



# Safety of hydroxyzine in the sedation of pediatric dental patients

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Hydroxyzine is one of the most popular oral sedatives used in pediatric dentistry. This study aimed to investigate the safety and possible side effects of sedation using hydroxyzine in pediatric dentistry. "Hydroxyzine," "Dental sedation," "Child," and "Safety" and their associated synonyms were searched using the Cochrane Library, Embase, PubMed, KISS, KMBASE, and KoreaMed databases. Academic information and portals of DBpia and RISS were also perused. Altogether, 340 papers were found, among which a total of 24 papers were selected according to the detailed criteria. Nine studies used hydroxyzine as monotherapy, and 10 studies compared its safety when hydroxyzine used as multitherapy. In addition, seven studies employed a drug regimen wherein hydroxyzine was one of the components. All these studies revealed that the adverse events specific to hydroxyzine usage were drowsiness and dryness of the mouth, and that there were respiratory complications due to a synergistic reaction of hydroxyzine. Although classified as a histamine blocker, hydroxyzine with its sedative, antiemetic, anticonvulsant, and anticholinergic properties is an oral sedative available without serious adverse events, if the proper dosage of the drug is used and its synergistic effects with other drugs are ascertained in the route of administration.

**Keywords:** Hydroxyzine; Pediatric Dentistry; Safety.



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## INTRODUCTION

If the degree of anxiety and fear in a child visiting a pediatric dentist is severe and it is difficult to treat with the generally used physical and psychological behavioral control method, sedation by drugs is often employed [1]. According to the level of sedation, it can be classified as minimal sedation or general anesthesia. Among these methods, general anesthesia is not preferred owing to its associated problems such as risks and costs. Thus, moderate sedation is often selected in pediatric dentistry wherever necessary [2]. Drugs for sedation can be

administered through various routes such as oral, nasal, intramuscular, intravenous, subcutaneous, and inhalation [3]. Oral sedation is the most common method that is used by pediatric dentists [4,5].

According to a survey conducted in Korea in 2014, chloral hydrate, hydroxyzine, and N<sub>2</sub>O/O<sub>2</sub> were the most frequently selected sedative drug combinations by pediatric dentists [6]. A study published by the American Academy of Pediatric Dentistry (AAPD) in 2016 reported that American dentists frequently used hydroxyzine alone or in combination with N<sub>2</sub>O/O<sub>2</sub>, chloral hydrate, meperidine, midazolam, etc. [7].

This study aimed to investigate the safety and side

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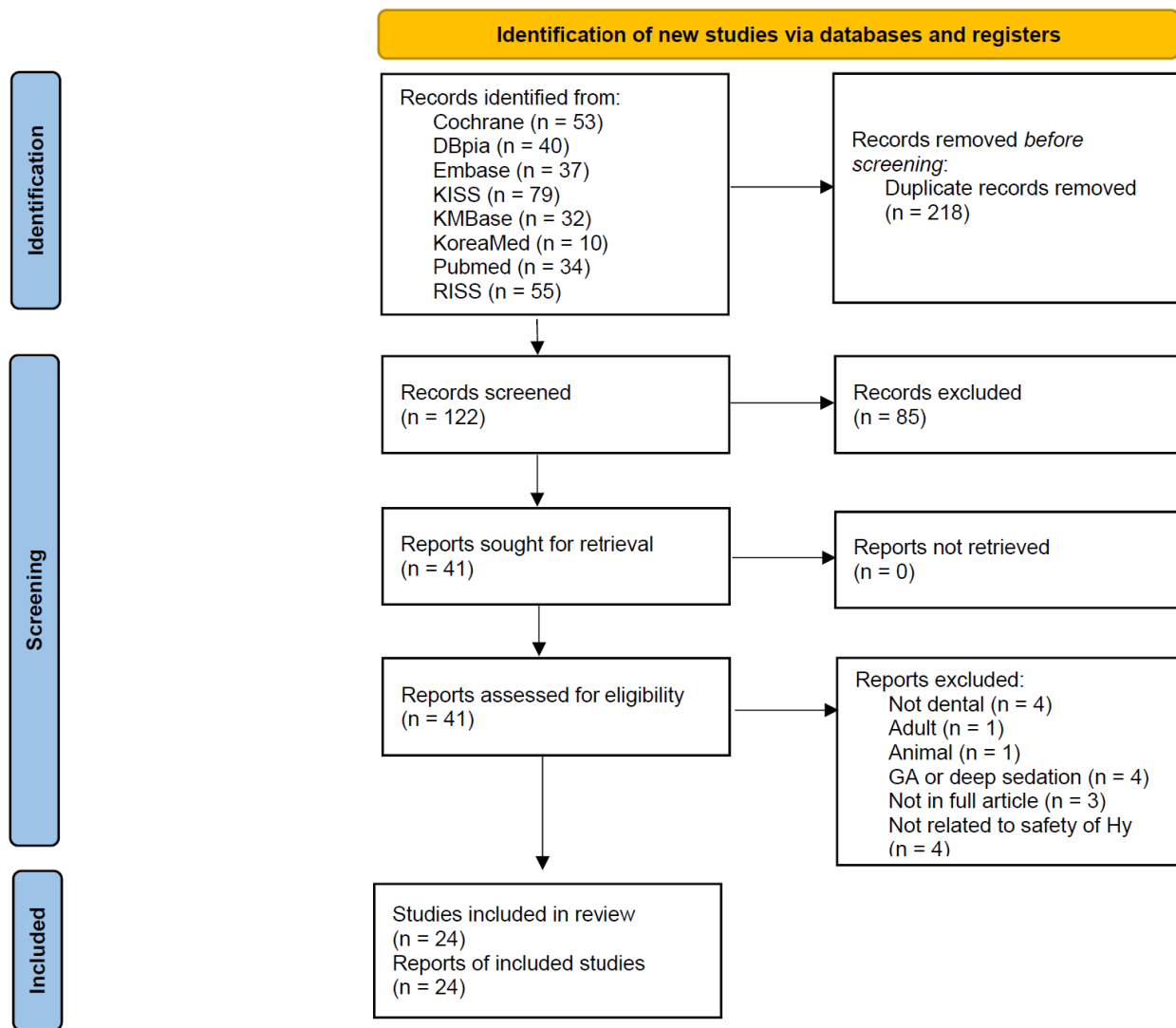


Fig. 1. PRISMA 2020 flow diagram showing the search results from the databases included in the study. Abbreviations: GA, general anesthesia; Hy, hydroxyzine; n, number; PRISMA, preferred reporting items for systematic reviews and meta-analyses.

effects of hydroxyzine by reviewing previously published literature.

## METHODS

To obtain relevant papers, the Cochrane Library, Embase, and PubMed databases were searched for foreign literature. For reports within the Korean literature, the databases KISS, KMBASE, and KoreaMed were perused in addition to academic information and portals from DBpia and RISS. Until June 2022, the data from each

of these databases were searched using the following keywords: “Hydroxyzine,” “Dental sedation,” “Child,” and safety. Besides, synonyms for these words were also used as keywords.

After the first search, 198 papers were found using domestic search engines and portals, and 142 papers were found using foreign search engines. Subsequently, 41 papers were selected by excluding duplicate papers and checking the titles and abstracts of the papers as a secondary screening process. Finally, articles unrelated to the safety of hydroxyzine or for which the original text was unavailable were excluded. The method employed

Table 1. Selected studies

First author	Publication year	Classification
Lang LL [8]	1965	Hydroxyzine monotherapy
Yoon DK [9]	1976	Hydroxyzine monotherapy
Doring KR [10]	1985	Hydroxyzine regimen
Moody Jr EH [11]	1986	Hydroxyzine multitherapy
Lee KY [12]	1990	Hydroxyzine multitherapy
Park HS [13]	1990	Hydroxyzine multitherapy
Kwon OY [14]	1994	Hydroxyzine multitherapy
Kim SH [15]	1997	Hydroxyzine monotherapy
Kupietzky A [16]	1998	Hydroxyzine monotherapy
Avalos-Arenas V [2]	1998	Hydroxyzine multitherapy
Ram D [17]	1999	Hydroxyzine monotherapy/multitherapy
Lee IC [18]	2001	Hydroxyzine multitherapy
Jung JH [19]	2001	Hydroxyzine regimen
Leelataweedwud A [20]	2001	Hydroxyzine regimen
Lee JH [21]	2002	Hydroxyzine regimen
Lima ARDA [22]	2003	Hydroxyzine multitherapy
Faytrouny M [23]	2007	Hydroxyzine monotherapy
Torres-Pérez J [24]	2007	Hydroxyzine monotherapy/multitherapy
Costa LRDRSD [25]	2007	Hydroxyzine multitherapy
Kim KH [26]	2007	Hydroxyzine regimen
Baygin O [27]	2010	Hydroxyzine monotherapy
Lenahan M [28]	2015	Hydroxyzine regimen
Kim GM [29]	2020	Hydroxyzine regimen
Pouliquen A [30]	2021	Hydroxyzine monotherapy

for the selection and exclusion of studies in each stage has been outlined in Fig. 1.

## RESULTS

Altogether, 24 papers met the criteria, and Table 1 lists them by the year of their publication. The contents in parentheses are citations that indicate the side effects reported for each of the articles. 1. Hydroxyzine Monotherapy (Table 2)

The reported side effects of moderate sedation using hydroxyzine alone in dental treatment of pediatric patients were drowsiness (age: 2.5–12 y, dose: 30 mg [9]), dryness of mouth (mean age: 6 y 3 mo, dose: 30 mg [8]), superficial thrombophlebitis (age: 4 y 6 mo, dose: 0.5 mg/kg [15]), nausea/vomiting, and cough (mean age: 5.33 y, dose: 1 mg/kg with 40%–60% N<sub>2</sub>O-O<sub>2</sub> [27]). As hydroxyzine is classified as a histamine blocker with antiemetic action, nausea/vomiting is not likely to be a

side effect caused by hydroxyzine. Superficial thrombophlebitis was treated by self-healing without special treatment. Oxygen desaturation was not reported in all studies that monitored oxygen saturation using a pulse oximeter, and physiological variables, including heart rate, were also within the normal range.

### 1. Multitherapy with Hydroxyzine (Table 3)

Among the literature that confirmed side effects or safety of administering hydroxyzine and other drugs in combination, only those that can be compared depending on the use of hydroxyzine were reviewed. A side effect that was found to be induced upon the use of only hydroxyzine was dryness of the mouth, which was mentioned in one study (mean age: 33.2 mo, dose: chloral hydrate 70 mg/kg, hydroxyzine 1–3 mg/kg [13]).

### 2. Regimen with hydroxyzine (Table 4)

Although there was no comparative analysis on the side effects of hydroxyzine usage in pediatric patients,

**Table 2.** Hydroxyzine monotherapy

Publication year/ First Author	Mean age	Sample size	Sedative drugs	Administration	Monitoring equipment/ interval	Adverse effects
1965 Lang LL [8]	6 y 3 mo	21	Hy: 50 mg (tablet)	60 min before appointment pO		Sleepy/Drowsy: 9 Dryness of mouth: 2
		21	Hy: 50 mg (syrup)			
	6 y 7 mo	20	Placebo tablet			
1976 Yoon DK [9]	2.5 y~12 y	18	Placebo syrup	30~45 min before appointment pO		Sleepy/Drowsy: 4 Nausea and vomiting: 3
		23	Hy: 30 mg syrup			
		20	Placebo			
1997 Kim HS [15]	4 y 6 mo	19	Control group	IV	PO	Drowsiness: 4 Drowsiness: 3 Drowsiness: 2
		1	Hy: 0.5 mg/kg			
1998 Kupietzky A [16]	30 mo	24	GA	50 min before treatment	PO, PC	Superficial thrombophlebitis Prolonged sedation
	35 mo	30	Hy: 5 mg/kg (Max. 100 mg), N <sub>2</sub> O-O <sub>2</sub> : 50%-50%			
1999 Ram D [17]	29 mo	30 (each drug once)	Met: 5 mg, Hy: 3.7 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 50%-50%	60 min before treatment (Met first, Hy 5~8 min later)	PO, PC	- PR, SaO <sub>2</sub>
			Hy: 3.7 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 50%-50%			
2007 Faytrouny M [23]	61.9 mo	15	Hy: 20 mg, Hy 3.7 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 50%-50%	24 hour before treatment (Hy 20 mg), 60 min before treatment (Hy 3.7 mg/kg)	PO	- HR, SaO <sub>2</sub>
	53.7 mo	15	Hy: 3.7 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 50%-50%			
2007 Torres-Pérez J [24]	3.9 y	18	Hy: 2 mg/kg, Hy: 1 mg/kg	2 hour before treatment (Hy 2 mg/kg)	- CR, SaO <sub>2</sub>	-
	2.83 y	18	Mid: 0.5 mg/kg, Hy: 1.5 mg/kg	20 min before treatment (Hy 1 mg/kg)		
				20 min before treatment		
2.94 y	18	CH: 50 mg/kg, Hy: 1.5 mg/kg	20 min before treatment	SaO <sub>2</sub> < 90: 1		
2010 Baygin O [27]	5.33 y	15	Hy: 1 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 40%-60%	60 min before treatment	PO, BIS	Nausea and Vomiting: 1 Cough: 4
	5.27 y	15	Mid: 0.7 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 40%-60%	60 min before treatment	SpO <sub>2</sub> , HR	Nausea and vomiting: 2 Cough: 4 Hiccough: 1 Enuresis: 2 Bronchospasm: 1
	5.2 y	15	Ket: 3 mg/kg, Mid: 0.25 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 40%-60%	15 min before treatment		Nausea and vomiting: 3 Hypersalivation: 8 Hallucination: 2
5.53 y	15	No medication, N <sub>2</sub> O-O <sub>2</sub> : 40%-60%			Nausea and vomiting: 4 Hiccough: 5 Otagia: 2 Epistaxis: 1	
2021 Pouliquen A [30]	6.8 y	184	Hy: 1-2 mg/kg (1.63 mg/kg mean)	90 min before treatment		

BIS, bispectral index; CH, chloral hydrate; CR, cardiac rate; GA, general anesthesia; HR, heart rate; Hy, hydroxyzine; IV, intravenous; Ket, ketamine; mo, months; Met, metoclopramide; Mid, midazolam; N<sub>2</sub>O, nitrous oxide; O<sub>2</sub>, oxygen; PC, precordial stethoscope; pO, per oral; PO, pulse oximeter; PR, pulse rate; RR, respiratory rate; SaO<sub>2</sub>, blood oxygen saturation; SpO<sub>2</sub>, peripheral oxygen saturation; y, years.

desaturation (mean age: 30 mo, dose: chloral hydrate 60 mg/kg, hydroxyzine 25 mg [19]) was the major side effect found in literature that investigated the safety of employing a regimen containing hydroxyzine. In addition, there were apnea, prolonged sedation, vomiting (mean

age: 47 mo, dose: chloral hydrate 50 mg/kg, meperidine 1.5 mg/kg, hydroxyzine 25 mg with 100% O<sub>2</sub> [20]), fever (mean age: 30 mo, dose: chloral hydrate 70 mg, hydroxyzine 2 mg/kg [26]), and rash (dose: meperidine 1-2.2 mg/kg, hydroxyzine 0.5-2.2 mg/kg with 50%-50%

Table 3. Multitherapy with hydroxyzine

Publication year/ First Author	Mean age	Sample size	Sedative drugs	Administration	Monitoring equipment/interval	Adverse effects
1986 Moody Jr EH [11]	39.6 mo	10	CH: 50 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 50%-50%	30 min before treatment Oral	PC, PO - PR, SaO <sub>2</sub>	
	42 mo	10	CH: 50 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 50%-50%	30 min before treatment Rectal	- 5 min	
	38.4 mo	10	CH: 30 mg/kg, Hy: 25 mg, N <sub>2</sub> O-O <sub>2</sub> : 50%-50%	30 min before treatment Oral		
1990 Lee KY [12]	37 mo	15	CH: 75 mg/kg	Rectal	PO, Manometer - BP, PR, RR, SaO <sub>2</sub>	Oxygen saturation < 95% more than 5sec.: 2 Excitement: 2
		15	CH: 75 mg/kg, Hy: 20 mg	1 hour before treatment (Hy), 30 min before treatment (CH) Oral	- 5 min	Oxygen saturation < 95% more than 5sec.: 2 Excitement: 1 Nausea: 1 Fever: 1
		15	CH: 75 mg/kg, Dzp: 3~4 mg	Rectal (CH) IM (Dzp)		Oxygen saturation < 95% more than 5sec.: 4 Vomiting: 2 Diarrhea: 1
1990 Park HS [13]	36.65 mo	20 (each drug once)	CH: 50 mg/kg	Oral	BPC, Manometer, PC	Vomiting: 1
			CH: 50 mg/kg, Hy: 25 mg	Oral	-	Xerostomia: 9
			CH: 50 mg/kg	Rectal	BP, HR, Respiratory reflex - 10 min	Vomiting: 1 Xerostomia: 1
1994 Kwon OY [14]	21-45 mo	22 (each drug once)	CH: 75 mg/kg	45 min before treatment	PO - HR, SaO <sub>2</sub>	Vomiting: 3 Nausea: 2 Diarrhea: 1
			CH: 50 mg/kg, Hy: 25 mg			Nausea: 1 Diarrhea: 1
1998 Avalos-Arenas V [2]	28.58 mo	40	CH: 70 mg/kg, Placebo CH: 70 mg/kg, Hy: 2 mg/kg	1 hour before treatment	PC, Manometer - HR, RR, BP, SaO <sub>2</sub> - 15 min	At least 10% of children had an SaO <sub>2</sub> of < 90%
1999 Ram D [17]	29 mo	30 (each drug once)	Met: 5 mg, Hy 3.7 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 50%-50% Hy: 3.7 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 50%-50%	60 min before treatment (Met first, Hy 5~8 min later)	PO, PC - PR, SaO <sub>2</sub> - 5 min	
2001 Lee IC [18]	33.2 mo	50 (each drug once)	CH: 70 mg/kg, Placebo		PO, BPC -	Vomiting: 6 Respiratory depression: 1
			CH: 70 mg/kg, Hy: 1 mg/kg		HR, BP, SaO <sub>2</sub> -	Vomiting: 1 Xerostomia: 4 Respiratory depression: 1
			CH: 70 mg/kg, Hy: 2 mg/kg		5 min	Vomiting: 1 Xerostomia: 6
			CH: 70 mg/kg, Hy: 3 mg/kg			Vomiting: 2 Xerostomia: 6 Respiratory depression: 2
2003 Lima AR [22]	40 mo	37 case (11 child)	Placebo Mid: 1 mg/kg Mid: 0.75 mg/kg, Hy: 2 mg/kg	30 min before treatment	PO - RR, HR, SaO <sub>2</sub> - 15 min	

N<sub>2</sub>O-O<sub>2</sub> [28]) in different cases. Among them, apnea was due to the respiratory depressive effect of the narcotic

used in combination. However, that could also be a result of a synergistic reaction of hydroxyzine.

**Table 3.** Multitherapy with hydroxyzine (continued)

Publication year/ First Author	Mean age	Sample size	Sedative drugs	Administration	Monitoring equipment/interval	Adverse effects
2007 Torres-Pérez J [24]	3.9 y	18	Hy: 2 mg/kg, Hy: 1 mg/kg	2 hour before treatment (Hy 2 mg/kg) 20 min before treatment (Hy 1 mg/kg)	- CR, SaO <sub>2</sub> -	
	2.83 y	18	Mid: 0.5 mg/kg, Hy: 1.5 mg/kg	20 min before treatment		
	2.94 y	18	CH: 50 mg/kg, Hy: 1.5 mg/kg	20 min before treatment		SaO <sub>2</sub> < 90: 1
2007 Costa LR [25]	40.6 mo	35 case (12 child)	Placebo	30 min before treatment	PO, BPC - RR, HR, SaO <sub>2</sub> , BP - 15min	Irritation: 7 Sleepiness: 9 Nausea, Vomiting: 3
			CH: 75 mg/kg  CH: 50 mg/kg, Hy: 2 mg/kg			

BP, blood pressure; BPC, blood pressure cuff; CH, chloral hydrate; CR, cardiac rate; Dzp, diazepam; HR, heart rate; Hy, hydroxyzine; IM, intramuscular; mo, months; Met, metoclopramide; Mid, midazolam; N<sub>2</sub>O, nitrous oxide; O<sub>2</sub>, oxygen; PC, precordial stethoscope; PO, pulse oximeter; PR, pulse rate; RR, respiratory rate; SaO<sub>2</sub>, blood oxygen saturation; y, years.

**Table 4.** Regimen with hydroxyzine

Publication year/ First Author	Mean age	Sample size	Sedative drugs	Administration	Monitoring equipment/ interval	Adverse effects
1985 Doring KR [10]	51.4 mo	36 case (26 child)	Alp: 0.6 mg/kg, Hy: 0.3 mg/kg, N <sub>2</sub> O-O <sub>2</sub> : 40%-60%	6min before treatment Submucosal (Maxillary vestibule)	ECG, PO, BPC - HR, BP, SaO <sub>2</sub> - 3 min	
2001 Jung JH [19]	30 mo	92 case (71 child)	CH: 60 mg/kg, Hy: 25 mg	45~60 min before treatment	PO	SpO <sub>2</sub> < 95%: 42
2001 Leelataweedwud P [20]	47 mo	195 case (111 child)	CH: 50 mg/kg, Mep: 1.5 mg/kg, Hy: 25 mg, 100% O <sub>2</sub>	45 min before treatment	PO, PC, Capnography - EtCO <sub>2</sub> , PR, RR, SpO <sub>2</sub> - 5 min	True apnea: 1 Prolonged sedation: 3 Vomiting: 1 True desaturation: 1
2002 Lee JH [21]	42.2 mo	40	CH: 60 mg/kg, Hy: 25 mg		PO, PC - - 5min	True desaturation: 0~3 times for each patient
2007 Kim KH [26]	30 mo	171 case (94 child)	CH: 70 mg/kg, Hy: 2 mg/kg, (N <sub>2</sub> O-O <sub>2</sub> induction if child not sedated in 60min)		- SpO <sub>2</sub> , HR, RR - 5 min	Vomiting: 2 Fever: 1 Desaturation: 1
2015 Lenahan M [28]		248 case	Mep: 1~2.2 mg/kg (Max 50 mg), Hy: 0.5~2.2 mg/kg (Max. 50 mg), (N <sub>2</sub> O-O <sub>2</sub> : 50%-50% for 238 case)	45~60 min before treatment	PO, BPC, PC - BP, PR, SaO <sub>2</sub> - 5 min	Nausea, Vomiting, Rash, Minor desaturation: 14
2020 Kim G [29]	36.4 mo	188 case (149 child)	CH: 50~70 mg/kg, Hy: 25 mg, N <sub>2</sub> O-O <sub>2</sub> : 55%-45% (mean)	30~60 min before treatment	PO, Capnography - SpO <sub>2</sub> , HR, RR, EtCO <sub>2</sub> - 15 min	Vomiting during procedure: 27 Vomiting after procedure: 4 Desaturation: 4

Alp, Alphaprodine; BP, blood pressure; BPC, blood pressure cuff; CH, chloral hydrate; ECG, electrocardiograph; EtCO<sub>2</sub>, end tidal carbon dioxide; HR, heart rate; Hy, hydroxyzine; mo, months; Max, maximum; Mep, meperidine; N<sub>2</sub>O, nitrous oxide; O<sub>2</sub>, oxygen; PC, precordial stethoscope; PO, pulse oximeter; PR, pulse rate; RR, respiratory rate; SaO<sub>2</sub>, blood oxygen saturation; SpO<sub>2</sub>, peripheral oxygen saturation.

## DISCUSSION

Hydroxyzine is classified as a histamine blocker (H1), but has sedative, antiemetic, anticonvulsant, and anticholinergic properties. After oral administration, it is absorbed through the gastrointestinal tract, and its clinical action is observed within 15–30 minutes. The maximum action is observed 2 hours after administration [31]. The sedative action of hydroxyzine is initiated when the hypothalamic nuclei are inhibited and then subsequently, the sympathetic part of the autonomic nervous system [32]. Since it amplifies the central nervous system depression of drugs such as barbiturates, narcotics, alcohol, sedative-hypnotics, and anxiolytics, the dose of these drugs in combination or hydroxyzine alone should be reduced to 50% [33].

Although the dosage of hydroxyzine has not been determined precisely, Ayd [34] described in 1957 that 25 mg was effective in children with neurotic and hyperkinetic disorders. In addition, Kopel [35] reported in 1959 that satisfactory results were obtained when 30–50 mg of the drug was taken at bedtime, a day before the appointment; and the same dose when taken one hour before treatment in “high-strung” children. In 1965, Lang [8] reported that a single dose of 50 mg of the drug was effective when it is taken one hour before the treatment. On the other hand, in 1992, Shapira et al. [36] reported that, since hydroxyzine (50 mg) prescription in heavier children showed high failure rates, an effective mg/kg ratio should be used. They also added that the 3.7 mg/kg ratio used along with 50% N<sub>2</sub>O-O<sub>2</sub> was the most appropriate. Tafaro et al. [37] used 2 mg/kg, and Needleman et al. [38] used 1 mg/kg in their studies. Kupietzky and Blumenstyk [16] reported no side effects even with higher doses of hydroxyzine (5 mg/kg, 100 mg max).

Among the side effects that were investigated in this study, drowsiness and dryness of the mouth are considered to be caused by hydroxyzine. These phenomena are considered to be helpful for pediatric

treatment.

The goal of sedation in pediatric patients is to ensure patient safety and minimize discomfort, anxiety, and psychological trauma. It is also aimed at maximizing the potential of amnesia, controlling behaviors for the safe completion of procedures, and ensuring safe discharge from the hospital [39]. The side effects of sedation treatment can cause brain damage or even death, and these side effects are mainly caused by respiratory failure [40]. Normal arterial oxygen saturation of healthy children in room air is 97–100%, and an oxygen saturation of 95% or more can provide oxygen to tissues at a normal level. Mild hypoxemia refers to an oxygen saturation of 91–95%, moderate hypoxemia an oxygen saturation of 75–90%, and severe hypoxemia an oxygen saturation of less than 75% [41]. An oxygen saturation of less than 95% does not occur under normal physiological conditions. Cyanosis of nails or mucous membranes is useful for detecting hypoxia, and changes in heart rate, electrocardiogram, and blood pressure can also be signs of hypoxemia [42]. However, these were not observed until the oxygen saturation fell from a moderate to a severe level [43]. When an overdose of drugs is used or inappropriate anesthesia is practiced, cardiovascular complications may also occur during sedation. However, these processes occur less frequently than when only local anesthesia is used [44]. Hypotension or hypertension refers to a case in which a patient's blood pressure changes by 20% or more from the baseline. When the cardiac rhythm is different from the patient's baseline sinus rhythm, it can be considered as arrhythmia [45].

To prevent such a situation, the patient should be continuously monitored by professional personnel using appropriate equipment before, during, and after the procedure [46]. According to the American Society of Anesthesiologists (ASA) guidelines, ventilatory and cardiovascular functions are not affected in cases of minimal sedation. Thus, no interventions other than observation or intermittent assessment of the sedation level are necessary. Moreover, for moderate sedation, no

interventions are required for airway maintenance or spontaneous ventilation. However, even in cases where minimal sedation is intended, individuals can be moderately sedated, which can progress to deep sedation. Therefore, it is stated that an operator needs to prepare the necessary equipment for deep sedation [39,45]. It should be able to monitor heart rates and oxygen saturation continuously, and capnography or precordial stethoscopes are recommended to monitor ventilation [39].

No serious adverse events induced by hydroxyzine were reported in this study. However, it was reported in 1994 that second-generation antihistamines could induce QT interval prolongation. Besides, some first-generation antihistamines (including hydroxyzine) could also cause ventricular fibrillation, which may result in torsades de pointes (TdP), leading to death [47]. Such QT interval prolongation is thought to be caused by cardiac potassium channel blockage involved in repolarization, and increased repolarization time and T wave disturbances have been reported with the use of hydroxyzine. However, since these adverse events only occur when the drug is overdosed and do not appear in most cases, hydroxyzine should not be administered to patients with hereditary long QT syndrome or cardiovascular disease [48]. In this regard, there was a pharmacovigilance review of hydroxyzine in 2017, in which [49] all 59 cases with QT prolongation and/or TdP reported from 1995 to 2016 had underlying risk factors (daily dose of 100 mg or more, systemic disease, concomitant medications).

## CONCLUSIONS

Hydroxyzine was developed in 1956 and has been widely used in over 30 countries. It is the 70th most-used drug with over 10 million prescriptions in the US in 2020. It is safe to use, with a very low incidence of side effects. Besides, there have been rare cases of fatal overdose, and no reported withdrawal symptoms following long-term treatment.

Upon the selection of an appropriate route and dose, there are no side effects except for drowsiness and dryness of the mouth when used alone. Since hydroxyzine can amplify central nervous system depression due to other drugs, more satisfactory sedative effects can be obtained by reducing nausea and vomiting and other side effects of drugs such as chloral hydrate.

However, the use of hydroxyzine alone is limited to the management of children with mild to moderate fear. Therefore, when used in combination with other drugs for pediatric patients who are more fearful, the patient's vital signs should be meticulously monitored before, during, and after treatment to maintain sedation at a minimal to moderate level.

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**Taegyeom Kim:** Writing - original draft, Writing - review & editing

**Keongah Kim:** Supervision

**Seungoh Kim:** Supervision

**Jongbin Kim:** Conceptualization, Supervision

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