Chloral Hydrate Administered by a Dedicated Sedation Service Can Be Used Safely and Effectively for Pediatric Ophthalmic Examination

MOHAMMED KARAOUI, VARSHINI VARADARAJ, BEATRIZ MUNOZ, MEGAN E. COLLINS, LEYLA ALI ALJASIM, ESAM AL NAJI, KARAM HAMWEYAH, MOHAMMED AL SHAMRANI, EARL RANDY CRAVEN, AND DAVID S. FRIEDMAN

• PURPOSE: To determine safety and efficacy of oral chloral hydrate sedation (CHS) for outpatient pediatric ophthalmic procedures.

• DESIGN: Prospective, interventional case series.

• METHODS: Setting: King Khaled Eye Specialist Hospital. Subjects: Children aged 1 month to 5 years undergoing CHS for ocular imaging/evaluation. Procedures: Details on chloral hydrate dose administered, sedation achieved, vital signs, and adverse events were recorded. Outcome Measures: Primary outcome was percentage of patients with a sedation level ≥ 4 at 45 minutes post chloral hydrate administration. Secondary outcomes were time from sedation to discharge and adverse events, including changes in vital signs following chloral hydrate administration.

• RESULTS: A total of 324 children were recruited with a mean age of 2.2 (SD: 1.3) years and mean weight of 10.9 (SD: 3.3) kg. Adequate sedation was obtained with a mean chloral hydrate first dose of 77.4 (SD: 14.7) mg/kg in 306 (94.4%) patients, with an additional 6 patients (1.9%) achieving adequate sedation with a second dose (overall adequate sedation: 96.3%). Mean reductions in heart rate, respiratory rate, and oxygen (O_2) saturation from pre-sedation to 25 minutes post-sedation were 11.7 (SD: 14.3) beats per minute, 1.2 (SD: 2.4) breaths per minute, and 0.81% (SD: 1.2%), respectively ($P < .001$ for all). In multivariable regression, odds of remaining sedated 45 minutes after chloral hydrate administration were 2.53 times higher for American Society of Anesthesiologists (ASA) class II or III patients than for ASA class I (95% confidence interval [CI]: 1.11–5.78, $P = .03$), 1.03 times higher per mg increase in initial dose of chloral hydrate (95% CI: 1.01–1.06, $P = .006$), and 2.70 times higher per unit increase in number of planned procedures (95% CI: 1.63–4.47, $P < .001$). Three patients developed minor adverse events: 2 cases of O_2 desaturation and 1 paradoxical reaction, none requiring significant intervention. Patients were discharged a median of 90 minutes after chloral hydrate administration.

• CONCLUSION: Chloral hydrate administered by a dedicated sedation service, as in this prospective assessment, can be used safely and effectively for outpatient pediatric ophthalmic procedures. (Am J Ophthalmol 2018;192:39–46. © 2018 Elsevier Inc. All rights reserved.)

POOR COOPERATION AMONG INFANTS AND YOUNG children undergoing diagnostic and therapeutic procedures often necessitates the use of sedation or anesthesia to allow for adequate immobilization and successful completion of the procedure. There has been considerable debate around the choice of sedative or anesthetic in the pediatric ophthalmology community[1–3] and beyond.[4–7] While general anesthesia (GA) is frequently used for its reliability in producing a uniform anesthetic response, it is time consuming, resource intensive, expensive, and not without complications.[6,8,9] A recent crossover study from Canada assessing costs of GA vs chloral hydrate sedation (CHS) in a pediatric ophthalmology clinic reported substantial savings with CHS; mean cost per patient was $406 (Canadian) for CHS compared to $1135 for GA.[10]

Results from earlier studies indicate that CHS might be an effective alternative to GA in children,[11] proving to be especially convenient in outpatient settings.[1] Chloral hydrate has been used historically for procedural sedation in many settings, including in the fields of pediatrics,[12] dentistry,[7] and radiology,[13–16] and to a lesser extent in pediatric ophthalmology.[1,17] While studies reporting CHS use date back to 1961,[18] it has not been consistently used for sedation in pediatric ophthalmology, and its use has overall decreased in recent decades for various reasons, including pungent taste, paradoxical agitation, hepatotoxicity, prolonged duration, and lack of reversal agent.

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From the King Khaled Eye Specialist Hospital and Research Center, Riyadh, Saudi Arabia (V.V., B.M., M.E.C., E.R.C., D.S.F.); and Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA (M.K., L.A.D., E.A.N., K.H., M.A.S., E.R.C.).

Inquiries to David S. Friedman, Wilmer Eye Institute, Johns Hopkins University School of Medicine, 600 N. Wolfe St, Baltimore, MD 21287; e-mail: David.Friedman@jhu.edu

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Reports of variability in success rates,[14,19] concerns about adverse effects,[20,21] and lack of agreement around the ideal dose for sedation[4] have likely limited its more widespread use.

While audits and retrospective reviews have indicated that CHS is overall both safe and effective,[17] prospective evaluations are limited.[1,22,23] We therefore, conducted a prospective study to determine the efficacy of oral CHS by assessing the success rate for performing a complete ophthalmic or imaging evaluation in young children, and its safety by assessing adverse events related to sedation. We also sought to determine the dose of chloral hydrate (CH) required to achieve adequate sedation, measure the time to sedation and recovery, and identify any risk factors for sedation failure.

METHODS

THIS WAS A PROSPECTIVE, NONRANDOMIZED STUDY CONducted at King Khaled Eye Specialist Hospital (KKESH), Riyadh, Saudi Arabia from April 1, 2014 to August 29, 2016 in collaboration with the Wilmer Eye Institute at Johns Hopkins Hospital, Baltimore, Maryland, USA. This study conformed to the standards set forth by the Declaration of Helsinki, and all study procedures were prospectively approved by the KKESH and Johns Hopkins Medicine Institution Review Boards. It was registered at ClinicalTrails.gov (NCT02985567). Informed written consent was obtained prior to study enrollment from parents of subjects who were undergoing tonometry (in a separate paper, we study the effect of CH on intraocular pressure). Oral consent was obtained from parents of all other subjects not undergoing tonometry, as only standard clinical procedures were being followed without any study-related intervention.

• **STUDY POPULATION:** Children aged 1 month to 5 years who were undergoing CHS for ocular imaging/evaluations or ophthalmic care at KKESH were eligible to participate. Children meeting any of the following criteria were excluded: (1) weight < 3 kg or > 20 kg, (2) ocular surface disease/infection, (3) medical contraindication to CH, including children requiring concurrent medications that contraindicated administration of CH as determined by the prescribing physician; green or gray nasal discharge, fever, productive cough, chest retractions, or other signs of respiratory infection; oxygen saturation $< 90\%$; active infectious disease such as rubella or varicella; rectal/tympanic temperature > 37.7 C, or oral/temporal artery temperature > 37.2 C; history of current vomiting and diarrhea; anemia (Hgb < 9 g/dL); or history of seizure within 6 weeks of the sedation procedure.

• **STUDY PROCEDURES:** A study ophthalmologist and 1 of 2 pediatricians overseeing sedation procedures reviewed subjects' medical and ocular history to exclude patients in whom CHS was contraindicated. As per standard protocol at KKESH, 2 designated pediatricians are responsible for careful evaluation (history, physical examination, and laboratory testing) of all children planned for CHS as well as the supervision of all CHS procedures taking place outside the operating rooms. For children with any history of a neurologic, cardiac, renal, or chronic respiratory issue, among others,[17] a detailed medical record was sought from the primary physician to ensure suitability for safe CHS.

American Society of Anesthesiologists (ASA) Classification of Physical Status was assigned to all patients.[24] Demographic (age and sex) and medical information (ocular diagnosis, current medications, and surgical history) were recorded from the clinical charts for all recruited subjects.

The established code of sedation procedures at KKESH is based on protocol recommendations of the American Society of Anesthesia[25] and American Academy of Pediatrics.[26] The details of the protocols followed for administration of CHS have been previously published.[17] Briefly, all solid food and nonhuman milk was withheld from patients 6 hours prior to procedures, human milk was withheld 4 hours prior to procedures, and all other fluids including water were withheld 2 hours prior to procedures, as per the protocol's nil per os (NPO) guidelines, and CH was administered orally as a pharmacy-prepared solution containing 150 g of CH, 250 cc of sterile water, and 500 cc of strawberry flavored syrup. Children younger than 6 months of age received a target dose of 50 mg/kg (0.25 mL/kg), and all others received a target dose of 100 mg/kg (0.50 mL/kg). Since patients >20 kg were excluded, the largest initial dose was no more than 10 mL. The drug was administered orally between the child's cheek and middle molar in 1-cc increments with close monitoring of spitting up/ingestion of the drug. A second dose, consisting of half of the first dose (therefore, total dose not exceeding 15 mL), was administered at the discretion of the overseeing pediatrician if a patient was not adequately sedated 45 minutes post ingestion of the first dose.

Following administration, we prospectively monitored the success rate of CHS and the occurrence of adverse events related to administration of CH. Sedation level ranging from 1 to 6 based on a modified Ramsay scale,[27] as shown in Supplemental Table 1 (Supplemental Material available at AJO.com), was documented every 10 minutes from 25 minutes post ingestion of CH up to a maximum of 135 minutes post ingestion. Sedation was considered adequate if a sedation level of 4 was achieved within 45 minutes of CH ingestion.

The monitoring of sedation included documentation of the following: (1) vital signs: heart rate (HR), respiratory rate (RR), and oxygen (O_2) saturation every 10 minutes from 25 minutes after start of sedation to a maximum of