



# Safety of chloral hydrate sedation in dental practice for children: an overview

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Chloral hydrate is the oldest and most common sedative drug used in moderate sedation for pediatric dental patients. Hence, the purpose of this article is to review the safety and possible adverse events of this drug when used for pediatric dental treatment. A bibliographic search in PubMed, MEDLINE, Cochrane Library and KMBase, KISS, DBpia, KoreaMed, and RISS databases was performed. Using the keywords “dental sedation,” “chloral hydrate,” and “children or adolescent,” 512 scientific articles were found. Subsequently, 183 studies were individually assessed for their suitability for inclusion in this literature review. Altogether, 24 studies were selected. They included 12 cases of death before, during, or after chloral hydrate sedation for dental treatment, majorly due to dosing error and use of multiple sedatives. Additionally, intraoperative adverse events were mostly respiratory problems such as hypoxia and apnea, but most events were temporary. After treatment, prolonged sedation, including excessive sleep and less activity were the most common postoperative adverse events, and even death cases were reported. Despite the wide acceptance of chloral hydrate as a sedative-hypnotic agent, the risk of adverse events and adequate dose should be of great concern when using it for pediatric dental sedation.

**Keywords:** Adverse Drug Reactions; Child; Chloral Hydrate; Conscious Sedation; Pediatric Dentistry; Safety.

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## INTRODUCTION

Dental fear and anxiety in children lead to problems with behavior management for treatment [1]. A child who had a negative experience during dental treatment develops even greater anxiety toward future dental visits, which makes future regular checkups and further treatment difficult [2]. Sedation is one of the behavior management methods that can be applied to pediatric patients who show the type of behavioral pattern that is likely to yield these results [3].

The drug is a critical factor in sedation. Drugs used for sedation must be able to induce a sedative state of

desired depth after administration, with rapid onset of action and recovery. Additionally, sedative agents or medication must be reversible and above all, safe for the patient. Individuals who perform sedation must be able to select the right drug for the intended treatment procedure, know the drug interactions of sedatives, and have life-saving skills that can save the patient from an adverse event [4].

According to a survey conducted among members of the American Academy of Pediatric Dentistry (AAPD), oral administration was the most commonly used method of sedation besides nitrous oxide (N<sub>2</sub>O) inhalation, and the combination of chloral hydrate (CH), hydroxyzine, and N<sub>2</sub>O inhalation was commonly used by American

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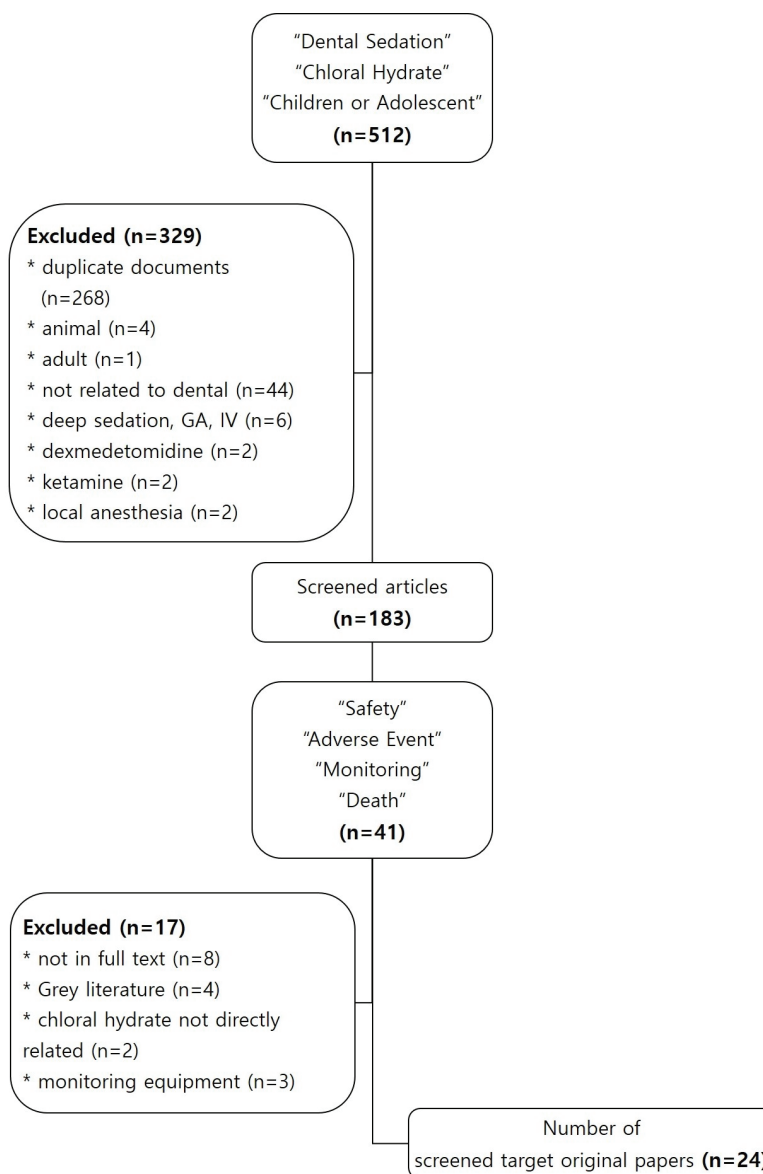
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**Table 1.** Paper selection criteria

Inclusion	Exclusion
Children, adolescent group	Adult age group
Minimal or moderate sedation	Deep sedation, general anesthesia
Dental procedure, sedation	Medical procedure, sedation
	Failure to secure the full text
	Gray literature (publisher's letter, thesis)



**Fig. 1.** Flow diagram of the literature selection progress

pediatric dentists [5]. A survey of sedation practices in pediatric patients among members of the Korean Academy of Pediatric Dentistry (KAPD) and Korean Dental Society of Anesthesiology also showed that the most preferred route of sedative administration for

children was oral, while the most preferred sedative combination was CH, hydroxyzine, and N<sub>2</sub>O inhalation sedation [6,7].

While CH oral sedation is frequently used and highly preferred in pediatric dentistry, there are still reports of

Table 2. Selected studies

First author	Year of publication	Type of study	Topic
Grissinger M [8]	2019	Review	Death
Abdulhamid I [9]	2016	Open-label study	Safety related to systemic condition
Huang A [10]	2015	Comparative study	Safety
Nordt SP [11]	2014	Case report	Death, safety
McCormack L [12]	2014	Nonrandomized cohort study	Safety
Kang J [13]	2012	Retrospective study	Safety related to systemic condition
Chicka MC [14]	2012	Review	Death, safety
Costa LR [15]	2012	Comparative study	Safety
Kupiec TC [16]	2011	Case report	Death
de Rezende GP [17]	2007	Case report	Safety
Martinez D [18]	2006	Prospective, pilot study	Safety
Park MK [19]	2006	Prospective randomized study	Safety
Myers GR [20]	2004	Randomized double-blind crossover study	Safety
Lee JH [21]	2002	Cross sectional study	Safety
Leelataweedwud P [22]	2001	Retrospective study	Safety
Dallman JA [23]	2001	Clinical trial	Safety
Jung JH [24]	2001	Cross sectional study	Safety
Avalos-Arenas V [25]	1998	Clinical trial	Safety
Engelhart DA [26]	1998	Case report	Death
McCann W [27]	1996	Clinical trial	Safety
Needleman HL [28]	1995	Retrospective study	Safety
Sams DR [29]	1993	Case controlled study	Safety
Wilson S [30]	1990	Clinical trial	Safety
Mueller WA [31]	1985	Data collection	Safety

significant adverse events during or after dental treatment under sedation, including death.

This study aims to evaluate the safety and adverse events of CH sedation for dental treatment in pediatric patients by reviewing previous studies and published literatures.

## METHODS

We conducted a literature database search of PubMed, Embase, and Cochrane Library, and also domestic literature databases such as the Korean Medical Database (KMbase), KoreaMed, and Korean Studies Information Service System (KISS), which are CORE search databases, and DataBase Periodical Information Academic (DBpia) and Research Information Sharing Service (RISS), which are academic search engines/web portals. The search terms used were “dental sedation,” “chloral hydrate,” and “children or adolescent”. The period of

literature search was from the release date of each database or journal publication to January 2020. There was no restriction on the year of publication.

The primary search included 512 papers. Of these, 183 papers remained after checking for duplication and considering the inclusion and exclusion criteria (Table 1). In the secondary search, we manually checked the title and abstract to screen for papers related to safety, adverse event, monitoring, and death and then selected 41 papers. Of these, we excluded papers without a direct relation to CH, papers whose original text was not provided, gray literature (editor’s letter, thesis paper), and papers on patient monitoring equipment (Fig. 1).

## RESULTS

Altogether, 24 papers that met the criteria were included in the review. The papers are listed by year in Table 2, starting from the most recent paper based on

Table 3. Death case report

First author/ publication year	Case number	Age (year)	Sedative drugs (mg/kg, %)	Administered by: / at:	Detailed description	Cause
Grissinger M 2019 [8]	1, 2			Unauthorized person	Failure to recognize overdose	Dosing error
	3	13	CH (6000 mg)	Dentist	Weight-based prescription	Overdose (Respiratory arrest)
	4, 5	Child		Parents Home	Pharmacy dispensed 500 mg/5 mL instead of 250 mg/5 mL	Dosing error
	6	Child		Parents Home	Pharmacy prescribed tenfold drug	Dosing error
	7	4M			Strapped onto papoose board without proper head position	Improper patient control during treatment
	8				Repeated "5 mL PRN" prescription	Dosing error
Nordt SP 2014 [11]	9	4F	CH (70)	Home prior to procedure	Discharge after 1 h, remained somnolent but arousable, ongoing somnolence for 6 h Dead after PICU	Resedation after discharge (Respiratory arrest)
Chicka MC 2012 [14]	10	2M	CH (unknown)	Unknown Dental office	Medical history of Russell-Silver syndrome Dentist noticed respiratory rate slowed CPR, intubation, pronounced dead upon arrival at emergency department	(Respiratory arrest)
Kupiec TC 2011 [16]	11	6M	Meth (2), Hy (1.64), CH (15), N <sub>2</sub> O-O <sub>2</sub>	Dentist Dental office	Medical history of asthma Patient appeared responsive but groggy after procedure, taken home and fell asleep Dead after few hours of procedure	Cocktail (Toxicity of methadone)
Engelhart DA 1998 [28]	12	2M	CH (95), N <sub>2</sub> O-O <sub>2</sub>	Unknown Not in dental center	Full arrest during surgical procedure Transported to emergency room after 2 h, dead after 2.3 h of administration	Combined effect of CH, lidocaine, N <sub>2</sub> O

CH, chloral hydrate; Meth, methadone; Hy, hydroxyzine; N<sub>2</sub>O-O<sub>2</sub>, nitrous-oxygen inhalation; PRN, pro re nata, as needed; PICU, pediatric intensive care unit

the year of publication.

### 1. Death case report (Table 3)

Altogether, 12 deaths before, during or after dental treatment under CH sedation in pediatric patients, caused by drug administration or dosing error, overdose, or combined use of multiple sedative medications have been reported. These include patients with underlying diseases that entail high risk of respiratory obstruction, drug administration by unauthorized person, and inadequate airway management after administration.

According to Cote et al. [32], drug overdose is defined as using > 1.25 times the maximum recommended dose. In the case of CH, the maximum recommended dose is 2 g, 100 mg/kg in one dose, and death from overdose of single use of CH is rare relative to its frequent usage.

While death of a patient with history of asthma has been reported [16], another patient with mild asthma was

treated safely using CH with single dose of 65 mg/kg [9]; thus, asthma itself cannot be a major factor of patient death.

There has been a report of death from improper head positioning on the papoose board [8]. Immobilization devices such as the papoose board must be applied without causing airway obstruction or chest compression during sedation. In addition, the patient's head position and breathing movement must be checked frequently to secure the airway during treatment [4].

### 2. Adverse events before and during sedation (Table 4)

In the dental treatment under CH sedation of pediatric patients, the most common adverse event that occurred during treatment after sedative administration was hypoxia (oxygen desaturation). Gastrointestinal problems, including vomiting, nausea, abdominal pain, and paradoxical

Table 4. Summary of preoperative and intraoperative adverse events

First author/ Publication year	Age (month)	Sample size	Sedative drugs (mg/kg, %)	Administered by: / at:	Monitoring Equipment Information Interval (minute)	Results
Grissinger M 2019 [8]	48	1 (1M)				Strapped onto the papoose board without proper head position Death cause: improper position to protect his airway
Nordt SP 2014 [11]	36	1 (1M)	CH (400)	Parents Home		Somnolent after 10 min, unresponsiveness Vomiting during ambulance Esmolol infusion Discharge after 30 h without sequelae
McCormack L 2014 [12]	55	40 (21M, 19F)	CH (30), Mep (2), Hy (2), N <sub>2</sub> O-O <sub>2</sub> (30-50) Mdz (1), Mep (2), Hy (2), N <sub>2</sub> O-O <sub>2</sub> (30-50)	Dentist Dental office	PO, PC, Visual observation SaO <sub>2</sub>	Mdz included regimen more body movement during treatment
Chicka MC 2012 [14]	96	1 (1M)	CH (75), Hy (4.4)			Medical history of attention deficit disorder, on medication 50 min after administration, stopped crying, turned blue, and no pulse when placed in papoose board Remained in coma for 3 days Hypoxic brain damage
	26.4	1 (1M)	Hydrocodone barbiturate, CH (25), Hy (5.8), Mep (4.6)	Mother Home		2% lidocaine (13.2 mg/kg) Patient turned blue, no breathing during treatment Naloxone administration Respiratory arrest, seizure CPR by parent Discharged satisfactory condition
Costa LR 2012 [15]	43.2	42 (22M, 20F)	CH (70) CH (100) Mdz (1.0) Mdz (1.5)	Dentist Dental office	PO, BPC, Visual observation HR, SaO <sub>2</sub> , BP, RR 15	1 case (10%) in CH 70 mg/kg group had oxygen desaturation (SaO <sub>2</sub> 90%), irritation
de Rezende GP 2007 [17]	35	1 (1M)	CH (100)	Dentist Dental office	HR, SaO <sub>2</sub> , BP, RR 15	Became active after 15 min Vomited twice during treatment Abdominal pain, thirst Observed aggressive behavior and fell asleep
Park MK 2006 [19]	44.5 34.3	15 (6M, 9F) 16 (11M, 5F)	CH (60), Hy (1), N <sub>2</sub> O-O <sub>2</sub> (50) CH (60), Hy (1), Mdz (0.1), N <sub>2</sub> O-O <sub>2</sub> (50)	Dentist Dental office	PO SaO <sub>2</sub> , PR 2	No hypoxia, vomit, nausea Mean SaO <sub>2</sub> : 99.1% No hypoxia, vomit, nausea Mean SaO <sub>2</sub> : 98.6% SaO <sub>2</sub> , 95% once
Myers GR 2004 [20]	48.9	40 (22M, 18F)	CH (50), N <sub>2</sub> O-O <sub>2</sub> (50) CH (50), Mdz (0.2), N <sub>2</sub> O-O <sub>2</sub> (50)		PO, BPC, ECG, Capno, PC HR, SaO <sub>2</sub> , BP, RR, ETCO <sub>2</sub> 5	2 oxygen desaturation (SaO <sub>2</sub> 85%, 88%) cases, resolved with head positioning and mouth suctioning No desaturation
Lee JH 2002 [21]	42.2	40 (22M, 18F)	CH (60), Hy (25 mg)	Dentist Dental office	PO, PC PR, SaO <sub>2</sub> , RR 5	Mean SaO <sub>2</sub> : 98.1% No true apnea True desaturation (SaO <sub>2</sub> under 95%) 0-3 times per patient

Leelatawe edwud P 2001 [22]	47	111 (57M, 54F)	CH (50), Mep (1.5), Hy (25 mg), O <sub>2</sub> (100)	Dentist Dental office	PO, PC, Visual observation, Capno PR, SaO <sub>2</sub> , BP, RR, ETCO <sub>2</sub>	2 true apnea cases (no visual sign of breathing, no breath sound, Capno 0 for 25 s) 3 prolonged sedation (need more than 30 min after treatment for discharge) cases 1 vomiting case
Dallman JA 2001 [23]	41.8	31 (23M, 8F)	Mdz (0.2), N <sub>2</sub> O-O <sub>2</sub> (25-50) CH (62.5), PZ (12.5 mg), N <sub>2</sub> O-O <sub>2</sub> (25-50)	Dentist Dental office	HR, SaO <sub>2</sub> , BP, RR	No vomit case 1 vomiting case
Jung JH 2001 [24]	30	71 (40M, 31F)	CH (60), Hy (25 mg)	Dentist Dental office	PO SaO <sub>2</sub>	Temporary hypoxia (SaO <sub>2</sub> under 95%) 42.2%
Avalos- Arenas V 1998 [25]	28.58	40	CH (40), Hy (2), N <sub>2</sub> O-O <sub>2</sub> (50) CH (40), Hy (2)	Dentist Dental office	PO HR, SaO <sub>2</sub> , BP, RR	At least 10% cases of hypoxia (SaO <sub>2</sub> under 90%)
McCann W 1996 [27]	45	40 (26M, 14F)	CH (40), Hy (2), N <sub>2</sub> O-O <sub>2</sub> (50) CH (40), Hy (2)	Dentist Dental office	PO HR, SaO <sub>2</sub> , BP, expired CO <sub>2</sub> level	No desaturation (SaO <sub>2</sub> under 95%) episodes
Needleman HL 1995 [28]	31.2	382 (216M, 166F)	CH (55), Hy (1), N <sub>2</sub> O-O <sub>2</sub> (40-60)	Dentist Dental office	PO, PC HR, SaO <sub>2</sub> , RR	Intraoperative vomiting 8.1% 21% of patients desaturation (SaO <sub>2</sub> under 95%)
Sams DR 1993 [31]	31 35.8	24	CH (50), PZ (1), N <sub>2</sub> O-O <sub>2</sub> ( $<$ 50) Mep (1), N <sub>2</sub> O-O <sub>2</sub> ( $<$ 50)	Dentist Dental office	HR, SaO <sub>2</sub> , BP, RR, Temp	2 desaturation (SaO <sub>2</sub> 90-95%)
Wilson S 1990 [30]	28.8 30.1	12 10	CH (40), Hy (2) CH (25, 50, 70)	Dentist Dental office	PO, BPC, CO <sub>2</sub> monitor, brain monitor HR, SaO <sub>2</sub> , BP, RR, expired CO <sub>2</sub> level, EMG	13% true desaturation (SaO <sub>2</sub> $<$ 95%) 10% true desaturation (SaO <sub>2</sub> under 95%) No significant difference between dosage of CH
Mueller WA 1985 [31]		20	CH (100), N <sub>2</sub> O-O <sub>2</sub> (50)	Dentist Dental office	PO HR, BP, RR	35% decreased SaO <sub>2</sub> (SaO <sub>2</sub> under 95%)

CH, chloral hydrate; Hy, hydroxyzine; Mdz, midazolam; Mep, meperidine; PZ, promethazine; PO, pulse oximetry; PC, precordial stethoscope; SaO<sub>2</sub>, oxygen saturation; BPC, blood pressure cuff/sphygmomanometer; BP, blood pressure; HR, heart rate; RR, respiratory rate; PR, pulse rate; ECG, electrocardiography; Capno, capnography; ETCO<sub>2</sub>, end tidal carbon dioxide; EMG, electromyogram

reaction (an hyperactivity reaction) were also observed during treatment. As with any sedative agent, CH sedation can result in residual sedation, disorientation, paradoxical excitement, delirium, ataxia, headache, nightmares, hallucinations, and paranoid behavior [33]. CH sedation for dental treatment in pediatric patients was often accompanied by respiratory problems like desaturation and apnea during treatment.

According to the American Dental Association (ADA) guidelines, sedation can be largely divided into four

stages: minimal sedation, moderate sedation, deep sedation, and general anesthesia [34]. Although deeper levels of sedation (moderate to deep sedation) can be achieved by adjusting the dose, given that pharmacological reaction cannot be reversed and individual patient response is highly diversified, only minimal to moderate sedation can be considered in the rational use of oral CH sedation [35]. For CH administration aimed at minimal and moderate sedation, the oxygen saturation, heart rate, blood pressure, and respiratory rate must be monitored during treatment,

**Table 5.** Summary of postoperative adverse events including death case

First author/ publication year	Age (month)	Sample size	Sedative drugs (mg/kg, %)	Monitoring period	Results
Huang A 2015 [10]	84	7	CH, Mep, Hy	24 hours after discharge	Excessive somnolence
Nordt SP 2014 [11]	48	1 (1F)	CH (70)		Discharge after 1 hour, remained somnolent but arousable Ongoing somnolence for 6 hours Post-discharge death by respiratory arrest
McCormack L 2014 [12]	55	40 (21M, 19F)	CH (30), Mep (2), Hy (2), N <sub>2</sub> O-O <sub>2</sub> (30-50) Mdz (1), Mep (2), Hy (2), N <sub>2</sub> O-O <sub>2</sub> (30-50)	Post-operation before discharge, 8, 24 hours after discharge	CH combination regimen exhibited significantly more sleeping after arriving home, less talking, and greater need for postoperative pain medications up to 8 hour after discharge
Costa LR 2012 [15]	43.2	42 (22M, 20F)	CH (70) CH (100) Mdz (1.0) Mdz (1.5)	24 hours after discharge	Minor post-discharge adverse events(falling asleep, difficult to awake) were common, significantly more associated with CH than Mdz
Kupiec TC 2011 [16]	72	1 (1M)	Meth (2), Hy (1.64), CH (15), N <sub>2</sub> O-O <sub>2</sub>		Medical history of asthma Patient appeared responsive but groggy after procedure, taken home and fell asleep Dead after few hours of procedure Post-discharge death by drug cocktail
Martinez D 2006 [18]	24-60	30 (14M, 16F)	CH (20-30), Mep (1-2), Hy (1-2), N <sub>2</sub> O-O <sub>2</sub> (50) Mdz (0.5-0.75), N <sub>2</sub> O-O <sub>2</sub> (50)	Post-operation before discharge, 24 hours after discharge	Children having combination regimen containing CH were more likely to sleep on the way home and at home than those received Mdz alone
Dallman JA 2001 [23]	41.8	31 (23M, 8F)	Mdz (0.2), N <sub>2</sub> O-O <sub>2</sub> (25-50) CH (62.5), PZ (12.5 mg), N <sub>2</sub> O-O <sub>2</sub> (25-50)	20 minutes after operation	Mdz group met discharge criteria more quickly than CH group 1 vomiting case
Engelhart DA 1998 [28]	24	1 (1M)	CH (95), N <sub>2</sub> O-O <sub>2</sub>		Following surgical procedure, patient transported to emergency room after 2 h of administration, dead after 2.3 h of administration Post-discharge death by overdose of CH, combined effect of CH, lidocaine, N <sub>2</sub> O
Sams DR 1990 [29]	31 35.8	24	CH (50), PZ (1), N <sub>2</sub> O-O <sub>2</sub> (< 50) Mep (1), N <sub>2</sub> O-O <sub>2</sub> (< 50)	30 minutes, 24 hours after discharge	2 postoperative pain 6 increased anxiety/irritability 2 fever 2 postoperative pain 1 increased anxiety/irritability

CH, chloral hydrate; Mep, meperidine; Hy, hydroxyzine; Mdz, midazolam; Meth, methadone; PZ, promethazine

while electrocardiogram (ECG) and capnography are recommended [4]. The name and dose of all administered drugs, route, site, and time of administration, including local anesthetic, must be recorded. Additionally, the heart rate, respiratory rate, blood pressure, oxygen saturation, and level of consciousness must be recorded at least every 10 min [4,34].

The literature on adverse events before and during CH

sedation of pediatric dental patients included data on patient monitoring, except for three papers. In papers on patient monitoring, oxygen saturation was monitored in all patients, given that children are likely to develop respiratory problems. However, six studies used inadequate monitoring interval, did not inscribe patients' heart rate and blood pressure in the monitoring data.

Considering that CH stimulates the gastric mucosa,

reports of abdominal pain or vomiting during treatment were common. If pretreatment fasting was not followed, pulmonary aspiration due to reflux of food cannot be avoided.

### 3. Adverse events after sedation (Table 5)

Most adverse events occurring after CH sedation treatment in pediatric dental patients were decreased activity and excessive sleep. Cases of death after treatment termination and discharge were also reported.

The onset of CH action is usually 15–30 min after oral administration, with maximal effect occurring after more than an hour. The duration of drug action ranges from 2 to 8 h and typically lasts at least 5 h, but individual patient response varies, and the sedative effect can last up to 24 h [10,11]. The mean elimination half-life of CH is  $9.7 \pm 1.7$  h [36]. However, it has been found that the half-life is longer in neonates and infants and that the effect of the drug outlasts the plasma half-life (related to influence of the central nerve system) [32]. Death at home after sedation treatment and discharge [11] may also be related to this.

## DISCUSSION

The goals of sedation in pediatric patients are to (1) protect the safety of patients; (2) minimize physical discomfort and pain; (3) control anxiety, minimize psychological trauma, and maximize the possibility of amnesia; (4) modify behavior or movement to complete procedures safely; and (5) discharge patients in a safe state under medical/dental supervision, as determined by accepted standards [4].

The drugs used for sedation in children include N<sub>2</sub>O/oxygen, benzodiazepines such as midazolam, diazepam, and nonbarbiturate sedative-hypnotics like CH. Histamine blockers like hydroxyzine, promethazine (PZ), narcotic analgesics like meperidine (Mep) are also used. In addition, sedative like ketamine and propofol can be included as a drug for sedation in children. Each drug

is used singly or in combination, and the routes of administration are oral, nasal, intramuscular, submucosal, and intravenous. Depending on the administered drug, patient characteristics, and pharmacological properties vary by route of administration [37].

CH is one of the oldest sedative-hypnotic used for sedation since it was first synthesized by Justus von Liebig in 1832 by ethanol chlorination and was introduced to medicine by Liebreich in 1869. It was first used in children in 1894 [38] and has been widely used as an oral sedative in pediatric dentistry since the mid-1950s. In Korea, it is the only oral sedative approved for use in children by the Ministry of Food and Drug Safety. It has been sold in a 95 ml bottle at 100 mg/ml concentration by one pharmaceutical company, but since June 2018, only 5 ml and 10 ml bottles at 100 mg/ml are being sold. In the USA, the manufacturing of CH solution was discontinued in 2012 under the US Food and Drug Administration (FDA) guidelines; thus, usage is limited [35]. CH is an alcohol derivative, which is rapidly absorbed through the gastrointestinal tract into the cardiovascular system after oral administration, it undergoes first-pass metabolism in the liver and kidneys, and converted to its active form, trichloroethanol (TCE). It is conjugated in the liver and then excreted in urine [35].

CH usage in pediatric dentistry for sedation has a recommended oral dose based on body weight of 25–100 mg/kg, the recommended hypnotic dose is 50 mg/kg and single maximum dose is 1 g [33]. Although there are reports of death at a dose of approximately 4 g, the toxic dose for oral administration is 10 g [39], and the maximum recommended dose is 100 mg/kg, up to 2 g [32]. However, even at the therapeutic dose, it can weaken the muscle tone of the tongue, causing tongue retraction toward the posterior oropharyngeal wall and airway problem. Therefore, proper patient monitoring is required for use in pediatric patients [35].

In pediatric dentistry, careful consideration should be taken in multiple sedative administrations. Since CH has the disadvantage of stimulating the gastrointestinal



**Table 6.** Recommended discharge criteria

1. Cardiovascular function and airway patency are satisfactory and stable
2. The patient is easily arousable, and protective airway reflexes are intact
3. The patient can talk (if age appropriate)
4. The patient can sit up unaided (if age appropriate)
5. For a very young child or a child with disability who is incapable of the usually expected responses, the premedication level of responsiveness or a level as close as possible to the normal level for that child should be achieved.
6. The state of hydration is adequate

mucosa and inducing adverse effects such as nausea and vomiting, it is often used in combination with hydroxyzine, which has anti-vomiting and sedative effects [35]. According to a survey of KAPD members by Yang et al. [6], a higher proportion of participants preferred a combination of two or more drugs and routes of administration including N<sub>2</sub>O inhalation to single-drug treatment, and 67.6% of participants used a combination of sedatives, CH, hydroxyzine, and N<sub>2</sub>O. However, administering two or more sedatives can increase the risk of adverse events [4]. Cote et al. [32] demonstrated a significant correlation between the use of a combination of three or more drugs and adverse events. Unlike single-drug administration, combined use with inhalation sedation or narcotics can prolong the drug action and increase the depth of sedation; thus, it is recommended to reduce the dose of CH [3].

Generally, in sedation other than general anesthesia, the American Society of Anesthesiologists (ASA) physical status classification (levels 1 and 2) correspond to the indications. In the case of ASA levels 3 and 4 and tonsillar hypertrophy, special attention is required as there is a high risk of respiratory obstruction [4]. Furthermore, as the case of preoperative oral administration at home and post-discharge death suggest [11], drugs for sedation should not be administered without direct supervision of a skilled medical practitioner [4].

In the case of deep sedation, ECG and capnography must be monitored including oxygen saturation, heart rate, blood pressure, and respiratory rate data. Moreover, the sedation depth may be greater than the intended depth; therefore, during CH sedation, the practitioner must be capable of airway management, suction, continuous

positive pressure ventilation, and bag-valve-mask ventilation at the level of deep sedation [4].

According to the preoperative fasting guideline proposed by the ASA, a minimum fasting period of 2 h is recommended for clear liquids like water or fruit juice, 4 h for breast milk, 6 h for infant formula, milk, light meal (e.g., toast and clear liquid). For fried or fatty foods, the fasting period must be longer than that for a light meal, as they take longer to digest [4,34].

In 2019, the AAPD proposed the discharge criteria in a guideline (Table 6). Patients who received moderate sedation must be postoperatively monitored in an environment equipped with a suction device and positive pressure ventilation (bag-valve-mask) that can supply  $\geq 90\%$  oxygen that is suitable for the age and body size of the pediatric patient. The patient's vital signs should be monitored every 5 min, and once the child begins to awaken, the recording intervals may be increased to 10 to 15 minutes. If the patient is not fully awake, oxygen saturation and heart rate should be continuously monitored until the discharge criteria is satisfied [4].

Cote et al. [32] showed that adverse events following procedural sedation in pediatric patients are strongly correlated with nonhospital-based facilities and dental practitioners. In pediatric dentistry, N<sub>2</sub>O which is commonly used for anxiolysis is known to have little effect on respiration and level of consciousness if used alone [32], but when used in combination with other sedatives, the depth of sedation may be shifted to excessive levels and special attention must be taken.

Moreover, dental treatment is performed under conditions vulnerable to airway obstruction, such as abnormal head, tongue positions and presence of foreign

bodies, including rubber dam, exogenous water, saliva, and blood. Since pediatric patients have poor airway management ability and respiratory problems are likely to occur, all responsible practitioners and personnel must be capable of pediatric advanced life support to cope with emergencies.

## CONCLUSIONS

CH has been used safely in pediatric patients for over 100 years. In countries such as USA, midazolam syrup is widely used, and it can be an alternative oral sedatives to CH. However, in Korea, CH syrup is the only oral sedative that can be used in pediatric patients.

Unlike sedation in adults, in pediatric patients, the younger the age and the worse the physical condition of the child, the faster and longer the drug acts and the deeper the sedation level can be, requiring close attention. Systemic condition of the patient must be assessed before sedation, and close monitoring is required, starting from drug administration. Keeping in mind that drug reaction is amplified when used in combination with other sedatives, dosage should be in great concern, as N<sub>2</sub>O/oxygen inhalation sedatives and local anesthetics are often used in combination in pediatric dentistry.

It should be remembered that the goal in oral CH sedation is minimal to moderate sedation, and patients' vital signs must be closely monitored during treatment. The practitioner should remember that sedation depth might be increased after drug administration, and should be capable of advanced life support to respond to respiratory problems. Following treatment termination, the patient should be closely monitored until discharge and full explanation of possible adverse events after discharge should be given to caregiver.

While it is a drug that has been used widely for a long time, there have been multiple cases of death; thus, full attention is required for oral CH sedation in pediatric dentistry.

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