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Chloral hydrate for sedation of children with asthma during dental treatment

ABSTRACT

Aim *We hypothesised that chloral hydrate is safe and effective for sedation during dental treatments for children with mild asthma. We evaluated the safety and efficacy of chloral hydrate by measuring changes in heart rate (HR), transcutaneous oxygen saturation, (SpO_2), asthma score, behaviour, types and frequency of adverse reactions associated with chloral hydrate were assessed throughout treatment.*

Materials and methods *Children (<10 years old) with mild asthma undergoing dental treatments received a single 65 mg/kg oral dose of chloral hydrate liquid 1 hour prior to treatment in an open label trial. Heart rate (HR), SpO_2, asthma score, behaviour, types and frequency of adverse reactions associated with chloral hydrate were assessed throughout treatment. Asthma score was obtained before and after treatment. Thirty minutes after treatment, SpO_2, HR, and level of consciousness was assessed.*

Results *Twenty four children were enrolled and 92% (22/24) recovered from sedation without respiratory depression. Two experienced mild respiratory depression related to chloral hydrate. Asthma was not a contributing factor as they did not experience wheezing, cough, tachypnoea, or retractions. Inhaled nitrous oxide supplemented chloral hydrate sedation in 63% (15/24) children to achieve effective cooperation. Three children had a SpO_2 <95% (2 during treatment, 1 during recovery).*

Conclusions *Chloral hydrate 65 mg/kg administered a as single oral dose appears to be safe with respect to disease exacerbation for children with mild asthma undergoing dental treatment. Due to ineffective sedation and mild respiratory depression associated with chloral hydrate, newer, easily titrated medications, such as midazolam, may offer advantages.*

Keywords *Asthma; Children; Chloral hydrate; Dental treatment.*

Introduction

Asthma is a chronic airway disease characterised by recurrent episodes of coughing, wheezing, and tachypnoea [Fredberg, 2004]. Approximately 5-10% of children in the United States are affected by asthma making the disease a major cause of school absenteeism [Mellon and Parasuramam, 2004; Yeatts et al., 2003]. Asthma is the leading cause of paediatric hospitalisation and is responsible for an annual health care cost of three billion dollars [Mellon and Parasuramam, 2004]. The disease has a more deleterious effect on racial and ethnic minorities as well as on poor urban children [Evans et al., 1997; Brown et al., 2004; Debley et al., 2005]. It is projected that 22 million persons will be diagnosed with asthma by the year 2010 [Debley et al., 2005]. With the incidence of asthma increasing, more studies are needed to evaluate the effects of various medications on asthmatic individuals to prevent adverse drug reactions [US Surveillance for asthma, 2002; Grant et al., 2005].

Chloral hydrate is commonly used for sedation in children of various ages undergoing outpatient dental procedures [Houpt, 2002]. Stress, anxiety, and hyperactivity experienced during dental procedures may precipitate an exacerbation of asthma in predisposed patients [Ten Thoren and Petermann, 2000]. Use of sedation to reduce stress and manage behavioural responses during the dental visit may decrease the incidence and severity of an asthma exacerbation [Steinbacher and Glick, 2001]. While chloral hydrate has a wide margin of safety, this agent may induce gastric irritation, nausea, vomiting, diarrhoea, clumsiness, hallucinations, drowsiness, and mild respiratory depression, especially when administered on an empty stomach [Zhu et al., 1996]. Chloral hydrate has been observed to affect diastolic blood pressure and expired carbon dioxide concentrations in healthy children undergoing various dental procedures [Pershad et al., 1999]. Asthma may place children at higher risk for chloral hydrate-induced respiratory insufficiency, therefore it is important to evaluate the safety of this agent in children with asthma [Cote, 2000]. There is a paucity of data on the respiratory effects of this agent in asthma.

A study evaluating the respiratory effects of chloral hydrate in adult subjects (n=24) with asthma and without asthma showed alterations in several respiratory

Mild-Intermittent	Symptoms less than or equal to 2 times a week; exacerbations brief (from a few hours to a few days), intensity may vary; nighttime symptoms less than or equal to 2 times a month
Mild persistent	Symptoms greater than 2 times a week but less than 1 time a day; exacerbations may affect activity; nighttime symptoms greater than 2 times a month
Moderate persistent	Daily symptoms; daily use of inhaled short acting beta2-agonist; exacerbations affect activity; exacerbations greater than or equal to 2 times a week, may last days; nighttime symptoms greater than 1 time a week
Severe persistent	Continual symptoms; limited physical activity; frequent exacerbations; nighttime symptoms are frequent

TABLE 1 Criteria from the National Asthma Education and Prevention Program used to determine subjects' asthma severity upon enrollment into the study.

and arterial blood gas parameters consistent with physiologic sleep-induced respiratory depression [Adrete and Itkin, 1969]. The alterations were longer and more pronounced in the asthmatic group, with the most pronounced effect on oxygen arterial pressure three hours after chloral hydrate administration. There are no known studies evaluating the effect of chloral hydrate in children with asthma.

We hypothesised that chloral hydrate is safe and effective when administered orally for sedation during dental procedures in children with mild asthma. Our aim was to evaluate the safety and efficacy of chloral hydrate in children with asthma undergoing dental procedures in an urban children's dental clinic as measured by transcutaneous oxygen saturation (SpO_2), heart rate (HR), asthma score, behaviour, and types and frequency of adverse reactions associated with chloral hydrate.

Methods

This open-label study was conducted at the Developmental Dental Clinic at Children's Hospital of Michigan (Detroit, USA). The Human Investigation Committee approved the protocol and informed consent was obtained from the parent of each child enrolled in the study. Parents of children with scheduled appointments for dental treatments were asked by study personnel for informed consent to participate.

Children less than 10 years of age were enrolled using the following criteria: 1) asthma (mild intermittent or mild persistent); 2) parental permission for dental procedure (e.g. filling of dental caries, extractions, pulpectomies, debridement of necrotic nerve tissue); 3) sedation requirement during dental procedure based upon previous dentist's assessment or child's history. Exclusion criteria were: 1) presence of medical contraindication for sedation with chloral hydrate; 2) known or suspected hypersensitivity to chloral hydrate or any component of chloral hydrate liquid; 3) moderate or severe persistent asthma; 4) asthma score of 1 or 2 prior to administration of chloral hydrate. Parents were instructed to have their child fast for four hours prior to the time of the dental appointment to minimise the risk of aspiration during the study procedures.

Upon enrollment into the study, the study dentist determined the child's asthma severity after consultation with the child's primary physician and parents using the criteria from the National Asthma Education and Prevention Program [National Asthma Education and Prevention Program, 1997]. Criteria are summarised in Table 1. On the day of the appointment, the child's asthma score, using the modified Wood's score was determined prior to initiation of study procedures by an experienced nurse from the Department of Pulmonary Medicine [Wood et al., 1972]. The scoring system is explained in Table 2. The child's weight was recorded. Baseline transcutaneous SpO_2 and HR were recorded using a pulse oximeter (Escort Prism SE, Arleta, CA). The study dentist evaluated the child's behaviour during monitoring of SpO_2 and HR values using the system developed by Leelataweewud et al. [2000]. The child's baseline level of consciousness was assessed and documented using the categories of "alert", "agitated or depressed" or "comatose" from the Woods scale (Table 3).

One hour prior to the start of the treatment, the study dentist administered a single 65 mg/kg oral dose of chloral hydrate liquid to the child. All doses were dispensed from the dental clinic medication inventory. As the study was open-label, the dentist, dental team and study personnel were aware that the child was receiving chloral hydrate.

One hour after administration of the chloral hydrate dose, the child was placed, but not initially immobilized, on a papoose board and the dental treatment was initiated. The child was restrained with parental consent if his or her behaviour was dangerous to him/herself or to

Indicator	0	1	2
SpO_2	>94% (room air)	<94% (room air)	<94% (40% FiO_2)
Cyanosis	No	Yes	Yes
Breath sounds	Equal	Unequal	Absent
Wheezing	None	Moderate	Marked
Accessory Muscles	None	Moderate	Marked
Level of consciousness	Alert	Agitated or depressed	Comatose

TABLE 2 Asthma scoring system used to classify asthma and level of consciousness during study procedures (modified from Wood et al., 1972).

the dental team. Nitrous oxide 50% via inhalation mask was administered to increase and maintain sedation if deemed necessary by the study dentist.

Local anaesthesia using lidocaine injection (lidocaine 2% with 1:100,000 epinephrine) was administered to each child. The study dentist determined the dose of lidocaine based on the child's individual requirements. Dental treatment was performed according to standard practice. Transcutaneous SpO_2 and HR were continuously monitored, with values for both parameters documented by the study dentist every five minutes throughout the treatment. Behaviour was also assessed throughout the entirety of the treatment and documented every 5 minutes. At the end of the treatment, final SpO_2 and HR values were documented and the pulmonary nurse assessed the child's asthma score.

Thirty minutes after the dental treatment, SpO_2 and HR were documented and the study dentist assessed the child's level of consciousness. Criteria for discharge home were normal vital signs, regain of consciousness, and normal response to verbal and physical stimulation.

Sample size was determined by convenience and subjects were screened and enrolled on a first come, first serve basis. All statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL). Demographic and univariate data were examined using descriptive statistics for continuously scaled variables (means, standard deviations), frequencies or proportions for discontinuously scaled dependent variables.

Mean differences in the primary outcome (SpO_2) and secondary outcome (HR), were compared across the study procedures using a multivariate General Linear Model, and (repeated measures ANOVA). Post hoc pair-wise comparisons were evaluated using a Bonferonni test to control for the problem of multiple tests of hypotheses. Alpha was set at a p-value ≤ .05, two-tailed.

Excellent	Treatment completed without difficulty, minimal crying and patient quiet and/or asleep for most of case
Satisfactory	Treatment completed with minimal difficulty, but alternating periods of crying and struggling with period of quiet and/or sleep
Unsatisfactory	Treatment completed with difficulty due to crying and struggling throughout treatment
Aborted	Treatment not completed due to combative behaviour that increased the risk of injury to the patient or dental team

TABLE 3 System used to assess behaviour during study procedures (modified from Leelataweewud et al., 2000).

Physical Measures	Mean ± SD(Range)
Weight (kg)	12.5 ± 0.4 (12.5-26)
Age (months)	57.8 ± 19.5 (34-102)
Ethnicity	**% Total (Number)**
African American	70.8% (17/2)
Caucasian	12.5% (3/24)
Hispanic	16.6% (4/24)
Gender	**% Total (Number)**
Male	54% (13/24)
Female	46% (11/24)

TABLE 4 Physical measures and demographics of study participants (n=24).

Medication	Number of subjects**
Montelukast sodium tablets	3
Budesonide inhaler	3
Fluticasone/salmeterol inhalation	1
Prednisone tablets	1
Albuterol inhaler	15

*4 Subjects were receiving no asthma medications at the time of the study at home.
** Includes those subjects receiving this agent in combination with other therapies.

TABLE 5 Home asthma medications of study participants (n=20)*.

Results

A total of 24 children were enrolled in the study with 23/24 children completing the protocol. Demographic and physical characteristics of the study population are in Table 4. Upon enrollment into study, 20 children were classified as having mild-intermittent asthma, and 4 children were classified as having mild-persistent asthma. The majority (20/24, 83%) of the children were receiving some type of asthma medication at home at the time of study enrollment (Table 5). The asthma score was 0 for all children at the beginning of dental treatment. Mean baseline SpO_2 was 98% and mean baseline HR was 99 beats/min. One dentist performed the treatments. All treatments were initiated 60 minutes after administration of the chloral hydrate dose and ranged in duration from 15 to 45 minutes. Dental treatments for the study population are in listed in Table 6. Mean SpO_2 was measured and documented at: baseline (time 0), 60, 65, 70, and 120 minutes after chloral hydrate administration. Mean SpO_2 decreased slightly from baseline 98% to 97.5% at 120 minutes after chloral hydrate administration (Fig. 1). There was no significant difference in mean SpO_2 between any two monitoring periods ($p>.05$). Mean HR increased significantly ($p<.05$) during the procedure but returned to baseline values 30 minutes into the recovery period (Fig. 1). In addition, mean HR values were significantly higher at the beginning and at the end of the treatment compared with baseline values ($p<.05$).

Mean HR values were also significantly higher at each time of recording during the treatment when compared with those at the beginning and end of the treatment

Procedure	Number of Study Participants *
Malgam fillings	5
Composite crown restoration	1
Crown extraction	1
Composite fillings	4
Coronal restoration	7
Crown placement/bonding	1
Crown restoration	1
Examination/Polishing	1
Extraction	9
Fluoride treatment	1
Partial caries removal	1
Pulpotomy	5
*30% of participants had more than one procedure performed during the study period.	

TABLE 6 Dental procedures for study participants (n=24).

(p<.05). After considering the potential correlation between repeated measures, the generalied estimation equation analysis indicated a significant increase in mean HR from the beginning of the treatment until 70 minutes after the start of the treatment. Mean HR increased significantly at the time of administering the local anesthetic for all subjects (p<.05). Mean HR continued to increase during the treatment and decreased when the child was released to his or her parents.

Twenty children (83%) were assessed as having excellent behaviour at baseline phase (Fig. 2). During the procedure, six children (25%) were assessed as having excellent behaviour, nine children (38%) as having satisfactory behaviour and eight children (33%) having unsatisfactory behaviour. Inhaled nitrous oxide supplemented the chloral hydrate sedation in 63% (15/24) children to achieve effective cooperation. The treatment had to be aborted for one child because of lack of cooperation (Fig. 2). The children's level of consciousness at baseline was compared with their level of consciousness at the completion of dental treatment. All (24/24) of the children completing treatment were assessed as "alert" at baseline compared with (7/24) 29% at the completion of the treatment (p<.05).

Twenty two (22/24) children had an asthma score of 0 at 30 minutes after completion of the dental treatment, compared with 24/24 at baseline. Two children developed SpO_2 concentrations of less than 94% after the treatment was initiated, requiring oxygen supplementation. However, none of the children had wheezing or retractions on physical examination.

During the study period, three subjects had a documented SpO_2 of less than 95%. Two children experienced an oxygen desaturation during the dental treatment leading to its termination and one child experienced an episode of desaturation during the

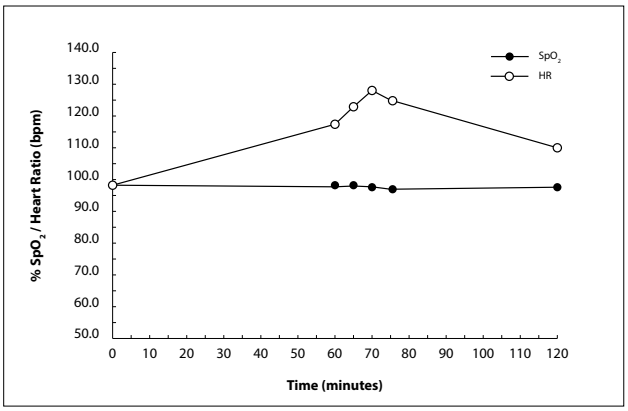

FIG. 1 Changes in % SpO_2 and HR beats per minute (bpm) during study procedures for study subjects (n=24).

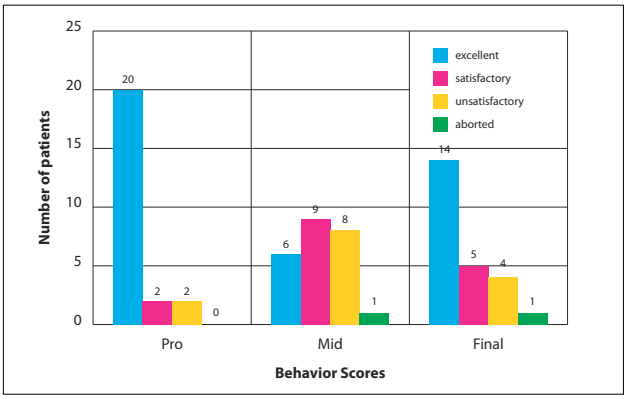

FIG. 2 Behaviour scores of study participants (n=24) using modified Leelataweewud et al. [2000] system.

recovery period. One of the two children who had oxygen desaturation during the treatment was also very combative, and had a high HR value at that time. The desaturation was most likely related to crying as the SpO_2 returned to normal range after interrupting the treatment and improvement of the behaviour.

The second child, a 46 month old, 16 kg, male was calm and alert, but was not able to take deep breaths due to sedation. He was receiving albuterol as needed for control of asthma at home. His SpO_2 decreased to 83% after 30 minutes of recovery time. Supplemental oxygen 3 l/min. via facemask was administered and the child was instructed to take deep breaths and his SpO_2 increased to 95%. His axillary temperature was 37.2, HR 100 beats/min and RR 28/min. The child was transferred to the emergency department (ED) for further observation where he received intravenous fluids 300 ml normal saline over one hour with a maintenance rate for hydration and mild hypotension of 95/47 mm. He was placed on continuous cardiorespiratory monitoring with pulse oximetry. The child continued to receive supplemental oxygen and was monitored for an additional three hours. While in the ED the child did not have any documented episodes of hypoxia. His blood pressure remained within the normal range. He ate lunch and did not experience any vomiting. The

child was discharged from the ED approximately 6 hours after chloral hydrate administration in stable condition. At the time of discharge home, the child was alert and had a SpO_2 of 97% on room air. The mild hypotension may have been related to either chloral hydrate or to an extended fasting period prior to the dental treatment.

The child experiencing oxygen desaturation during the recovery period, completed the procedure and was calm and alert, but could not maintain acceptable oxygen saturation most likely secondary to sedation. Supplemental oxygen was administered for 30 minutes prior to weaning to room air. The child was discharged home, one hour later, alert, with normal vital signs. None of these three children experienced any wheezing during treatment or at the time of discharge. Hospitalisation was not required for any child and all children, except the one discharged from the ED, were discharged home from the dental clinic on the day of the treatment.

Discussion

The results of this study indicate that chloral hydrate administered as a single oral dose of 65 mg/kg did not cause acute asthma exacerbation in children 34 to 102 months of age with mild asthma undergoing dental treatments. These findings assist in filling the gaps in our knowledge about the respiratory effects of commonly used medications in paediatric asthmatic patients. To our knowledge, there are no other reports of the safety of chloral hydrate in children with asthma.

Chloral hydrate is commonly used in oral doses of 25 to 100 mg/kg total body weight to sedate children prior to dental treatments and diagnostic examinations [Barone, 1996; Wheeler et al., 2001]. Doses of 80 to 100 mg/kg, with a maximum of 2 gr are referred to as "high dose" [Greenberg et al., 1993]. The dose of 65 mg/kg used in the study protocol is within the therapeutic dosage range. However, this dose failed to successfully sedate 33% (8/24) of the children in the study who were assessed as having "unsatisfactory" behaviour. Heart rate was a reliable predictor of behaviour, as HR values increased as the children became more agitated. Chloral hydrate doses must be individualised to obtain the desired clinical effect. Duncan et al. reported an 85% successful sedation rate using oral doses of 75 mg/kg of chloral hydrate supplemented by inhaled nitrous oxide in children undergoing dental treatments [Duncan and DeBall, 1994]. However, with the chloral hydrate dose of 65 mg/kg 71% (17/24) of the children in the study were sedated at 30 minutes after completion of the treatment resulting in a prolonged recovery time.

The use of asthma medications and a history of frequent ear problems may be possible risk factors for increased anxiety in children undergoing dental procedures [Wogelius et al., 2003]. Due to the location of dental pain, and similarities in treatment situations, children with ear problems may recall previous negative experiences associated with ear treatments while visiting the dentist. These findings further support the need to identify safe and effective sedative medications for asthmatic children undergoing dental treatment. The number of children with a history of ear problems in our study population is unknown. It would be interesting to determine if cases of inadequate sedation were associated with this factor.

The majority, 92% (22/24), of children in the present study recovered from sedation without documented respiratory depression. Two children experienced mild respiratory depression related to chloral hydrate administration and asthma was not a contributing factor as they did not experience wheezing, cough, tachypnoea, or retractions. Respiratory depression and hypoventilation were closely related to level of consciousness in these children. While asleep, their SpO_2 decreased to less than 95% most likely secondary to shallow breathing. As the effects of chloral hydrate wore off, these two children became increasingly alert with concomitant increases in SpO_2. Both children were slightly sedated, yet conscious when the SpO_2 monitor alarm indicated a reduction of SpO_2 below 95% prior to clinical signs of cyanosis or pallor. Therefore, SpO_2 is an earlier and more useful indicator of hypoxia secondary to respiratory depression compared with clinical observation [Wilson, 1995]. The incidence of mild respiratory depression associated with the administration of chloral hydrate for sedation prior to diagnostic procedures has been reported to be as high as 4% [Wilson, 1992; Slovis et al., 1993; Cote, 2000]. However, in the present study, we had a higher incidence of respiratory depression, since it occurred in 8% (2/24) of our study subjects ($p>.05$).

Fasting prior to the administration of chloral hydrate has been associated with an increased failure rate of initial sedation in 200 infants undergoing auditory brainstem response for evaluation of hearing loss [Keidan, 2004]. Therefore, infants who fasted required an increased total dose of chloral hydrate, and associated prolonged sedation time. The investigators concluded that this was due to increased irritability of hunger, making sedation more difficult. This may have been a confounding factor for the 33% (8/24) of the children in the study who were assessed as having "unsatisfactory" behaviour.

Chloral hydrate is a commonly used oral sedative hypnotic, alone or in combination with other agents such as hydroxyzine or midazolam for children during dental treatments [Avalos-Arenas et al., 1998; Reeves et al., 1996; Campbell et al., 1998]. The use of chloral hydrate in combination with hydroxyzine increased the effect of chloral hydrate in a study of children 21 to 36 months of age randomised to receive either 70 mg/kg chloral hydrate alone or with 2 mg/kg hydroxyzine in terms of decreased crying and movement during dental procedures [Avalos-Arenas et al., 1998]. Overall, there were more oxygen desaturations and deep sedations

in the chloral hydrate and hydroxyzine group compared with children who received chloral hydrate alone. Therefore caution is advised when using chloral hydrate in combination with another sedative agent.

Upon oral administration, chloral hydrate undergoes rapid absorption and reduction to tricholoethanol (TCE), by alcohol dehydrogenase. The pharmacological effects of chloral hydrate are caused by TCE which probably exerts barbiturate-like effects on GABAA receptor channels [Keidan, 2004]. Effects of chloral hydrate are dose-related with hypnotic doses producing deep sleep and higher doses producing general anaesthesia and depression of vasomotor and respiratory centers. The onset of chloral hydrate-induced sleep is usually within 30 to 60 minutes. Children usually wake up 30 to 45 minutes after dose administration. However, the effects of chloral hydrate may persist for 4 to 8 hours [Kao et al., 1999]. There is a paucity of information on the post-discharge side effects of chloral hydrate sedation for dental treatments in children. Because of the long half-life of the active TCE metabolite, 6 to 10 hours, injury or death has been reported after releasing patients from medical care [Lovinger et al., 1993]. Adverse effects were reported after discharge in children who had received chloral hydrate in doses of 72 mg/kg and 78 mg/kg for sedation prior to Computed Tomography and Magnetic Resonance imaging [Hubbard et al., 1992]. These effects included sleepiness lasting longer than 4 hours post discharge, unsteadiness, hyperactivity, vomiting, and poor appetite. We did not monitor this data in our study protocol. To our knowledge, none of the children who had participated in the study reported any serious study-related adverse events to the study dentist.

Chloral hydrate continues to be prescribed for procedural sedation for dental treatments for infants and children in spite of the availability of agents with a rapid onset, shorter duration of action such as midazolam [Kil et al., 2003]. Disadvantages of chloral hydrate include a steep dose-response curve relationship making it difficult to titrate the desired level of sedation against adverse effects [Wilson, 1995]. Limitations to the present study include lack of comparison of the effects of chloral hydrate in a non-asthmatic control group. Therefore, these observations may be due to an overall effect of chloral hydrate rather than a specific effect on asthmatic patients. Post-discharge adverse effects related to chloral hydrate were not monitored. Further investigation of alternative agents to chloral hydrate for pediatric sedation is necessary.

References

› Adrete JA, Itkin IH. Effects of chloral hydrate on the respiration of nonasthmatic and asthmatic patients. J Allergy 1969;43(6):342-348.
› Avalos-Arenas V, Moyao-Gracia D, Nava-Ocamp AA, Zayas-Carranza RE, Fragoso-Riso R. Is chloral hydrate /hydroxyzine a good option for paediatric dental outpatient sedation? Curr Med Res Opin 1998;14(4):219-226.
› Barone MA. The Harriet Lane handbook: a manual for pediatric house officers. 14th ed. St. Louis: Mosby; 1996. p. 505.
› Brown P, Mayer B, Zavestoski S, Luebke T, Mandelbaum J, McCormick S. Clearing the air and breathing freely: the health politics of air pollution and asthma. Int J Health Serv 2004; 34 (1):39-63.
› Campbell RL, Ross GA, Campbell JR, Mourino AP. Comparison of oral chloral hydrate with intramuscular ketamine, meperidine, and promethazine for pediatric sedation-preliminary report. Anesth Prog 1998 Spring;45(2):46-50.
› Cote CJ. Adverse sedation events in pediatrics: analysis of medications used for sedation. Pediatrics 2000;106(4):633-644.
› Debley JS, Carter ER, Gibson RL, Rosenfeld M, Redding GJ. Asthma morbidity and treatment in the Chicago metropolitan area: one decade after national guidelines. Ann Allerg Asthma Immunol 2005;95(1):95-25.
› Duncan WK, DeBall S. Chloral hydrate sedation: a simple technique. Compend Contin Educ Dent 1994;15(7):884-893.
› Evans D, Mellins R, Lobach K et al. Improving care for minority children with asthma: Professional education in public health clinics. Pediatrics 1997;99:157-164.
› Fredberg JJ. Bronchospasm and its biophysical basis in airway smooth muscle. Respir Res 2004 Feb 26; 5(1):2.
› Grant EN, Malone A, Lyttle CS, Weiss KB. The prevalence of ibuprofen-sensitive asthma in children: a randomized controlled bronchoprovocation challenge study. J Pediatr 2005;147(2):233-238.
› Greenberg SB, Faerber EN, Aspinall CL, Adams RC. High dose chloral hydrate sedation for children undergoing MR imaging: safety and efficacy in relation to age. AJR 1993;161:639-641.
› Houpt M. Project USAP 2000-of sedative agents by pediatric dentists: 15-year follow-up survey. Pediatr Dent 2002;24:289-294.
› Hubbard AM, Markowitz RJ, Kimmel B, et al. Sedation for pediatric patients undergoing CT and MRI. J Comput Assist Tomgr 1992;16:3-6.
› Kao SC, Adamson SD, Tatman LH, Berbaum KS. A survey of post-discharge side effects of conscious sedation using chloral hydrate in pediatric CT and MR imaging. Pediatr Radiol 1999;29:287-290.
› Keidan I, Gozal D, Minuskin T, Weinberg M, Barkaly Augarten A. The effect of fasting practice on sedation with chloral hydrate. Pediatr Emerg Care 2004;20(12):805-807.
› Kil N, Zhu FJ, Van Wagnen C, Abdulhamid I. The effects of midazolam on pediatric patients with asthma. Pediatr Dent 2003;25(2)137-142.
› Leelataweewud P, Vann WF, Dilley DC, Lucas WJ. The physiological effects of supplemental oxygen versus nitrous oxide/oxygen during conscious sedation of pediatric dental patients. Pediatr Dent 2000;22:125-133.
› Lovinger DM, Zimmerman SA, Levitin M, Jones MV, Harrision NL. Trichloroethanol potentiates synaptic transmission mediated gamma-aminobutyric acidA receptors in hippocampal neurons. J Pharmacol Exp Ther 1993;264(3):1097-1103.
› Mellon M, Parasuramam B. Pediatric asthma: improving management to reduce cost of care. J Manag Care Pharm 2004 Mar-Apr; 10(2):130-41
› National Asthma Education and Prevention Program. Expert Panel Report 2: guidelines for the diagnosis and management of asthma. NIH publication 97-4051. Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health, 1997.
› Pershad J, Palmisano P, Nichols M. Chloral hydrate: the good and the bad. Pediatr Emerg care 1999;15(6):432-435.
› Reeves ST, Wiedenfeld KR, Wrobleski J Harden CL, Pinosky ML. A randomized double-blind trial of chloral hydrate/hydroxyzine versus midazolam/acetaminophen in the sedation of pediatric dental outpatients. ASDC J Dent Child 1996;63(2):95-100.
› Slovis TL, Parks C, Reneau D et al. Pediatric sedation: short-term effects. Pediatr Radiol 1993;23:345-348.
› Steinbacher DM, Glick M. The dental patient with asthma: An update and oral health considerations. JADA 2001;132;1229-1239.
› Surveillance for asthma-United States, 1980-1999. MMWR 2002;51;1-12.
› Ten Thoren C, Petermann F. Reviewing asthma and anxiety. Resp Med 2000;94:409-415.
› Wheeler DS, Jensen RA, Poss WB. A randomized, blinded comparison of chloral hydrate and midazolam in children undergoing echocardiography. Clin Pediatr (Phila) 2001;40(7):381-387.
› Wilson S. Chloral hydrate and its effect on multiple physiological parameters in young children: a dose response study. Pediatr Dent 1992;14:171-177.
› Wilson S. Review of monitors and monitoring during sedation with emphasis on clinical applications. Pediatr Dent 1995;17(7):413-418.
› Wogelius P, Poulsen S, Sorenson HT. Asthma, ear problems, an dental anxiety among 6 to 8 yr olds in Denmark: a population-based cross-sectional study. Eur J Oral Sci 2003;111:472-476.
› Wood DW, Downes JJ, Lecks HI. A clinical scoring system for the diagnosis of respiratory failure. Am J Dis Child 1972;123;227-228.
› Yeatts K, Davis KJ, Sotir M, Herget C, Shy C. Who gets diagnosed with asthma? Frequent wheeze among adolescents with and without a diagnosis of asthma. Pediatrics 2003;111:1046-1054.
› Zhu JF, Hildalgo HA, Holmgreen WC, Redding SW, Hu J, Henry RJ. Dental management of children with asthma. Pediatr Dent 1996;18:363-370.