in cases with compromised immunity [275]. Otherwise, steroids in a single larger dose or multiple smaller doses for a shorter period is generally considered safer. If steroid medication is extended for a longer period ranging over many weeks to months, gradual tapering of dose must be considered [8, 11, 26, 27, 69, 70, 118, 122]. Among the cases with steroid medication, dexamethasone (41% of cases) and prednisolone (33% of cases) were most commonly reported. Some cases have reported other steroids such as prednisone [8, 27, 51, 82, 132], hydrocortisone [34, 35, 59, 62, 66], and betamethasone [27, 100, 102, 130]. Among these steroids, dexamethasone is more advantageous because it is a long-acting steroid with greater anti-inflammatory activity and can be administered in a single dose. However, as it takes longer time for onset of anti-inflammatory action, it is preferable to combine it with NSAIDs such as ibuprofen [71]. Although the dose and duration of steroid medication have varied among the NaOCl accident cases, none of the cases have reported any steroid-related complications.

Apart from steroids, antihistamines have also been employed for their anti-inflammatory effect. Since the acute inflammatory response following NaOCl accidents involves the release of chemical mediators such as histamine, antihistamines would minimize inflammation and associated swelling [5, 9, 51, 66, 67, 88, 89, 101, 118, 128]. Similarly, leukotriene antagonists such as montelukast can be prescribed to nullify the effect of inflammatory mediators [128]. If the use of steroids is a concern, particularly in an immunocompromised patient, proteolytic enzymes such as serratiopeptidase [101] bromelain, papain, trypsin, and chymotrypsin could be prescribed as an alternative for anti-inflammatory effect [106, 113, 121].

Although not commonly prescribed, medications such as aescin, rutinascorbin, and vitamin C have also been employed for further actions of anti-inflammatory, anti-oedematous, antioxidant, vasoprotective with increased stability and reduced permeability of blood vessels, immunity boosting, and tissue healing effects [74, 85]. Depending on the patient's prevailing medical status, the need for prescribing and/or continuing additional medications must be considered as well [10, 22, 55, 62, 69, 106, 121, 130]. Apart from systemic medications, nasal douching or lavage [136] and nasal steroid and/or decongestant can be prescribed when the maxillary sinus is involved [9, 37, 54, 71, 82, 96, 136]. Antiseptic rinse such as CHX and cetylpyridinium chloride mouthwash can be recommended for topical antimicrobial effect [41, 74, 97, 108] [74, 108]. If any initial sign of tissue necrosis manifests, prescribing gel, ointment, or adhesive paste containing topical antiseptic and/or anaesthetic agent is beneficial [74]. Overall, although clinical evidence regarding the choice or type and effectiveness of medications on the outcome of NaOCl accident is limited, medications play a major role in aiding recovery.

Informing and Explaining the Incident of NaOCl Accident to Patient and/or Patient Party

NaOCl accident being an iatrogenic event, lapse in duty of candour could be invoked against the clinician [273]. Hence, it is vital for the clinician to document the incident and inform [94, 114, 122] and explain to the patient and/or patient party in detail [24, 63, 76, 112, 133, 145]. However, the timing of this step is critical considering the patient's state of severe distress and the importance of rendering emergency treatment to control the clinical manifestations and extent of the NaOCl accident [5, 97, 99, 114]. Following emergency treatment and with patient reassurance, the patient can be expected to be in a better receptive and responsive state for patient-clinician communication to explain the incident of the NaOCl accident and the treatment measures taken to manage it. It is also important to inform the patient about potential consequences or outcomes of the incident and further management measures that would be needed under such circumstances [6, 24, 27, 76, 77, 94, 112, 131, 145]. It is preferable to carry out this step during the patient monitoring period, as it provides an opportunity to explain in detail while watching or observing the patient's status.

Documenting the Incident of NaOCl Accident

It is equally important to document the details of the incident of NaOCl accident due to its potential medico-legal implications [24] though the number of claims is reported to be a few [272]. The details such as time, date, and location of the incident of NaOCl accident, concentration and volume of NaOCl used, precautionary measures taken before and during the endodontic procedure to avoid or prevent it and protect the patient, and

treatment measures taken to manage it must be carefully recorded and documented with clinical photographs [28, 112, 125, 274]. Apart from documentation, photographs also help in the assessment of clinical progress of NaOCl accident [28, 122, 130]. It is also important to document radiographic or radiologic images taken before and after the NaOCl accident as evidence regarding whether the causative or contributory factor was pre-existing or an iatrogenic one [21]. Additionally, as a NaOCl accident is mostly an iatrogenic incident, thorough documentation facilitates sharing of incident-related details when the patient is referred to or presents to, or self-reports to, secondary or other care, and standardized case reporting as per reporting guidelines [112, 114, 127]. The latter is crucial because well-documented and reported cases are one of the main sources of clinical data or evidence for case analysis and reporting [10, 105, 110] and/or systematic review and synthesis of data about NaOCl accidents. However, a major challenge in this aspect is missing details and/or heterogeneity in the available data, which can be mostly attributed to a lack of uniformity in recording and/or reporting the details of an incident of a NaOCl accident [17, 27, 30, 274]. Hence, documenting the incident by adopting a standard or uniform format is valuable. In this regard, an original and its modified template can be employed to document an incident of a NaOCl accident [9, 27, 112]. However, as only a couple of cases have reported employing such a template [27, 124], a strong emphasis is needed on documenting and reporting all future incidents using such a template. It is also important to report the documented incident and seek advice from the indemnifier to safeguard oneself [112].

Patient Instruction and Follow-up

The patient must be given both verbal and written home care and postoperative instructions, and a soft diet must be advised [9, 141, 273, 284]. The symptomatology of NaOCl accident mostly shows initial worsening, the extent of which depends on application of emergency treatment and various factors related to the patient, tooth involved, NaOCl irrigant, and irrigation aspects [14, 15, 22, 50, 271, 273]. At times, the patient may initially experience only pain or a burning sensation, which can be easily mistaken for operative or post-operative pain [19], and other features or complications of NaOCl accident start to manifest any time following the patient discharge. Hence, it is crucial to strictly follow up the patient on an hourly basis, at least telephonically [44, 112], for the initial 24 hours (Fig. 4). In case of any clinical worsening or complication during follow-up, the patient must be immediately referred to secondary care and then followed up under primary care when the patient's condition becomes stable [7, 10, 11, 34, 51, 55, 56, 59, 67, 91, 92, 108, 112, 113, 117, 119, 122, 126, 129, 273].

Progression Phase Management

Irrespective of initial treatment measures, the symptomatology of NaOCl accident mostly progresses, with or without tissue damage or complications, due to acute tissue response to cytotoxic NaOCl. Therefore, progression phase management aims to stabilise the patient and facilitate recovery. It includes early and/or later treatment measures carried out after the initial 24 hours and can extend over a period ranging from a few days to many weeks depending on the presence and extent of tissue damage or complications and patient response to treatment.

Patient Recall Assessment, Monitoring, Reassurance, Instruction, Medications, and Other Measures

The patient must preferably be recalled after 24 hours. A detailed clinical examination and assessment, including any radiographic investigation, must be carried out, particularly if this was not performed during the initial phase of management. The patient must be informed and reassured regarding the status of progress of manifestations, given any necessary protective instructions such as avoiding sunlight and/or applying sunscreen cream or calamine lotion for facial ecchymosis or cutaneous manifestation [33, 59, 80, 90, 95, 117, 120-122, 124-126, 128, 131, 133]. Any additional or adjunctive measure, such as LLLT, can be continued if initiated during initial phase or its application can be started during the progression phase considering its beneficial role in facilitating the resolution of manifestations and recovery [84, 102, 108, 113, 135]. Again, pharmacological measures play either a main or adjunctive role during the progression phase. It mainly includes continuation of already prescribed and/or administered medications with or without any further change or additional medications [33, 36, 44, 51, 62, 66, 81-83, 85, 92, 136, 137]. Even as a late measure, medications have played a main role with other supportive measures, in ensuring recovery, though the recovery period varied, even in those cases, without or with tissue damage, where NaOCl accident was detected or confirmed after a time elapsed ranging from a couple of days to a few days following the incident [38, 104, 108, 126, 127, 134].

Advising Warm Compression and/or Warm Oral Rinses

This measure is recommended to improve local microcirculation to facilitate resolution of swelling and/or ecchymosis and prevent tissue necrosis and/or accelerate healing in case of tissue necrosis [5, 9, 32, 64, 103]. Both warm compression and warm saline rinses can be advised for extraoral and intraoral effects, respectively. They must be advised after the initial 24 hours of cold compression and must be applied at 15-minute intervals or as frequently as possible daily for at least 1-2 weeks or for the following several days to obtain their beneficial effects [40-42, 87, 89, 106, 113, 121, 146, 273, 274].

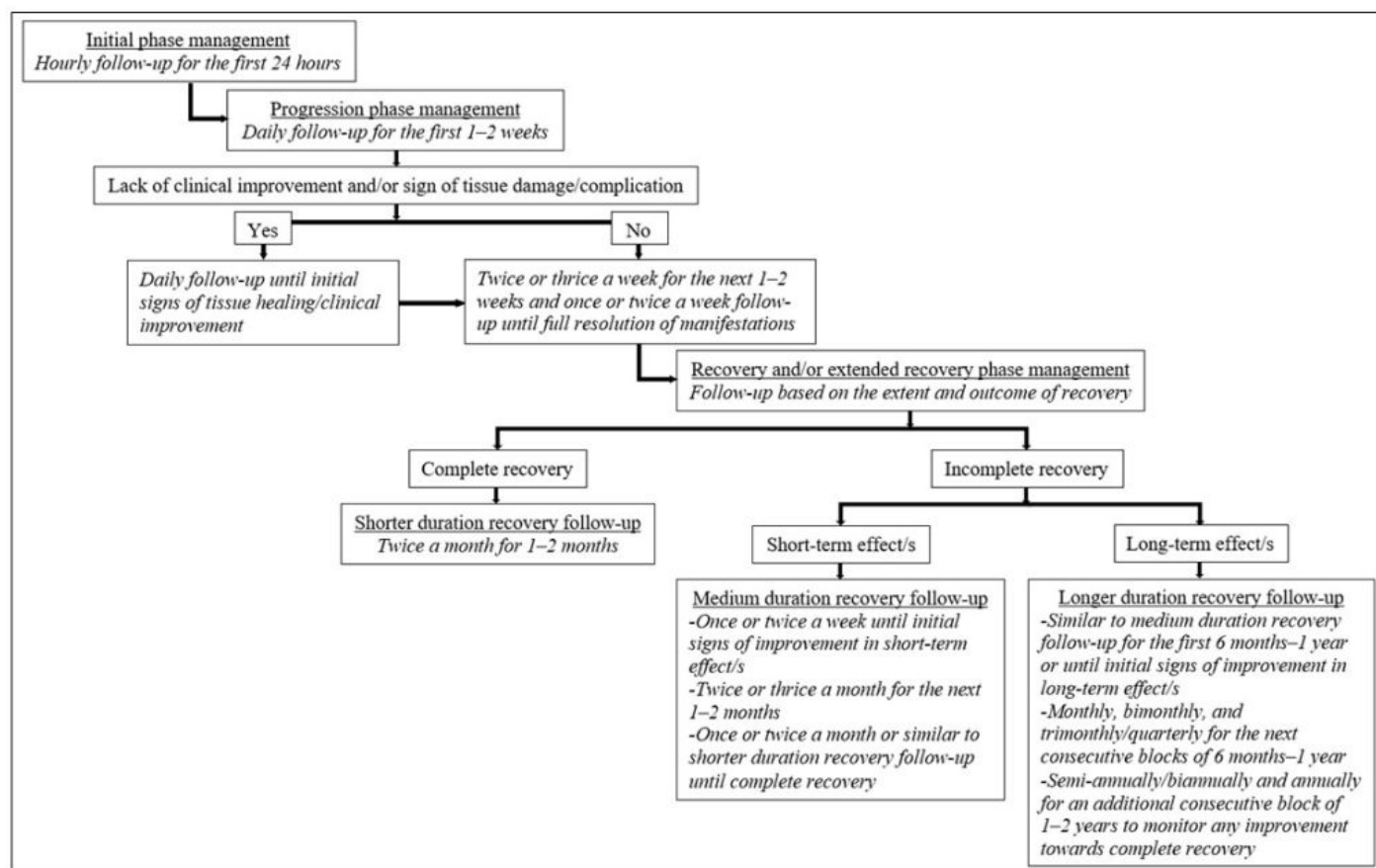


Figure 4. Planning the patient follow-up on a case-to-case basis in the management of sodium hypochlorite accident

Closing the Open Access or Reopening the Closed Access

In cases where the access has been left open for the first 24 hours or more following a NaOCl accident, the access must be closed after verifying and ensuring that intracanal bleeding or drainage has ceased [32, 44, 62, 75, 87, 133]. However, in cases with closed access but still showing signs of worsening or progression of symptomatology, the access can be reopened to allow drainage and release of pressure either before closing it again [80] or leaving it open for the next 24 hours [112] depending on whether drainage continues or ceases. Although some cases have reported root canal cleaning and shaping in the progression phase using NaOCl or an alternative irrigant such as saline, CHX, and EDTA, and without or with an intracanal medicament such as $\text{Ca}(\text{OH})_2$ and IKI, depending on the pulpal and periapical status of the involved tooth [37, 45, 48, 55, 80, 110, 113, 115, 122, 128] it is safer and preferable to close the access without any further endodontic manipulation or procedure until the recovery phase.

Similarly, extraction of the involved tooth for any reason, such as perforation with poor prognosis, must be postponed to

the recovery phase or until tissue healing occurs because it can further injure the already damaged tissues and increase the risk of complications or infection, especially in an immunocompromised patient [10]. However, if such a tooth is affecting the healing of the damaged soft and/or hard tissues [73, 111], extraction can preferably be considered under the coverage of the same medications employed for NaOCl accidents [28, 41, 58]. Following extraction, additional measures such as surgical and chemical debridement, bone graft deposition, and platelet-rich fibrin membrane insertion can further facilitate tissue healing [73, 111].

Patient Follow-up

The patient must be followed up daily for the initial couple of weeks (Fig. 4) to monitor and reassure the patient because of the potential for worsening of symptoms during the 1st week [17, 40, 271, 273]. Although the patient could be followed up telephonically, it is preferable to recall the patient for clinical follow-up due to the unpredictable course of NaOCl accident. Further patient management during follow-up in the progression phase must be considered based on the following 2 clinical scenarios.

A Patient with Clinical Improvement and/or No Signs of Tissue Damage or Complication

Apart from pharmacological, supportive, and additional or adjunctive measures, such a patient only needs follow-up for recall examination and assessment at regular intervals until complete recovery is evident (Fig. 4). The complete resolution of symptomatology can be expected with a recovery period mostly ranging from 2-6 weeks. In case of non-classic or mild category of NaOCl accidents, recovery can occur in less than 1-2 weeks [77, 137].

A Patient with Lack of Clinical Improvement and/or Signs of Tissue Damage or Complication

In case of unconfirmed diagnosis or clinical worsening or complication or lack of clinical improvement during the progression phase, immediate consultation with a dental or medical specialist or referral and admission to a secondary care or hospital must be considered for patient assessment and investigations [8, 41, 51, 56, 62, 64, 76, 78, 83, 87, 108, 117, 134, 136, 137] and appropriate management [24, 32, 43, 69, 73, 92, 95, 108, 136, 137], including any medical and/or multidisciplinary approach [10, 11, 36, 41, 66, 104, 134], airway management [7, 8] surgical measures under GA [11, 26, 36, 41, 64, 66], parenteral administration of medications and nutrition, and intensive care supportive measures and monitoring including vital signs [7, 8, 10, 11, 56, 64, 74, 92, 113, 122, 123, 129, 132, 134].

Under such circumstances, apart from regular orofacial examination and assessment [51, 57, 76, 136], ophthalmological and neurological assessments [24, 25, 56, 83, 136], neurosensory testing and mapping [122], conventional radiographic imaging such as orthopantomogram (OPG) [62, 69, 78, 82, 87, 100, 134, 136] and paranasal radiographs [36, 103, 118], advanced radiological imaging such as computed tomography (CT), cone-beam computed tomography (CBCT) or dental volumetric tomography (DVT) [26, 27, 41, 43, 60, 62, 78, 87, 100, 122, 123, 126, 129, 134, 136, 137], magnetic resonance imaging (MRI) [64], and ultrasonography/ultrasound, anterior rhinoscopy and/or nasoendoscopy or nasofibroscopy [10, 11, 26, 62, 82, 123, 136, 137], and medical or laboratory investigations such as blood tests, immunological tests, histopathological examination, and tissue culture or culture sensitivity tests must be considered on a case-by-case basis [8, 34-36, 48, 51, 117, 123, 136, 137].

Apart from assisting in identifying the causative or contributory factor for the incident NaOCl accident, these measures will help to assess the extent of complication/s and measures needed to effectively address them, plan and/or change accordingly the course of management of NaOCl accident, formulate any contingency treatment plan, and evaluate the prognosis for resuming endodontic treatment following patient recovery [38, 43, 63, 87, 100, 103, 105, 108, 113, 134, 136].

In case of neurological complication, although altered sensation can return to normal sensation without further measures other than follow-up [34, 38, 46, 47, 56, 57, 92, 98, 107], an additional pharmacological measure in the form of early vitamin B12 administration twice a week, preferably via IM route, has shown successful outcome [107, 127]. However, delay in the administration of vitamin B medication was not effective in resolving the altered sensation [62]. For neuropathic pain, apart from analgesics, use of tricyclic antidepressant drugs such as nortriptyline and amitriptyline and anticonvulsant medications such as gabapentin and carbamazepine have been reported, though their effectiveness in complete resolution of neuropathic pain cannot be ascertained [64, 83].

In a severe case of NaOCl accident with swelling or hematoma or cellulitis extending into fascial spaces, especially sublingual, submental, and submandibular spaces, and risk of complications involving airway or danger area of face, I&D [44][31,44,67,68,93,120] and surgical decompression [7] of fascial spaces must be considered [7, 9, 41, 59].

In case of tissue necrosis, the option of pharmacological and/or non-pharmacological measures must be considered based on the extent and type of necrosed tissues and the patient's clinical response. It must be noted that diminished or minimal pain after the initial intense pain and/or burning sensation can indicate rapid necrosis of soft and/or hard tissues and can be attributed to destruction of underlying nerves and/or neurological complications such as hypoesthesia and paraesthesia [32, 103, 119, 122]. Although this can be misleading, pain can still arise from the inflamed peripheral areas around the necrotic lesion, with a need for analgesics [122, 127]. Similarly, steroid administration, including delivery via local or intraoral infiltration, can be an option on a case-to-case basis to control inflammation around the necrotic lesion and facilitate tissue healing [11]. As tissue necrosis is prone to secondary infection, antibiotics are important prophylactically and/or therapeutically irrespective of whether necrosed tissues are already infected or not [6, 8, 22, 26, 32, 34, 36, 38, 41, 45, 46, 69, 85, 101, 108, 112, 134]. As antibiotic therapy is mostly empirical, selection of antibiotic regimen or changes to antibiotic dosage must be based on the patient's clinical response or improvement [10, 26, 36, 130, 134, 136]. However, when improvement is not seen, changing or adding antibiotics to the regimen based on culture or sensitivity tests is highly recommended [36]. Additionally, antimicrobial and/or anaesthetic gels, creams, and ointments [88,95,110,119], CHX [108] or metronidazole mouthwash [85,95], and methylene blue [74] can be considered for topical application in tissue necrosis. Alternatively, herbal agents such as Commiphora myrrh-based mouthwash [93] have also been employed for topical application. Similarly, herbal or natural

agents such as honey can be useful for topical application for any extraoral or cutaneous manifestations [93,143]. Necrotic lesions involving only soft tissues and a smaller area can heal with pharmacological measures and/or follow-up alone [8,27,32,34,38,45,46,49,57,64,69,95,101,122]. However, if tissue necrosis involves both soft and hard tissues or is extensive or non-responsive to pharmacological measures, then non-pharmacological measures such as chemical and/or surgical debridement, surgical ostectomy, and lasers must be considered. When soft tissue necrosis is extensive, chemical debridement by tissue irrigation with a solution such as saline, hydrogen peroxide [92], CHX [92, 108], and povidone-iodine [85] and/or surgical debridement with or without drainage must be carried out [9, 34, 36, 64, 127]. The latter procedure, preferably under LA [85, 127], is recommended to remove necrotic tissue and directly irrigate the affected site to facilitate healing [41, 64, 85, 92, 120, 127, 273]. If the patient is uncooperative or has a medical indication, surgical debridement can be carried out under GA [34, 35, 41, 64, 66]. Eugenol pack can be employed for wound dressing following debridement [127]. A Penrose drain could be inserted to facilitate drainage or decompression, prevent hematoma formation, and promote irrigation [41, 64, 66, 273]. In case of extensive necrosis of alveolar bone, ostectomy of the alveolar plate with bone milling and curettage of necrotic bone must be considered. Bone milling is a conservative surgical measure to identify bleeding points and facilitate revascularization. This procedure can be carried out under LA or GA depending on the extent of involvement [119]. On the other hand, laser therapy can be a non-surgical alternative or adjunctive treatment option for tissue necrosis. Although the current level of evidence is limited to a few case reports [88, 103, 108, 110], LLLT in conjunction with other conservative measures facilitated relatively faster and complete tissue healing [88, 103, 108, 110] and satisfactory outcome without the need for any surgical intervention. It is also effective for the resolution of the paraesthesia [103]. These beneficial effects of LLLT could be attributed to its ability to improve microcirculation, stimulate cellular proliferation, migration, and differentiation and facilitate regeneration of tissues including nerve fibres [9, 108, 267]. They can be obtained through the process of tissue and/or systemic photobiomodulations by local and/or remote applications of LLLT [108, 267, 285].

In case of non-resolving localized chronic granulomatous reaction or foreign body like reaction in the affected tissues with persistent symptomatology or no clinical improvement, a deep surgical exploratory debridement, including microbiologic culturing and histopathological assessment, within the first 2 weeks of NaOCl accident has been recommended [11]. Although this recommendation has limited clinical evidence to back it up, it is expected to improve the treatment outcome and

minimize long-term effects of NaOCl accident [11]. Extensive damage to the maxillary sinus, with or without complications such as ocular or nasal involvement, may need endoscopic endonasal sinus surgery, meatal antrostomy, or anterior antrostomy via canine fossa approach, along with supportive measures such as nasal steroid and/or decongestant, nasal douching or lavage, sinus saline lavage, and steam inhalation [26, 43, 80, 118, 123, 136]. It is also important to continue daily follow-up until initial signs of tissue healing or clinical improvement become evident (Fig.4).

Recovery and/or Extended Recovery Phase Management

The recovery phase involves full resolution of symptomatology but with signs of complete or incomplete recovery depending on the extent and outcome of recovery. It involves those subsequent treatment measures which must preferably be carried out after signs of recovery are evident. In case of incomplete recovery with unsatisfactory outcome/s, extended recovery phase management matters to facilitate complete recovery. Any failure to see complete recovery even after recommended extended recovery phase management and follow-up can be deemed as a partial recovery. Recovery and/or extended recovery phase management can extend from many weeks or months to years depending on the extent of recovery and/or outcome of tissue damage or complication.

Continuation or Completion of Endodontic and/or Post-endodontic Treatment or Other Management of Tooth and Its Surrounding Tissues

Since NaOCl accident by itself generally does not affect the long-term endodontic prognosis of the involved tooth [16, 76], root canal treatment (RCT) can be resumed when the patient fully recovers. However, this would require regaining the trust and compliance or cooperation of the patient, as the affected patient may hesitate to undergo further endodontic treatment due to the fear or distress associated with the experience of an incident of NaOCl accident [8, 27, 62]. In addition, the prognosis of the tooth, especially in the presence of other iatrogenic mishaps such as perforation, must be thoroughly evaluated before resuming RCT to avoid its extraction later or during the follow-up period [57, 111, 119, 131]. When a NaOCl accident occurs in the presence of perforation, the focus on managing the former may delay repair of the latter. This, apart from any delay in resuming endodontic treatment due to patient factors such as fear and reluctance, can affect the surrounding or supporting tissues of the tooth and its eventual prognosis [122]. If prognosis is deemed favourable, it is also important to correct procedural errors such as perforation and over-instrumented or widened apex, by non-surgical and/or surgical means, before resuming RCT to prevent irrigant extrusion [34, 38, 45, 48, 57, 63, 79, 92, 101, 110, 120, 122].

Although many cases did not report on post-incident management of the tooth, nearly 48% of cases completed RCT by employing NaOCl irrigant, either alone [5, 21, 92, 113, 120] or combined with other irrigants such as distilled water, saline, and EDTA [55, 94, 122, 135] and supplemented with laser disinfection [135], or by using alternative irrigants, either alone or combined, such as electrochemically active water [45, 79], saline [44, 48, 62, 69, 72, 85, 86, 99, 105, 107, 124, 135], hydrogen peroxide [51, 81], CHX [27, 45, 56, 69, 79, 81, 85, 105, 107, 110, 126, 133], and EDTA [69, 72, 126]. Irrigants such as 0.2% CHX combined with cetrimide [161] and povidone-iodine [6, 9, 25, 69, 79, 81, 112, 271, 279] have also been recommended as an alternative to NaOCl [93, 112, 131, 271]. When NaOCl irrigation is deemed indispensable, using NaOCl irrigant again in a case of NaOCl accident can be considered safer provided predisposing factors are identified and/or addressed, and all the preventive measures are taken [20, 21, 27, 55, 63, 92, 94, 113]. If RCT has already been completed at the time of the NaOCl accident, then the tooth can be considered for appropriate post-endodontic restorative management [23, 92, 97, 122, 128, 136].

On the other hand, approximately 20% of cases reported extraction of the involved tooth. Although a radical option, extraction could be a last resort in case of persistent pain [9, 41, 58, 69], poor restorability [75, 100], endodontic prognosis [82], or periodontal prognosis [73, 84, 100], root perforation with poor prognosis or repairability [73, 111], lack of soft and/or hard tissue healing [109], persistent mobility with periapical or periradicular lesion or extensive necrosis of alveolar bone [22, 43, 119, 127], primary tooth [36, 41, 70, 76, 92], or patient's decision due to adverse outcome or unpleasant experience or fear associated with the incident of NaOCl accident or failed treatment [25, 58, 62, 74]. Additionally, debridement of the socket, with or without histopathological examination, must be considered when a tooth is extracted for a periapical and/or periodontal reason or lack of tissue healing [69]. In case of a maxillary molar extraction, a buccal advancement flap would be required when a risk of oroantral communication exists [82].

Additional Patient Management and/or Follow-up

The duration taken for recovery following NaOCl accident depends on many factors such as patient's age, body resistance and healing or repair ability, medical status, habits like smoking, extent and severity of NaOCl accident, how soon the NaOCl accident was detected and managed effectively, presence and correction of any other iatrogenic complications such as perforation, and nature and extent of tissue damage or complications [9, 10, 73, 98, 108, 122, 130, 266]. However, it is unpredictable and can vary from case to case, as many patients, despite higher age and/or contributory medical status, had good

recovery within a satisfactory period and/or without hospitalization [21, 55, 57, 73-75, 100, 106, 113, 117, 124, 130]. On the contrary, some young and/or medically fit patients had significant complications, hospitalization, or prolonged recovery period [7, 8, 36, 43, 62, 67, 70, 83, 116, 119, 122, 134, 136].

The symptomatology involving pain and swelling or haematoma, including ecchymosis, mostly resolves within 1-1½ months (4-6 weeks). Soft and hard tissue necrosis needs around 1½-2 months (6-8 weeks) to heal. However, neurological, ocular, facial, and other such complications can take many months to years to recover [53, 59, 122, 127, 128]. Thus, the recovery duration can be broadly categorised into shorter, medium, and longer recovery periods. Shorter recovery period ranges from 1-2 weeks to 1-1½ months. It is mostly expected in cases without tissue damage or complications. A medium recovery period can extend from 1½-2 months to 6 months or less than 1 year, as seen among cases with tissue necrosis or neurological complications. Whereas cases with severe neurological, ocular, or facial complications might require a longer recovery period, which can range from 1-5 years. In this context, when the symptomatology fully resolves, the need for additional measures and/or follow-up in the form of extended recovery phase management can be considered according to the following 3 clinical circumstances on the basis of extent and outcome of recovery (Table 1).

A Patient with Complete Recovery

No further management is required in such a case. However, it is prudent to carry out a shorter-duration recovery follow-up (Fig. 4) for a couple of months to confirm the satisfactory and uneventful orofacial outcomes. Around 74% of the reported cases had a complete recovery [5-8, 10, 16, 21, 23, 27, 28, 33, 34, 36, 37, 39-42, 44, 45, 48, 49, 51, 53-55, 57, 60, 61, 63, 65-73, 75-77, 79, 81, 82, 85-91, 93, 94, 96, 97, 99-106, 108-113, 115-117, 119-121, 124, 126, 129-136, 149, 265], which overall can be considered as good if not excellent. Except a couple of cases [36, 67], which took a medium recovery period; otherwise, most of these cases needed a shorter recovery period.

A Patient Showing Incomplete Recovery with Short-term Effect/s

Although no further management is needed in such a case too, measures to facilitate the reversal of short-term effect/s (Table 1) must be considered. Additionally, a medium-duration recovery follow-up (Fig. 4), which can extend over a period ranging from a few months to a year, can be planned to monitor the reversal of effect/s towards complete recovery. Approximately 18% of cases reported incomplete recovery with short-term effects [11, 22, 34, 38, 40, 43, 46, 47, 52, 56, 59, 64, 74, 92, 95, 98, 107, 122, 123, 127, 128]. Such cases need a medium recovery period and can either show a complete recovery [34, 43, 46, 47, 56, 74, 98,

107[Patel, 2017 #32] or have a potential for gradual improvement towards complete recovery [11, 59, 95, 128] with regular follow-up. On the contrary, the patient may fail to show improvement even after a period of medium-duration recovery follow-up [38, 40, 64, 92, 122, 123, 127]. Such a patient can be considered a case of incomplete recovery with a long-term effect.

A Patient Showing Incomplete Recovery with Long-term Effect/s

Such a case may need additional or further management in the form of corrective (*i.e.*, surgical or cosmetic), rehabilitation, or replacement measures for long-term or persistent effect/s (Table 1). A neurological complication manifesting as chronic neuropathic orofacial pain involving peripheral and central sensitization would require an interdisciplinary approach involving a general dentist, dental and medical specialists, and an orofacial pain clinician, and long-term multimodal management with oral analgesic, topical anaesthetic, topical analgesic, and neurological medications, and local/oral delivery devices such as an acrylic neurosensory stent [83]. Long-term medication therapy could be needed for chronic or prolonged state of altered sensation [62, 83].

Soft and hard tissue complications such as thickened lining or oro-antral communication involving the maxillary sinus due to extensive necrosis of alveolar bone and/or extraction of involved and adjacent teeth [43, 57, 81, 84, 119] would need endoscopic and/or flap surgery in association with an otolaryngologist [43]. Use of advanced buccal flap [43, 82] or reverse pedicled buccinator flap to seal oro-antral communication followed by vestibuloplasty to gain the vestibular depth has been reported [119].

Any cosmetic deformity caused by soft tissue damage and loss of facial adipose tissues and connective tissues [34, 92, 114] can be corrected by subcutaneous augmentation using free vascularised tissue [58], fillers, implants, or coleman fat transfer [11, 64, 114, 147, 271] though these procedures with their associated risks, including unpredictable outcome, have limited clinical evidence in this regard [226, 236, 242]. Since it is difficult to predictably restore the symmetry of the face with these procedures, removal of subcutaneous fat from the normal side of the face has also been suggested as an alternative treatment option. But this option carries the risk of facial nerve damage with an unpredictable treatment outcome [58].

Rehabilitation measures involving neurological treatment, ophthalmological care, otolaryngology intervention, speech and language therapy, and physiotherapy can be considered to address any associated long-term effect/s [43, 271]. Similarly, replacement measures in the form of removable, fixed, or implant-based prostheses can be considered when the involved and/or adjacent teeth are lost due to extraction [22, 43, 62, 91, 119]. Furthermore, a longer duration recovery follow-up (Fig. 4) must be planned to monitor any

progress towards complete recovery. Any lack of improvement or complete recovery even after a longer duration recovery follow-up for a period of more than 3 to 5 years could be considered as a case of only partial recovery with residual or permanent effect/s.

It must be noted that irrespective of the extent and/or outcome of recovery, a longer duration recovery follow-up is also recommended for cases with a compromised medical status [22, 113], long-term medication such as bisphosphonate therapy [21, 113], or extreme complications with a risk for permanent damage or tooth failure [24-26, 35, 83, 84, 92]. Although only around 8% of cases had incomplete recovery with long-term effects [24-26, 35, 36, 38, 69, 83, 85, 114], such cases have a greater potential for partial recovery with residual or permanent effect/s [24-26, 35, 36, 38, 69, 83, 85, 114] as only a couple of cases showed signs of potential for gradual improvement towards complete recovery [32, 83].

Overall, although the prognosis for complete recovery can be considered good, the outcome of a NaOCl accident is unpredictable. The risk of residual or permanent effect/s (Table 1) with associated medico-legal liability becomes greater when complete recovery does not occur even after a longer duration of recovery follow-up for more than 1 year. The residual or permanent effect/s can be mainly in the form of neurological deficit such as altered sensation and nerve paralysis with loss of mimic musculature [12, 18, 24-26, 32, 34, 35, 53, 62, 64, 69, 74, 83, 98, 114, 123], soft tissue changes, which can be mucosal and/or cutaneous, such as fibrosis [41, 59, 98, 125], scar or granulation tissue [26, 34, 35, 40, 41, 57, 92, 123], reduced vestibular depth [74, 125], mucosal [122] or facial discolouration [95], defect, or dimple [35, 38, 64, 114] and progressive shrinkage of facial tissues on the affected side [58] which can lead to cosmetic deformity [33, 35, 58, 59, 64], and loss of involved tooth and its adjacent teeth with associated repercussions [11, 25, 36, 41, 43, 62, 69, 70, 73, 76, 91, 119]. Permanent ocular damage in the form of dystonia and enophthalmos also exists [26]. When a NaOCl accident involves a primary tooth, the potential for permanent damage to the underlying successor tooth must be anticipated [155, 161].

The flow chart depicting clinical decision making towards management of NaOCl accident is shown (Fig. 5). Management of NaOCl accident is summarized in Table 2.

Management of a Referred or Self-reported Case of NaOCl Accident

A case of NaOCl accident might require management under another care or set up, with or without the prior diagnosis of NaOCl accident, following referral or presentation [7, 8, 41, 55, 108, 113][[11, 26, 34, 41, 51, 55, 58, 64, 73-75, 82, 90, 93, 100, 108, 113, 116, 117, 119, 122, 126, 127, 129, 130, 134-136] or patient self-reporting [10, 24, 27, 38, 46, 47, 59, 74, 80, 81, 83, 88, 91, 101, 104, 108, 122, 123, 132, 137] due to clinical worsening, lack of improvement,

Table 1. Categorization of the extent of recovery, including associated outcome/s and other related details, following the management of sodium hypochlorite accident and full resolution of symptomatology

Extent of Recovery	Outcome of recovery	Duration for recovery and/or its outcome	Extent of satisfactory/unsatisfactory nature of outcome	Need for extended recovery phase management	Prognosis for reversal of unsatisfactory outcomes/effects towards complete recovery	Unsatisfactory outcomes/effects
Complete Recovery	Uneventful	2-4 weeks to <1½ months	Satisfactory	No	--	--
Incomplete Recovery	Short-term effect/s	2-6 months to <1 year	Partly unsatisfactory	Yes	Good/fair	Paraesthesia/hypoesthesia, neuropathic pain, weakness or palsy of nerves or mimic musculature, chronic tissue alterations, facial discoloration, and blepharospasm
Incomplete recovery	Long-term effect/s	>1 year to <3-5 years	Unsatisfactory	Yes	Guarded/average	Persistent paraesthesia/hypoesthesia/dysaesthesia/anaesthesia, neuropathic pain, weakness or palsy of nerves or mimic musculature, soft tissue fibrosis/lump, and thickening/hypertrophy of maxillary sinus mucosal lining
Partial Recovery	Residual/permanent effect/s	>3-5 years	Highly unsatisfactory	Questionable	Poor	<u>Oral/dental:</u> Mucosal scar, fibrosis, or discoloration, oro-antral fistula (in case of maxillary tooth), loss of tooth, and damage to permanent tooth follicle (in case of primary tooth) <u>Facial:</u> Facial scar, defect/dimple, shrinkage/atrophy, and asymmetry <u>Maxillary sinus:</u> Irreversible scarring of sinus mucosal lining with loss of function <u>Neurological:</u> Permanent paraesthesia/hypoesthesia/dysaesthesia/anaesthesia, and weakness/palsy of nerves or mimic musculature <u>Ocular:</u> Dystonia and enophthalmos

or complications. Although management of such a case is similar to that explained before in this article, it is important to contact clinician of the set-up, where the incident of NaOCl accident occurred, to collect all the details and/or access the treatment notes or files [38, 41, 55, 108, 114]. This is crucial to confirm NaOCl accident, particularly in a self-reported case, or where the diagnosis cannot be made only based on patient's presenting clinical features such as swelling, tissue necrosis, and epistaxis or nasal bleeding [32, 38, 41, 46, 55, 69, 81, 101, 108, 113, 122, 129, 137], and avoid any misdiagnosis and/or mismanagement [27, 28, 32, 59, 88, 90]. From a medico-legal perspective, it is equally important to obtain written informed consent from the patient and thoroughly document the details even though the clinician or the set-up where the patient is being managed is not involved with the occurrence of the incident of NaOCl accident [93]. This also facilitates enhanced quality of

case reporting due to the emphasis on the need to follow standardized reporting guidelines [127]. The management of a referred or self-reported case depends on the extent of time elapsed following a NaOCl accident. If the time elapsed is not more than a few hours or less than 24 hours, the management involving initial, progression, and recovery and/or extended recovery phases becomes applicable. However, the initial phase management depends on what initial measures were already carried out before the referral or self-reporting. When the time elapsed is more than 24-48 hours, initial measures could be less effective, though they can still be applied to obtain any beneficial effect towards recovery [32, 51, 81, 87, 134]. In cases where referral or self-reporting is significantly delayed by many days or weeks, the management depends on the prevailing clinical features, which tend to be mostly in the form of chronic complications or tissue changes [11, 43, 73, 74, 78, 83, 95, 114, 123, 127].

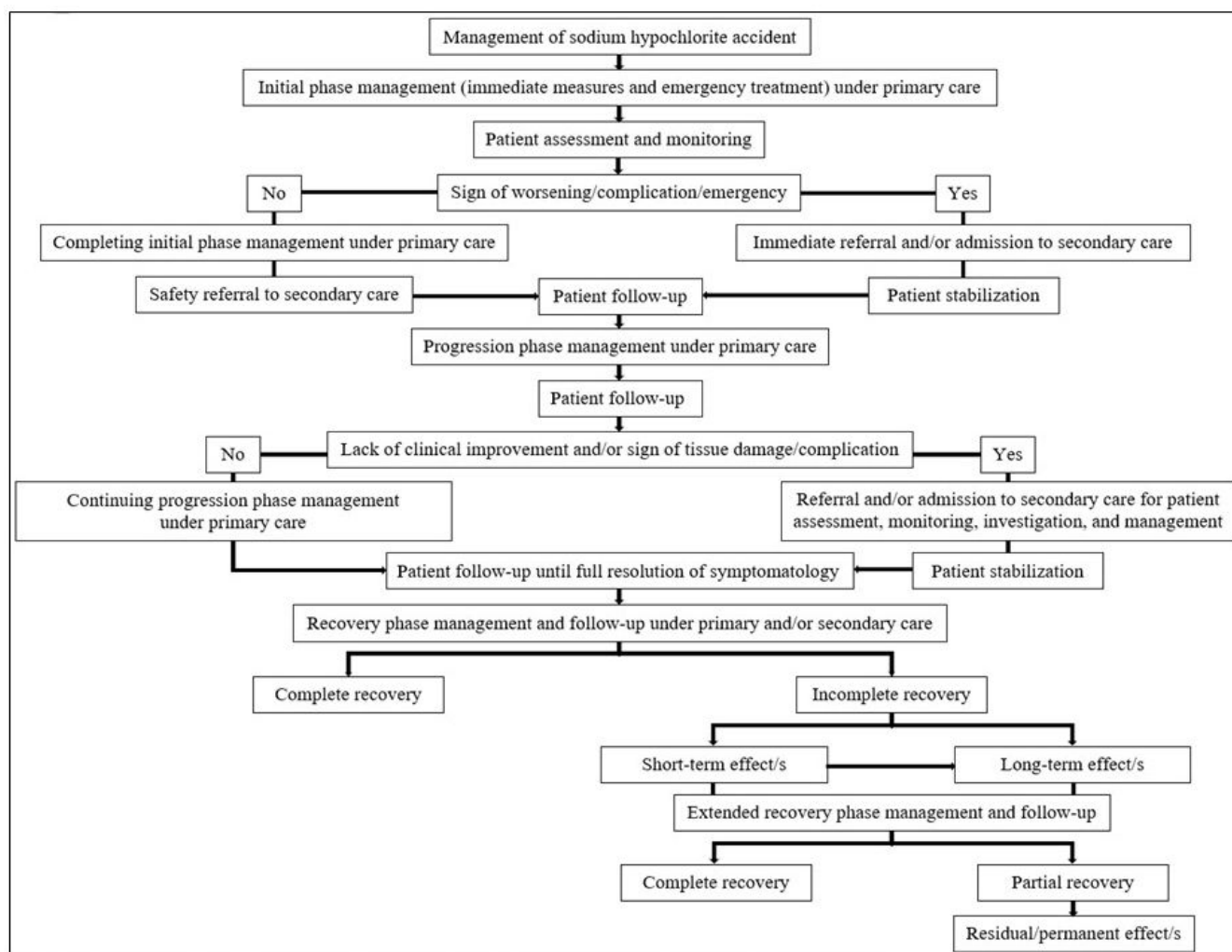


Figure 5. The flow chart depicts the clinical decision-making towards the management of sodium hypochlorite accidents

Prevention of NaOCl Accidents

This is an important aspect considering the medico-legal liability associated with NaOCl accidents [24–28]. As NaOCl is a widely used irrigant, clinicians must ensure all the preventive measures [6, 273, 279] by presuming that every endodontic case has the potential for an incident of NaOCl accident until the irrigation phase is over uneventfully. Additionally, awareness, concentration, and focus of the clinician during irrigation phases are important to prevent NaOCl accidents [27, 122]. The preventive measures can be broadly categorized as patient-, tooth-, irrigant (NaOCl)-, and irrigation-related measures.

Patient-related Measures

Patient Information and Consent

Before starting endodontic therapy, it is important to provide detailed information to the patient on the potential adverse effects of NaOCl and the precautionary or protective measures that would be taken, and obtain written informed consent [25]. This is

important particularly when any predisposing or risk factor for NaOCl accident is identified during pre- endodontic history taking, examination, and assessment of the patient. This can be considered a good practice because the act of immediately informing the patient following an unfortunate incident of a NaOCl accident may still not be justifiable from a medico-legal point of view [24, 112]. Displaying in the operatory a poster depicting preventive measures can be beneficial to conduct pre-treatment discussion, positively reassure the patient, and reinforce the cautious approach which must be followed by the clinician during NaOCl irrigation [274].

Medical and Dental History

The clinician must seek from the patient any history of orthodontic treatment and carefully evaluate such a patient to identify potential alveolar bony fenestration or root resorption due to tooth movement, which is a major predisposing factor for NaOCl accidents [20]. Similarly, the patient's medical and drug history must be obtained, particularly to identify cases involving

Table 2. Summary of measures to manage sodium hypochlorite accident

Management	Measures	
Initial phase management	<u>Under primary care</u> • Quickly detecting a NaOCl accident. • Staying calm and composed. • Stopping further NaOCl irrigation and endodontic treatment. • Positioning the patient in an upright posture. In case of NaOCl extrusion into the maxillary sinus, position the patient in a reclined posture. • Aspirating and/or diluting extruded NaOCl. • Removing rubber dam. • Informing and reassuring the patient. • Controlling pain with local anaesthetic injection and parenteral analgesic administration. • Controlling swelling with cold compression. • Controlling inflammation with parenteral steroid administration. • Allowing bleeding from the canal and leaving the tooth open. • Relieving tissue pressure by incision and drainage on a case-to-case basis. • Carrying out patient assessment, categorization of NaOCl accident, and monitoring to decide on continuing management under primary care or any immediate referral for management under secondary care in case of worsening/complication/emergency. • Applying additional or adjunctive measures such as low-level laser therapy (LLLT). • Prescribing and/or administering medications. • Explaining the incident of the NaOCl accident to the patient. • Documenting all the details about the incident. • Giving patient instructions. • Strict hourly follow-up of the patient.	<u>Under secondary care</u> (For any local/oral/facial/maxillary sinus/ophthalmological/neurological complications) Out-patient/consultation basis: • Referral for consultation with a concerned specialist or for patient assessment, investigations, and monitoring. (For any airway/systemic complications/emergency) In-patient/admission basis: • Medical assessment and investigations. • Airway management. • Management under general anaesthesia. • Surgical management and/or drain insertion. • Intravenous administration of medications and nutrition. • Multidisciplinary management. • Medical supportive measures. • Patient intensive care monitoring and stabilization.
Progression phase management	<u>Under primary care</u> • Patient recall assessment, monitoring, reassurance, medications, and additional or adjunctive measures such as low-level laser therapy (LLLT). • Advising warm compression and/or warm oral rinses. • Closing the open access or reopening the closed access. • Referral for management under secondary care in case of lack of clinical improvement and/or signs of tissue damage or complication. • Drainage to relieve tissue pressure and/or debridement of necrotic tissues. • Providing adjunctive therapy for local or oral tissue management or complication or healing. • Strict daily follow-up of the patient.	<u>Under secondary care</u> (For lack of clinical improvement and/or signs of tissue damage or complication) • Similar to initial phase management measures under secondary care.
Recovery and/or extended recovery phase management	<u>Under primary care</u> • Continuing/completing endodontic and/or post-endodontic treatment or extraction of involved tooth, including management of surrounding tissues, depending on prognosis of tooth. • Non-surgical/surgical correction of any iatrogenic error before continuing with endodontic treatment of the involved tooth. • Referral and/or management under secondary care for any short-term/long-term effects. • Regular follow-up of the patient to monitor progress towards complete recovery.	<u>Under secondary care</u> (For any short-term/long-term effects) • Referral for consultation with a concerned specialist. • Measures to facilitate reversal of short-term effects. • Non-surgical/surgical treatment in the form of corrective, rehabilitation, or replacement measures for long-term effects.

NaOCl: sodium hypochlorite

postmenopausal women [21, 113], bisphosphonate therapy [21, 113], immunocompromised status [16, 275], or comorbidities [127]. Such cases have a greater predisposition to NaOCl accidents, exacerbated tissue inflammatory response, severe manifestations with extensive tissue damage or complications including systemic involvement and life-threatening situations, chronic tissue damage, reduced tissue repair or healing ability, and prolonged recovery period with adverse or unfavourable or unsatisfactory outcomes [10, 15, 127, 130]. Similarly, patients with haemorrhagic disorders or on anticoagulant therapy may risk excessive tissue bleeding and associated complications in case of NaOCl accident [129]. Hence, all the precautionary measures must be taken to prevent NaOCl accidents in such patients.

Patient Assessment and Examination

A thorough pre-endodontic evaluation of the patient must be carried out by employing appropriate clinical examinations and investigations to identify any factor which can influence the occurrence and extent and/or outcome of NaOCl accident. Such a factor could be related to gender, age, density and thickness of cortical bone, amount of marrow space, proximity of vital structures, and specific location of venous vasculature with surrounding tissues around the tooth which is to be endodontically operated [6, 12, 15-17, 54, 70, 76, 81, 275, 286].

Patient Position on the Dental Chair

When the effect of patient position on a dental chair in influencing head or jaw position, gravitational force during NaOCl irrigation [154, 182, 189, 217, 233] and cerebral blood flow and tissue perfusion is considered along with the vascular mechanism involved behind NaOCl accident [6, 19, 162, 179, 208, 259], the patient position on a dental chair might have the potential to affect the orofacial venous pressure, which in turn can influence the infusion of actively extruded NaOCl into the vasculature, particularly when a positive pressure-based irrigation technique is employed, though the clinical evidence on their direct association is lacking. The type of apex (i.e., open or closed apex) can also matter when the influence of patient or jaw position and gravity on NaOCl extrusion is considered. A recent study that employed samples simulating immature teeth with an open apex reported that mandibular jaw position (vertical) had a relatively greater volume of extruded NaOCl compared to maxillary jaw position (45° inclined), though the difference was not statistically significant. It highlighted that clinicians must therefore exercise caution regarding the patient or jaw position during irrigation procedures involving immature teeth, especially while carrying out regenerative endodontic procedures [258].

On this basis, hypothetically, a supine or semi-supine position may seem to be more favourable than a sitting or upright position towards the measure of reducing the probability of NaOCl accident involving vascular pathway. Although the former position is most commonly employed during an endodontic procedure, it must be noted that the latter position is indicated in certain situations such as pregnancy and spinal deformities [189]. On the contrary, the patient is mostly positioned in a supine position when a NaOCl accident occurs during endodontic treatment under GA [36, 66, 76]. Additionally, in the case of maxillary posterior teeth, the supine position might tend to facilitate passive extrusion and stagnation of NaOCl along the periapical area and its eventual leaching into the maxillary sinus [5, 6, 19, 78].

Overall, although clinical evidence is lacking at this juncture, there is a scope and need to conduct clinical research regarding the influence of patient position on extrusion of NaOCl during intracanal irrigation. Additionally, there is also a potential to carry out studies employing teeth with immature (open apex) and mature (closed apex) roots and compare the extent of NaOCl extrusion under the influence of patient or jaw position. Clinically, irrespective of the patient position on a dental chair, employing a negative pressure-based irrigation technique is preferable to prevent NaOCl accidents because it is less influenced by factors such as jaw or head position and gravitational force. On the other hand, as these factors can significantly influence the extent of NaOCl extrusion when a positive pressure-based irrigation technique is adopted, applying an endodontic aspirator or high-volume evacuator to the access opening during irrigation is beneficial to reduce NaOCl extrusion or risk of NaOCl accident, especially when a conventional syringe- and needle-based irrigation is employed [233].

Tooth-related Measures

Evaluating Tooth and Its Surrounding Soft and Hard Tissues

Pre-endodontic assessment of the tooth must be done both clinically and radiographically (Figs. 6A-6D) to identify any predisposing factors such as open apex, large periapical lesion causing apical resorption and/or bony fenestration, widened apical foramen or defect due to resorption, apical bony fenestration, and proximity of root apex to maxillary sinus and surrounding vital structures before initiating endodontic therapy [6, 9, 15, 16, 18, 37, 40, 54, 70, 81, 136, 139, 284, 286, 287]. Although conventional radiographs are useful to identify such predisposing factors, computerised tomography (CT) and cone-beam computer tomography (CBCT) are recommended for a thorough 3-dimensional (3D) evaluation of the tooth and its surrounding periapical/periradicular bone when conventional

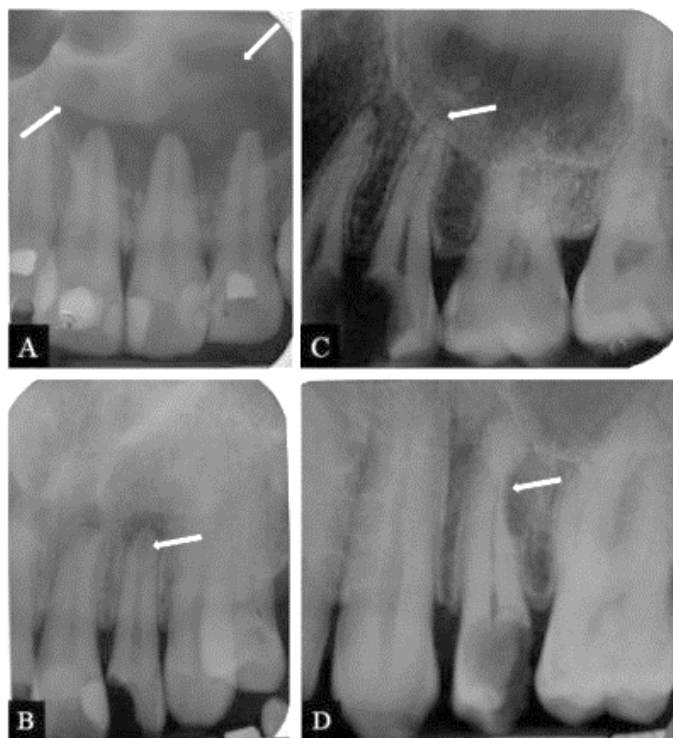


Figure 6. A) Pre-endodontic assessment for the risk of sodium hypochlorite accident by thorough radiographic examination to identify any predisposing factor (white arrow), such as large periapical lesion; B) Apical defect or resorptive lesion; C) Proximity of root apex to maxillary sinus; D) Root defect

radiographs have limitations in identifying such factors [22, 68, 107, 125, 136, 284]. A clinical study by Souza *et al.* [20] reported the presence of apical bony fenestration with an open-ended or widened foramen as an important risk factor for NaOCl accidents and recommended 3D imaging modalities such as CBCT, particularly with a smaller field of view, in preoperative identification of such a risk factor involving hard tissues [19]. Cho-Kee *et al.* [138] conducted clinician surveys with retrospective analysis of NaOCl accident cases that were encountered by dental practitioners and found that a greater number of cases involved maxillary teeth and female patients. Based on the CBCT images that were available, they reported the presence of apical bony fenestration in all the analysed cases and concluded it as a highly prevalent anatomical risk factor. They also noted the presence of apical pathosis and iatrogenic perforations as other risk factors, though to a lesser extent. They emphasized the importance of pre-endodontic and/or early detection of these factors, particularly in maxillary teeth of female patients, to prevent NaOCl accidents and highlighted the role of CBCT in this regard. Similarly, other advanced 3D imaging modalities such as magnetic resonance imaging (MRI) can be effective in preoperative identification

of the association between predisposing factors and surrounding soft tissues [19]. Additionally, there is scope to explore the application of other advanced imaging modalities such as conventional angiography (CA) using contrast medium, digital subtraction angiography (DSA) [197], high-resolution ultrasonography or ultrasound with or without colour Doppler and spectral analysis [236, 241, 242], fluoroscopy, magnetic resonance angiography (MRA), and computed tomography angiography (CTA) [132, 226] to assess the orofacial vasculature in relation to the predisposing factors.

Although the availability or applicability of these advanced modalities for pre-access preparation assessment of teeth in routine endodontics is questionable [127], considering the potential for life-threatening complications of NaOCl accidents, the role of these advanced modalities for pre-endodontic assessment on a case-to-case basis can be valuable, especially in a medically or immunocompromised patient with evident predisposing factor/s and greater risk for NaOCl accident and/or its worst outcome/s. Interestingly, a clinical case study analysed the role of mixing NaOCl with a radiopaque or X-ray diagnostic contrast agent and using this mixture as an irrigant in visualizing and monitoring the depth of irrigation needle insertion and irrigant penetration with conventional or digital radiography during the irrigation phase and developing an algorithm of actions to prevent and/or immediately address any NaOCl extrusion accordingly [221]. This method has the potential for regular radiographic assessment of the tooth in routine endodontics for the risk of NaOCl extrusion/accident, particularly in the presence of any predisposing factor. Unlike pre-endodontic or pre-access preparation assessment, this is a post-access preparation assessment applicable before and/or during the irrigation procedure. However, currently it lacks clinical evidence. Hence, there is scope to conduct further research in this regard.

Choosing an Appropriate or Alternative Endodontic Procedure

With the broadening scope for the application of vital pulp therapy (VPT), it can be considered as an alternative option to pulpectomy or RCT in certain circumstances, depending on meticulous clinical assessment and stringent case selection criteria [288]. Thus, in applicable cases such as a non-necrotic tooth with a large canal and immature apex, particularly in paediatric patients, pulpotomy can be considered instead of pulpectomy to avoid the need for root canal or intracanal irrigation and the probability of NaOCl accidents [76]. NaOCl application via direct passive irrigation or soaked cotton pellet during VPT, which is mainly for haemostasis and disinfection, can be considered safer because it is mostly limited to the pulpal surface level or confined to the coronal pulp or pulp chamber [288, 289].

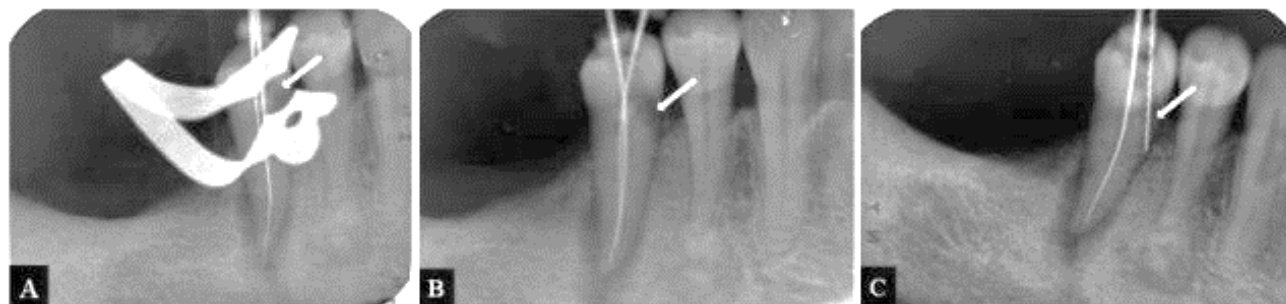


Figure 7. Iatrogenic or procedural errors such as root perforation (white arrow); A) during endodontic therapy must be detected and confirmed; B & C) and corrective measures must be taken before carrying out sodium hypochlorite irrigation to prevent sodium hypochlorite accident

Applying Clinical Skill with Sound Knowledge and Proper Armamentarium

The clinician must have a comprehensive knowledge of internal and external anatomy of the tooth, take good pre-operative radiographs, including angled radiographs, and use recommended armamentarium including magnification aids [27] to correctly design and prepare the access opening and to prevent iatrogenic errors such as perforation, which predisposes to NaOCl accidents [57].

Preventing or Minimizing or Correcting Iatrogenic Errors

Measures must be taken to prevent or rectify iatrogenic errors such as perforation, use of compressed air, faulty working length, overinstrumentation, and under- or over-enlargement of the apical 3rd of the root canal, which predispose to NaOCl accidents [9, 15, 16, 139]. Although rubber dam application is a part of standard endodontic practice, it may not have a direct role in the prevention of NaOCl accidents. However, whether it is applied before or after access opening can matter regarding the predisposition to NaOCl accidents. Rubber dam must preferably be applied after access opening is initiated and the pulp chamber is located. This is because a rubber dam can obstruct the viewing or assessing of crown-root angulation during access preparation, with a risk of cervical or subgingival perforation (Fig. 7A) [280], which has a major predisposition to NaOCl accidents [15]. This risk is greater especially when a tooth is misaligned, tilted, or crowned with changed or altered crown-root angulation [275]. On the contrary, a well-applied rubber dam with a proper gingival margin inversion and seal can reduce the probability of NaOCl accidents or damage to the surrounding tissues by minimizing extrusion or leakage of NaOCl via such a perforation, particularly an undetected one [108].

Likewise, the location of the apical foramen and correct working length must be determined using tactile sense [76], radiograph [63], and electronic apex locator [45, 66, 79] to prevent overinstrumentation [45, 66]. In case of occurrence of any iatrogenic error such as faulty working length and perforation [38,

57, 101], it must be detected early using radiograph (Figs. 7B & 7C) [63, 122] or CBCT [137] and electronic apex locator [45, 66, 122] followed by immediate corrective measures before carrying out NaOCl irrigation to prevent NaOCl accident. It must also be noted that an underprepared apical 3rd can lead to binding or wedging of the irrigation delivery device or needle, with increased risk of NaOCl extrusion, while an overprepared apical 3rd increases the risk of taking the device or needle closer to the apical foramen, irrespective of the irrigation method employed, with greater potential for NaOCl extrusion. Hence, the apical 3rd preparation must be optimal to ensure both effective apical irrigation and prevent NaOCl accidents [174, 245]. Use of compressed air to dry the root canal during endodontic therapy or irrigation carries the risk of causing NaOCl extrusion along with air or subcutaneous emphysema [36, 99, 100]. Hence, it must be avoided to prevent NaOCl accidents.

Irrigant (NaOCl)-related Measures

Employing Alternative Irrigants or Disinfection Modalities

Choosing an alternative irrigant to NaOCl is a better option to avoid NaOCl accident, especially if any predisposing factor is present and the use of NaOCl is not crucial or risky when the patient is immunocompromised [10]. Irrigants such as electrochemically active water [45, 72, 79, 163] or super-oxidized water [229], saline, CHX [69, 161], 0.2% CHX combined with cetrimide [161], and povidone iodine [112] can be considered as an alternative to NaOCl [6, 9, 25, 69, 79, 81, 271, 279], particularly in high-risk cases such as deciduous or young permanent teeth with open apex or teeth with apical fenestration or widened apical foramen due to pathologic or iatrogenic reasons [156, 161]. Since saline and electrochemically active water lack the desired antimicrobial effect [45, 66, 275] 0.12% or 2% CHX is mostly suggested as an alternative to NaOCl. CHX is relatively less toxic [161] with excellent antimicrobial property [142, 156, 163] and seems to be an effective alternative to NaOCl in many aspects [119]. As a main irrigant, CHX has shown overall high endodontic

success rates in RCT involving vital or non-vital pulps, with or without periapical lesion, and primary, secondary, or retreatment [148]. However, CHX lacks tissue-dissolving properties [156] and is also cytotoxic [159] with a tendency to cause damage like NaOCl when extruded into the tissues [9, 146, 159]. Hence, measures such as using a lower concentration of CHX combined with cetrimide [161], using CHX in gel form [79, 163], and using CHX alternately with diluted or lower concentration NaOCl [66] could be considered. CHX solution as an alternative irrigant in a case of NaOCl accident must also be used with all the precautionary measures because its accidental extrusion in such a case has led to a far worse or unfavourable outcome compared to an initial NaOCl accident [109]. Hence, when such a risk exists, CHX gel can be considered as an alternative irrigant [79].

When the requirement of having an alternative irrigant belonging to the hypochlorite category is considered, then calcium hypochlorite [$\text{Ca}(\text{OCl})_2$] has the potential to be such a one [239]. Although $\text{Ca}(\text{OCl})_2$ is less effective in removing inorganic or smear layer, like NaOCl, it can dissolve soft tissue or organic matter [175]. Moreover, it has better antimicrobial effectiveness due to its ability to generate more hypochlorous acid and $\text{Ca}(\text{OH})_2$ upon reaction with water [175, 186]. Efficacy of $\text{Ca}(\text{OCl})_2$ is found to be similar to or better than NaOCl, though the clinical evidence on its cytotoxicity is limited. One study reported that $\text{Ca}(\text{OCl})_2$ is more biocompatible than NaOCl, with the former showing less cytotoxicity compared to various concentrations of the latter. The cytotoxicity of even higher concentration 5% $\text{Ca}(\text{OCl})_2$ was as low as that of the less cytotoxic 0.5% NaOCl [194]. A recent study showed that when compared to NaOCl, $\text{Ca}(\text{OCl})_2$ has a more favourable influence on the viability, proliferation, and osteogenic differentiation of human apical papilla cells and caused less structural damage to them. Moreover, it did not impair cell chemotaxis. Overall, $\text{Ca}(\text{OCl})_2$ has the potential to be an alternative irrigant, especially in regenerative endodontic procedures [257]. However, more clinical research is warranted in this regard.

On the other hand, herbal or natural irrigants have the potential to serve as a non-chemical-based alternative to NaOCl [268, 290]. The currently available level of evidence indicates that the antimicrobial efficacy of some natural irrigants, either as single (castor oil, noni, and papain) or combined (garlic-lemon), is similar to NaOCl. The effectiveness of another natural irrigant, neem, is either similar to or superior to NaOCl, with less postoperative pain. On the contrary, few other natural irrigants such as propolis, miswak, and garlic as a single irrigant are inferior to NaOCl. However, a natural irrigant combined with a chemical irrigant (papain-chloramine, neem-NaOCl, and neem-CHX) has superior efficacy to NaOCl alone. When criteria of clinical or radiographic success are considered,

papain-chloramine and garlic have no significant difference with NaOCl [268]. Hence, although natural irrigants do not seem to be more effective than NaOCl and cannot totally replace it, they have the potential to be used as an additional irrigant along with NaOCl to reduce the concentration and/or volume of the latter and compensate for any decrease in the latter's efficacy. They can also serve as a substitute irrigant for NaOCl in selected cases. However, there is ample scope to conduct further research towards obtaining an herbal or natural irrigant formulation as an effective alternative to NaOCl [268].

As chemical-based alternative irrigants are also cytotoxic, though to a varying extent, employing an alternative disinfection modality is another measure to prevent NaOCl accidents. Laser application is one such alternative for intracanal disinfection. Although employing laser-based application alone as a disinfection modality has its own limitations and cannot totally substitute for irrigants [291-293], considering its application in a form such as direct laser irradiation of the root canal and antimicrobial photodynamic therapy (APDT) employing a dye can be a useful option as an alternative disinfection modality, particularly in cases that carry a greater risk for extrusion of NaOCl or other chemical irrigants [135, 293]. Although the evidence to link laser activation and irrigant extrusion seems inconclusive due to contradictory study outcomes, a couple of studies have reported that laser application modalities such as photon-induced photoacoustic streaming (PIPS) and shock wave enhanced emission photoacoustic streaming (SWEEPS) showed no significant effect on the extrusion of dyes that are generally employed for APDT [238, 250].

Reducing the Potential for NaOCl Extrusion

When use of NaOCl is indispensable, the potential for extrusion of NaOCl must be minimized, particularly in the presence of predisposing factors. This could be met by employing NaOCl gel instead of NaOCl solution [196, 224]. NaOCl gel showed significantly less extrusion compared to NaOCl solution when the apical diameter was ≤ 2.5 mm [211]. Similarly, in a primary tooth with a widened apex due to physiologic resorption, the former led to less extrusion compared to the latter [231]. In cases of larger apical diameter or wider apex, the potential for extrusion can be further reduced by depositing or coating NaOCl gel onto the canal wall rather than injecting it [294].

[172, 196, 224, 227] Although NaOCl gel has antibacterial effectiveness, effective removal of debris and smear layer, and reduced risk of extrusion, including apical debris, with lesser post-operative pain [231, 294]. Currently, clinical evidence is still limited to widely advocate it instead of NaOCl solution as a

routine irrigant. However, considering the importance of NaOCl as an irrigant and the dynamics of effective intracanal irrigation, along with the impact of life-threatening or adverse effects of NaOCl accidents, there is a strong reason and a good scope to conduct more focused research on improving NaOCl gel for clinical application as a regular and safer irrigant. There is also a scope to evaluate whether the application of an irrigant activation or agitation method to enhance the effectiveness of NaOCl gel has any influence on the latter's extrusion potential.

Controlling the Factors that Influence the Extent of Toxic Effects of NaOCl

When NaOCl irrigation is deemed necessary, measures to reduce the toxicity of NaOCl must be considered. One such measure is using a lower or diluted concentration of NaOCl [54, 69, 279, 295]. NaOCl with a concentration as low as 1% is found adequate to dissolve the entire pulp tissue during endodontic treatment [164] with satisfactory antimicrobial effect [296]. However, a concentration as low as 1% has also led to NaOCl accidents [22, 36, 38, 44, 56, 64, 71, 91, 295]. Therefore, NaOCl with a concentration less than 1% must be preferred [54, 69, 279, 295]. Additionally, it is preferable to use NaOCl solution with a neutral or physiological pH [54, 69, 295] and a solution osmolality approximating that of serum osmolality because such a solution would be better tolerated by the patients in case of extrusion [152]. NaOCl with a concentration $\leq 0.5\%$ and a pH around 8.9 is relatively less toxic with good antimicrobial effect, dissolves mainly necrotic tissues, less affecting vital and normal tissues, and is quickly cleared by draining vasculature [40, 44, 69, 244, 273, 295, 297]. However, NaOCl at a lower or diluted concentration would be less efficacious because it takes more time to act [151, 163]. This can be compensated with additional measures such as longer irrigation time [158, 273], frequent irrigation with a higher volume of solution [29, 295], using another irrigant such as CHX in combination with NaOCl [45, 51, 66, 81, 156, 296], using preheated or NaOCl solution heated to 45–60°C temperature [81, 164, 285], and sonic, ultrasonic, or laser activation of NaOCl solution [81, 153, 165, 285, 298–300]. Laser activation is shown to increase the efficacy of low-concentration NaOCl while ensuring the antimicrobial effect [232].

Although use of preheated NaOCl has been reported with NaOCl accident [72], there is no available evidence to indicate the role of temperature in aggravating the damaging effect of NaOCl. Preheated NaOCl solution may not cause any damage to surrounding tissues as temperature equilibrium is attained rapidly [150]. Sonic, ultrasonic, or laser activation techniques can also carry a risk of NaOCl extrusion, especially as the apical canal preparation size becomes greater and/or when factors related to safer irrigation are not controlled, which increases the risk of extrusion irrespective of the techniques employed

for irrigation and/or irrigant activation or agitation [174, 187, 245, 246]. However, any extrusion of lower-concentration NaOCl while employing these techniques to increase its efficacy can be minimal when correctly applied [17, 174, 181], or still be considered relatively safer compared to extrusion of higher-concentration NaOCl [244]. It must be noted that ultrasonic activation can increase the concentration of NaOCl during the activation phase [216]. Hence, from a safety point of view, this could become counterproductive when any extrusion during ultrasonic activation of lower-concentration NaOCl is considered. However, further research is needed on this aspect to understand its clinical implications. On the other hand, employing an additional disinfection modality such as APDT can help to reduce the need for a fuller or higher concentration of NaOCl, with or without activation technique, and/or to compensate for any decreased effectiveness of reduced-concentration NaOCl through a synergistic action towards ensuring patient safety [63]. When use of NaOCl at the full recommended concentration is preferred, then using it in a lesser or smaller volume is better.

On the other hand, even irrigation with a lower concentration of NaOCl but in larger amounts and too often may not be a safer option, as volume and frequency of irrigation are also related as factors influencing the probability of NaOCl extrusion [15]. Hence, irrespective of the concentration, using NaOCl in copious amounts must be avoided to minimize the extent of toxic effects under the influence of its volume [45, 51, 81, 156, 296]. NaOCl can also be used in combination with an additional irrigant as an adjunctive measure to reduce its volume. Overall, irrespective of the concentration, volume, and temperature of the NaOCl used and the method of irrigation or agitation or activation of NaOCl employed, all the precautionary measures must be ensured to prevent NaOCl accidents.

Irrigation-related Measures

Selecting the Irrigation Technique and/or Irrigant Agitation or Activation Method and Accessories

Since classic or non-classic NaOCl accidents occur when the pressure during the irrigation phase exceeds tissue back pressure and/or central venous pressure, it is important to carefully select the irrigation technique and/or agitation or activation method that generates less pressure, particularly in the presence of risk factors, to prevent NaOCl accidents. It must be noted that when the case reports on NaOCl accidents are considered, such incidents have mostly occurred while carrying out conventional syringe- and needle-based irrigation techniques. Hence, it is preferable to use an apical negative pressure-based irrigation technique such as EndoVac and GentleWave™ System instead of a positive pressure-based one such as conventional syringe and needle irrigation and RinseEndo [6, 191, 193, 200, 209, 218, 225, 240, 260, 264, 279, 301]. Although EndoVac microcannula,

compared to its macrocannula, might tend to cause NaOCl extrusion in an immature tooth [183], overall, EndoVac causes minimal extrusion [17, 170, 174] irrespective of apical preparation diameter or size when compared with conventional syringe and needle irrigation [174]. This can also be beneficial in cases where RCT needs to be resumed, and use of NaOCl irrigant is deemed necessary following the incident of a NaOCl accident [20]. However, EndoVac may not be suitable for primary teeth due to their shorter crown height [76]. Apart from the reduced tendency for extrusion of NaOCl [264], the available evidence suggests that apical negative pressure-based irrigation is also more effective than conventional syringe and needle irrigation in terms of apical penetration, canal debridement, and periapical repair [218, 261, 265, 301]. Hence, the former can ensure both efficiency and safety [167, 301].

When irrigant delivery needles are considered, closed-ended needles such as side-vented, double side-vented, and multi-vented needles must be employed rather than open-ended ones such as flat tip, beveled tip, and notched tip needles [6, 169, 279]. Conventional needle irrigation with an open-ended design carries a greater risk for NaOCl accidents, while a closed-ended design can significantly reduce that risk [181, 192, 193]. However, binding of closed-ended needles should be avoided, as this can still generate pressure high enough to cause extrusion of NaOCl [54, 160].

Irrigant activation or agitation employing manual (static or dynamic), thermal (intracanal or extracanal), active (machine-assisted or automated or mechanical), or combined methods are recommended to increase the efficiency of NaOCl. Additionally, these methods provide a scope to employ NaOCl at a lower concentration that can be considered safe. It must be noted that the reported cases of NaOCl accidents have mostly occurred during NaOCl delivery or the irrigation step, and such incidents have hardly been reported during the NaOCl activation or agitation step. Currently, clinical evidence on the influence or association of NaOCl activation or agitation methods, or their comparison among themselves or with the NaOCl irrigation or delivery techniques in relation to the risk of NaOCl extrusion is less clear, as systematic reviews and clinical (in vivo) and laboratory (in vitro) studies in this regard have reported varying results or outcomes. Hence, more research with standardized or uniform study designs and/or by developing new experimental or in vivo models is recommended to overcome the drawbacks associated with the existing study methodologies [262]. Nevertheless, it must be borne in mind that NaOCl activation or agitation methods carry the risk of NaOCl extrusion due to the need for intracanal delivery of NaOCl, application of energy for activation or agitation, and pressure generation. Moreover, the ability of these techniques to break the vapor lock, ensure flow

of NaOCl along the entire length of the canal, and allow effective apical 3rd penetration or irrigation can paradoxically facilitate the risk of NaOCl extrusion. The extent of risk of NaOCl extrusion would depend on various factors such as the type of root apex (*i.e.*, open or closed apex), root or canal curvature, size and/or extent of apical preparation, mode or source of energy (*i.e.*, manual, thermal, or mechanical including rotary, sonic, ultrasonic, or laser based) applied for NaOCl activation or agitation, power of the applied energy, type, design, size, and motion (*i.e.*, oscillatory/vibratory, rotatory, helical/spiral, pecking, or stationary) of the tip employed for activation or agitation, speed of motion of the tip, depth of intracanal insertion of the tip, direction of action or force generated for activation or agitation (*i.e.*, apical, lateral, or both), amount of pressure exerted or created during activation or agitation, and duration of application of the activation or agitation method [14, 15, 17, 19, 166, 174, 177, 181, 184, 187, 199-202, 204, 209, 210, 213, 215, 222, 225, 230, 234, 235, 237, 240, 243-247, 252-254, 256, 258, 263-265, 269, 297, 300, 302-304]. Overall, NaOCl activation or agitation methods have the potential to cause NaOCl accidents, particularly in the presence of tooth-related predisposing factors such as an open or immature apex or iatrogenic risk factors such as an overprepared apical area and not following the recommended steps for safer irrigation procedures, though the diameter or limit of apical canal preparation showed no significant influence on the volume of extruded NaOCl [251]. Hence, from a patient safety point of view, a NaOCl activation or agitation method must be carefully selected on a case-to-case basis following the thorough evaluation of the tooth and canal preparation to prevent NaOCl accidents.

Ensuring Measures and Steps that Facilitate Safer Irrigation Procedure

When a positive pressure or conventional irrigation technique is employed, a safety measure to prevent NaOCl accidents involves depositing NaOCl solution in the pulp chamber and/or working it into the root canal instead of its direct intracanal delivery during irrigation. This measure could be achieved by a few techniques such as 'Paper point' and 'Reservoir' techniques [157, 305]. These techniques intend to carry NaOCl solution passively and incrementally or progressively into the canal by employing a paper point, file, or gutta-percha (GP) point [157, 294, 305]. However, these techniques can be relatively more time-consuming. Also, their ability for deeper or apical 3rd irrigation can be limited [157]. Moreover, they are mostly based on anecdotal evidence, as scientific studies are lacking. On the other hand, maintaining a reservoir of NaOCl in the pulp chamber and applying an activation or agitation method involving sonic, ultrasonic, or laser energy can be useful to facilitate apical penetration with less risk of extrusion [167].



Figure 8. Placing a rubber stopper and bending the irrigation needle to control the length of needle insertion during intracanal irrigation and prevent sodium hypochlorite accident

When a conventional syringe and needle-based irrigation technique is employed for intracanal delivery of NaOCl solution, factors pertaining to the syringe size, operator applied plunger force, needle design and gauge or diameter, depth of needle insertion, irrigation force applied on the syringe, apical irrigation pressure, and NaOCl flow rate must be controlled [15, 206, 223, 228]. In this regard, irrespective of the needle design employed, it is important to ensure to select the needle gauge by considering type of apex (*i.e.*, open or closed apex), size and/or extent of apical preparation [202, 223], and canal taper [198], measure and place a rubber stopper on the needle [59] or bend the needle (Fig. 8) to limit its insertion beyond apical 3rd of the canal [279, 280][279,280], insert the needle passively 1–3 mm short of working length; do not wedge the needle into the root canal [6, 279, 306], control the fluid flow rate of NaOCl by injecting it slowly and gently [45, 181, 193, 228], do not apply excessive pressure during injection by using the index/forefinger rather than the thumb or palm to press the plunger of the syringe [6, 58, 112, 279, 280, 295], confirm coronal outflow or backflow of NaOCl through the access during irrigation [45] and further facilitate it during irrigation by carrying out simultaneous suction with a saliva ejector or high-volume evacuator [23], oscillate the needle in and out of the canal to deliver NaOCl freely without resistance [280], and stop irrigation in case of needle binding or resistance to NaOCl delivery [280]. Although moving the needle away from the apical area as NaOCl is injected reduces the apical pressure and NaOCl extrusion, particularly in case of immature teeth with open apex [169, 178, 180, 181, 193], it may compromise the effectiveness of apical irrigation. Hence, considering both efficiency and safety from a point of view, it is advisable to gently move the needle up and down while injecting NaOCl to facilitate better apical irrigation with manual-static form of activation and reduced risk of NaOCl extrusion.

When an irrigant activation or agitation method is coupled with a conventional irrigation technique to overcome the limitations of the latter and/or facilitate effective apical 3rd

irrigation or deeper apical 3rd dentinal penetration [265], additional measures must be ensured to prevent NaOCl accidents. With a manual-dynamic method of NaOCl activation or agitation employing a file or GP point, it must be borne in mind that a closely fitting file or GP point can act as a piston or plunger and generate sufficient hydraulic pressure to cause NaOCl extrusion [30, 157, 181, 294]. Hence, the file or GP point must be selected smaller than the prepared canal size and applied in a gentle pumping motion with controlled up-and-down strokes short of the working length. A clinical observational study that employed an open-ended needle for intracanal delivery of NaOCl solution but without pressure and used a GP point in a manual-dynamic motion for NaOCl activation reported a low rate of NaOCl accident or extrusion [14]. It must be noted that this study was conducted by well controlling those factors that are generally attributed to the occurrence of NaOCl accidents or extrusion. This study highlights the importance of adopting measures or steps to control such factors to ensure a safer irrigation procedure and to reduce or minimize the risk of NaOCl accident or extrusion despite employing conventional techniques of irrigation and manual-dynamic method of activation or agitation.

When an active method of NaOCl activation or agitation (*i.e.*, rotary, sonic, ultrasonic, or laser-based) is employed as an important part of the irrigation protocol, it is most preferable to use it in conjunction with an apical negative pressure irrigation technique to prevent NaOCl accidents. It is important to note that irrespective of the irrigant delivery or irrigation technique (*i.e.*, positive pressure/conventional or apical negative pressure-based), the active method of NaOCl activation or agitation must be carried out by adopting certain safety measures to prevent NaOCl accidents. These measures include choosing an activation tip having a design, preferably with a safety end (*i.e.*, for rotary, sonic, or ultrasonic mode) or a side firing tip rather than a front firing tip (*i.e.*, for laser mode), that facilitates the motion of action and generation of pressure in a lateral direction rather than in an apical direction, the tip must be of suitable shape and size or diameter to control the force of action or application and pressure gradient across the coronal to apical section, the chosen tip must be loosely fitting and inserted passively to a depth at least 2-5 mm short of working length or root apex to minimize apical pressure, and controlling the activation device by appropriately setting power, duration, and specifications or parameters of application on case-to-case basis. [173, 176, 177, 185, 187, 188, 199, 203, 213, 214, 218, 220, 237, 243, 246, 248, 249, 253, 255, 265]. Although higher power settings can enhance the effectiveness of an active irrigant activation or agitation method, it can also significantly increase

the generation of apical pressure, with a greater tendency to cause NaOCl extrusion, even if the intracanal depth of insertion of the tip is farther away from the root apex or much shorter than the working length [199]. Hence, it is crucial to ensure that power settings are well controlled while applying an active method of irrigant activation or agitation. Additionally, in case of laser-based activation or agitation following intracanal delivery of NaOCl, compared to the conventional method of laser activation with intracanal insertion of the laser tip, modified methods such as coronal laser assisted irrigation (CLAI), photon-induced photoacoustic streaming (PIPS), and shock wave enhanced emission photoacoustic streaming (SWEEPS) can be considered to facilitate effective irrigation with reduced potential for NaOCl extrusion by restricting the application of the laser tip to the canal orifice instead of inserting it into the canal [199, 210, 213, 219, 235, 238, 244, 250, 252, 253, 256, 300]. However, intracanal deposition of NaOCl followed by application of CLAI, PIPS, or SWEEPS might still carry the risk of NaOCl extrusion, though the pressure gradient decreases from the coronal to the apical end [184, 200, 213, 244]. Hence, employing these modified methods by confining both NaOCl and the laser tip to the pulp chamber and not beyond the canal orifice level seems beneficial from both efficacy and safety points of view. A couple of clinical studies have shown that the modified method of laser activation or agitation by depositing NaOCl in the pulp chamber and access preparation (*i.e.*, as a reservoir) and applying the laser tip within the boundaries of the pulp chamber with appropriate power settings was still effective in ensuring flow of NaOCl along the entire length of the canal up to the apex and without any sign of NaOCl extrusion, even in teeth with open or wide root apex and periapical lesion [177, 205].

In case of a tooth with an immature apex or a widened apex, apart from the aforementioned safety measures, the collagen apical barrier (CAB) technique can be considered to prevent NaOCl accident. The bioresorbable collagen is placed in the access opening, pushed through the root canal, and packed beyond the apical 3rd or root apex to form a barrier or plug periapically before initiating NaOCl irrigant delivery or irrigation and/or its activation or agitation steps, and to minimize NaOCl extrusion. The barrier can be either left behind or removed following the completion of the irrigation procedure [222, 303]. Although this technique sounds beneficial, presently the available clinical evidence is limited. Additionally, any issue related to the periapical seepage of NaOCl through and/or around the porous collagen barrier or the potential for the collagen barrier to absorb and remain soaked with NaOCl and allow it to leach into the periapical tissues until the barrier is

either resorbed or removed, cannot be ruled out. More importantly, any clinical implication of this potential issue is not known, and more research is needed in this regard.

Finally, irrespective of the irrigation technique and/or irrigant activation or agitation method employed, residual NaOCl must be flushed out from the canal by gentle lavage with normal saline or other irrigants before beginning the next sequence of irrigation or as a last step [45, 66, 279].

The flow chart regarding clinical decision-making towards prevention of NaOCl accident is depicted (Fig. 9). The measures for prevention of NaOCl accident are summarised in Table 3.

Conclusions

NaOCl accident is an iatrogenic event with potentially serious consequences and medico-legal implications. When the reported cases are considered, although the overall percentage of complete recovery is good, the course and outcomes of NaOCl accidents are unpredictable and vary from case to case. Additionally, the risk of incomplete recovery with long-term effects or partial recovery with residual or permanent effects, with greater medico-legal liability, also exists. Hence, in the event of an unfortunate NaOCl accident, the clinician must act briskly to render initial phase management involving quick detection and emergency treatment to aspirate and/or dilute extruded NaOCl to minimize tissue damage and/or complications. It is also equally important to monitor and appropriately refer the patient, well document the incident, and strictly follow up with the patient because clinical symptomatology mostly worsens or progresses initially with a varying or unpredictable course. Hence, progression and recovery phase management are crucial for patient recovery. Extended recovery phase management must be considered in case of any short- and/or long-term effects. Since prevention is always the best strategy, clinicians must adopt patient-, tooth-, irrigant (NaOCl)-, and irrigation-related measures to prevent NaOCl accidents. Finally, considering the various associated limitations and challenges, it is essential to emphasize the need for measures such as developing a local incident reporting system, strongly reinforcing the use of templates and online databases for a standardized form of documenting and reporting an incident of NaOCl accident, synthesizing a neutralizing agent for NaOCl, and conducting more clinical research on irrigation procedures and NaOCl extrusion to obtain a higher level of evidence and enhance clinical protocols for the management and prevention of NaOCl accidents.

Table 3. Summary of measures to prevent sodium hypochlorite accidents.

Category	Measures
Patient-related	- Obtaining informed consent from the patient. - Seeking information from the patient - History of orthodontic treatment. - Medical history. - History of medication, particularly bisphosphonate therapy. - Ensuring detailed pre-endodontic assessment of the patient to identify any predisposing factor for NaOCl accident. - Seating the patient in a semi-reclined position. Avoiding upright or supine position.
Tooth-related	- Carrying out thorough pre-endodontic clinical and radiographic evaluation of the tooth to detect any predisposing factors for NaOCl accident such as open apex, apical resorption, and apical bony fenestration. - Preferring vital pulp therapy such as pulpotomy over pulpectomy when such a choice is available. - Having optimal knowledge, clinical skill, and armamentarium before initiating endodontic treatment. - Preventing procedural errors such as perforation, faulty working length determination, overinstrumentation, under- or over-enlargement of apical 3rd, and use of compressed air for canal drying during endodontic treatment. - Immediately detecting and rectifying or correcting any procedural error before carrying out NaOCl irrigation procedure.
Irrigant (NaOCl)-related	- Preferably using other irrigants or disinfection modalities as an alternative to NaOCl irrigation, especially in the presence of any predisposing factor for NaOCl accident. - When NaOCl irrigation is indispensable, use NaOCl - At a lower concentration ($\leq 0.5\%$) with or without an irrigant activation or agitation method. - With neutral pH. - In smaller volume. - Along with alternative or additional irrigants or disinfection modalities. - In gel form instead of solution form. - With an apical negative pressure-based irrigation method such as EndoVac. - Preferring apical negative pressure-based irrigation technique over positive pressure-based or conventional syringe and needle irrigation technique. - Carefully choosing NaOCl irrigant activation or agitation method, particularly in the presence of any risk factor for NaOCl accident, and using it - With a proper selection of type, design, size, and motion of the tip for activation or agitation. - With appropriate device settings to control the power, speed, duration, and other specifications or parameters for the application of tip. - With tip insertion confined to the pulp chamber or canal orifice, or insertion depth at least 2-5 mm short of the working length or root apex. - With tip application as gently and passively as possible. - With tip application and pressure generation directed laterally rather than apically. - When a laser-based irrigant activation or agitation method is employed, it is preferable to use modified methods such as coronal laser assisted irrigation (CLAI), photon-induced photoacoustic streaming (PIPS), and shock wave enhanced emission photoacoustic streaming (SWEEPS) by confining both NaOCl and the laser tip to the pulp chamber and not beyond the canal orifice. - When a positive pressure-based or conventional syringe and needle irrigation technique is employed, preferably confining the deposition of NaOCl solution to the pulp chamber and/or access preparation and using a technique or method to carry or allow the flow of NaOCl passively into the canal towards the apical 3rd. - When a positive pressure-based or conventional syringe and needle irrigation technique is employed for intracanal delivery of NaOCl solution, it must be carried out - Ensuring optimal canal preparation. - Using a smaller-sized syringe. - Selecting an irrigation needle of proper diameter. Avoiding needles with very wide or narrow lumen. - Using a closed-ended irrigation needle instead of an open-ended needle. - Bending the needle and/or placing a rubber stopper to insert the needle short of the working length. - Avoiding wedging or binding the irrigation needle in the root canal during irrigation. - Injecting NaOCl slowly or gently using the forefinger or palm to press the plunger of the syringe. Avoiding using the thumb to press the plunger. - Injecting NaOCl at a lower flow rate. - Passively moving the needle in and out of the canal during irrigation. - Avoiding the use of higher apical irrigation pressure or forceful injection of NaOCl into the deeper or apical 3rd portion of the root canal. - Ensuring backflow of NaOCl through the access opening with simultaneous application of a saliva ejector or high-volume evacuator during irrigation.
Irrigation-related	- When irrigation with intracanal delivery of NaOCl solution and its activation or agitation with a manual-dynamic method is preferred, then a smaller size file or gutta-percha point must be used to minimize plunger-like action. - Avoid the use of endodontic instruments in piston-like motion during cleaning and shaping following NaOCl irrigation. - When NaOCl gel is employed, it is preferable to apply the gel by coating onto the canal walls instead of injecting it. - Applying the collagen apical barrier (CAB) technique before initiating the NaOCl irrigation procedure in a tooth with an immature apex or a wide apex. - Removing or flushing out any traces of or residual NaOCl from the root canal before the next sequence or step of irrigation or the final irrigation.

NaOCl: sodium hypochlorite

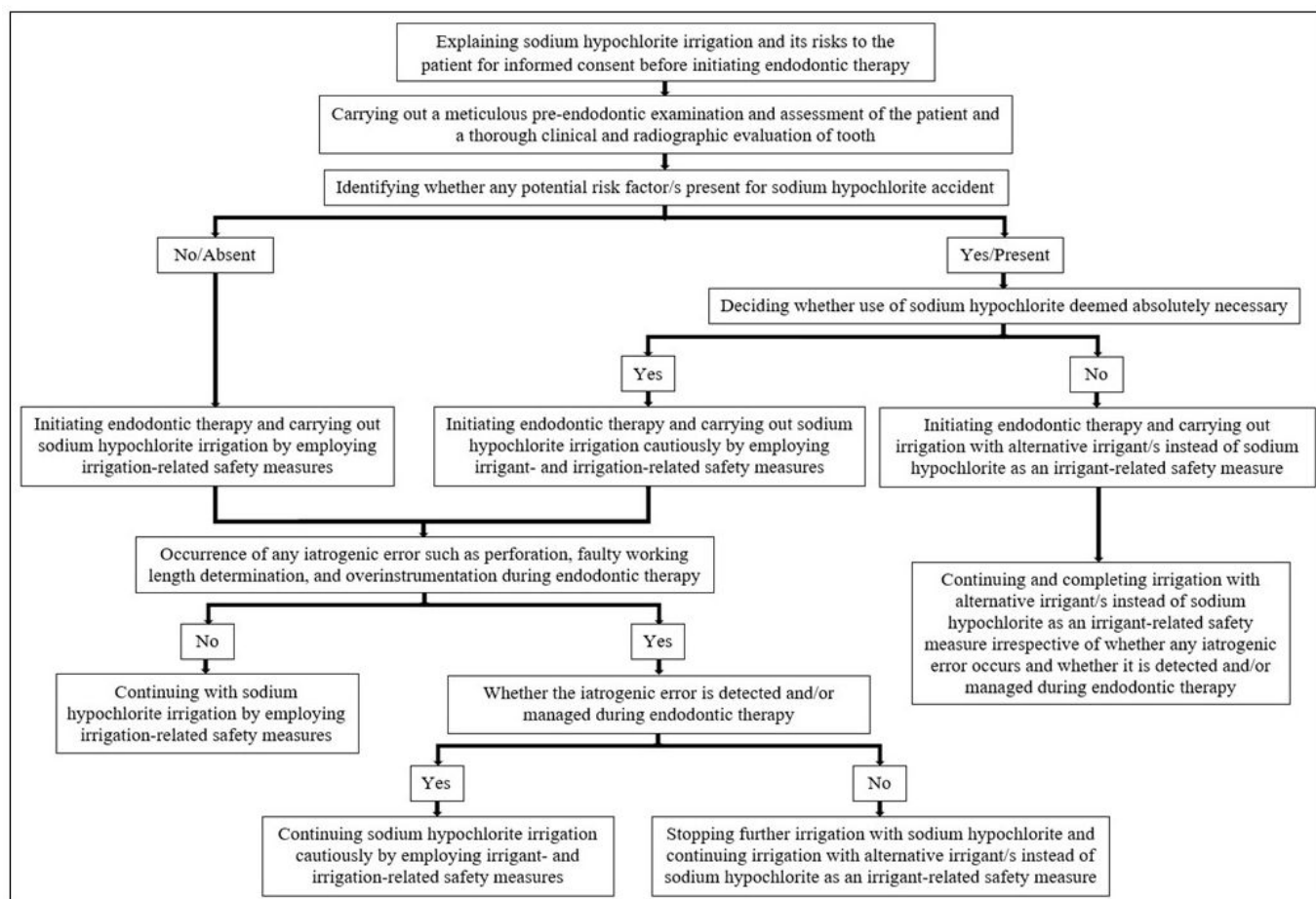


Figure 9. The flow chart depicts the clinical decision-making towards prevention of sodium hypochlorite accident

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