Oral chloral hydrate versus intranasal dexmedetomidine for sedation of children undergoing computed tomography: a multicentre study

VMY Yuen *, DKL Cheuk, TWC Hui, ICK Wong, WWM Lam, MG Irwin

KEY MESSAGES

1. Intranasal dexmedetomidine at 3 µg/kg can be used as primary sedative for young children during non-painful procedures. The rate of successful sedation is similar to that achieved by oral chloral hydrate at 50 mg/kg.

2. Intranasal dexmedetomidine is associated with better acceptance by young children compared with oral chloral hydrate.

3. Adverse effects of vomiting and gastrointestinal problems associated with chloral hydrate sedation may be avoided with the use of intranasal dexmedetomidine.

4. The time to resume normal activities after chloral hydrate and dexmedetomidine sedation is similar.

[1] VMY Yuen, [2] DKL Cheuk, [3] TWC Hui, [4] ICK Wong, [5] WWM Lam, [5] MG Irwin

[1] Department of Anaesthesiology, The University of Hong Kong Shenzhen Hospital
[2] Department of Pediatric and Adolescent Medicine, Queen Mary Hospital
[3] Department of Anaesthesiology, Queen Mary Hospital
[4] UCL School of Pharmacy, London, UK
[5] Department of Anaesthesiology, The University of Hong Kong

* Principal applicant and corresponding author: vtang131@hku.hk

Introduction

Chloral hydrate is a widely used sedative for young children undergoing imaging studies, with a high success rate. However, post-discharge adverse effects of chloral hydrate sedation are significant, including sleepiness for >4 hours, unsteadiness, hyperactivity, poor appetite, and vomiting.[1] In 54% of the children, normal activity is not resumed within 4 hours of discharge.

Dexmedetomidine is a highly selective alpha-2 agonist for paediatric sedation. It produces sedation similar to natural non-rapid eye movement sleep and has respiratory-sparing effect. It can be administered in an intravenous formulation or intranasally at 1-2 µg/kg to produce sedation before anaesthesia induction in children.[2,3] As dexmedetomidine has a much shorter half-life than chloral hydrate, its recovery profile is better. This study aimed to determine whether children sedated with intranasal dexmedetomidine resume normal activity more quickly than those with oral chloral hydrate.

Methods

This double-blinded, randomised controlled trial was approved by the Institutional Review Board of The University of Hong Kong / Hospital Authority Hong Kong West Cluster. It was conducted at Queen Mary Hospital and Guangzhou Women and Children's Medical Center. Children with American Society of Anesthesiologists physical status of 1 or 2 who required sedation for computed tomography study were recruited. After obtaining written informed consent from parents or legal guardian, children were enrolled. Exclusion criteria included allergy or hypersensitivity to dexmedetomidine, organ dysfunction, cardiac arrhythmia, congenital heart disease, or mental retardation.

The primary objective was to compare the proportion of children who could resume normal activity within 4 hours. Secondary outcomes included the success rate of sedation and completion of the imaging studies, the incidence of poor behaviour with oral and nasal drug administration, adverse respiratory and haemodynamic events, sleepiness for >4 hours, unsteadiness, hyperactivity, poor appetite, and vomiting.

Recruited children was randomly allocated to the chloral hydrate or dexmedetomidine group. The oral and nasal drug and placebo was produced by the Department of Pharmacy of either hospital. The pharmacists who prepared the drugs were not involved in recruitment or data collection.

After baseline blood pressure, pulse rate, and oxygen saturation were recorded, children in the chloral hydrate group received oral chloral hydrate at 50 mg/kg 30 minutes before imaging study and intranasal placebo. Children assigned to the dexmedetomidine group received 3 µg/kg intranasal dexmedetomidine 30 minutes before imaging study

and oral placebo. The acceptability of intranasal drug and oral drug was assessed using the behavioural scale, with crying or resisting defined as 1, anxious but accept as 2, and calm and cooperative as 3. All adverse events including vomiting, desaturation to <95%, apnoea episodes, requirement of airway support and intervention, and haemodynamic disturbances were recorded. Blood pressure, pulse rate, and oxygen saturation was recorded every 5 minutes. Sedation status was assessed and recorded every 5 minutes using the University of Michigan Sedation Scale, with awake/alert defined as 0, minimally sedated (tired/sleepy, appropriately responds to verbal conversation and/or sounds) as 1, moderately sedated (somnolent/sleeping, easily aroused with light tactile stimulation) as 2, deeply sedated (deep sleep, arousable only with significant physical stimulation) as 3, and unarousable as 4. Children was judged to be successfully sedated when the sedation score was ≥2 and computed tomography was performed as planned.

Before discharge, parents were given a post-sedation survey related to their child's behaviour and recovery at home to be completed over the next 24 hours. Parents were contacted the following day for collection of data on the time of resumption of normal activity, duration of sleepiness, presence of unsteadiness, and adverse effects including hyperactivity, poor appetite, and vomiting. Children was considered to have resumed normal activity when their University of Michigan Sedation Scale score was 0 or 1, when they were able to tolerate clear fluid or normal diet, ambulate or support himself, and communicate in the usual way.

Only 46% of the children could resume normal activity within 4 hours of discharge.[1] Our sample size estimation was based on the number of children needed to demonstrate clinically significant difference in return to normal activity within 4 hours of discharge. A total of 93 children per group is required if the proportion of children who resumed normal activity within 4 hours was increased by 20% with intranasal dexmedetomidine, with 80% power and 5% false positive rate.

The Chi-squared test was used to compare the proportion of children who resumed normal activity within 4 hours of discharge. The time taken for children to resume activities was shown in cumulative frequencies and compared using the log-rank (Mantel-Cox) test. The association between drug, age, and successful sedation was assessed using binomial logistic regression analysis. Behaviour during oral or nasal drug administration was categorised as poor when the behaviour score was 1, and acceptable when the score was 2 and 3. The incidence of poor behaviour and vomiting of the two groups was compared using Chi-squared test or Fisher's exact test. Hypotension and bradycardia was defined as blood pressure and heart rate of <20% of the age-specified normal range.[4] Hypoxia is a decrease of oxygen saturation to <95% or >5% from baseline. Statistical analyses were performed using SPSS (Windows version 20; IBM Corp, Armonk [NY], US). A P value of <0.05 was considered statistically significant.

FIG. Time to resume normal activities after sedative discharge

Results

A total of 196 children were randomised to receive allocated sedation. Of them, two withdrew after drug administration: one from the chloral hydrate
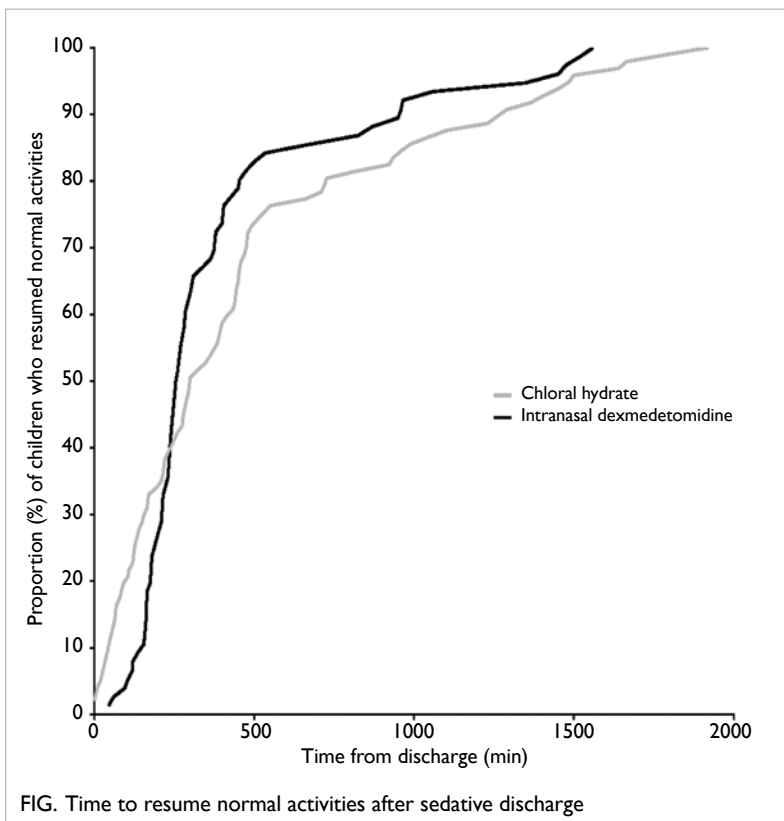
TABLE. Proportion of patients who experienced hypotension, bradycardia, and hypoxia

	Chloral hydrate (n=107)	Dexmedetomidine (n=87)	P value
Incidence of hypotension			0.0058
<12 months	0/21	0/8	
13-36 months	5/64	4/52	
>36 months	4/23	5/28	
Incidence of bradycardia			0.0016
<12 months	3/21	6/8	
13-36 months	0/64	4/52	
>36 months	0/23	4/28	
Incidence of hypoxia requiring oxygen therapy	2/108	0/88	0.048

group because of high fever and the other from the dexmedetomidine group because of refusal of data collection by the parent. Ten patients from the chloral hydrate group and 11 from the dexmedetomidine group failed to return the post-sedation survey. Therefore, data of 194 children were analysed for association between drug and successful sedation, behaviour, and adverse effects. Data from 175 children were analysed for the time to resume normal activities and post-sedation adverse effects.

The chloral hydrate and dexmedetomidine groups were comparable in terms of the proportion of children who resumed normal activities within 4 hours of discharge (39% vs 42%, P=0.76), the mean time to resume normal activities (469.9 vs 396.4 minutes, P=0.129, Fig), and the proportion of children with successful sedation (75.7% vs 73.6%, P=0.459). More children from the chloral hydrate group had poor behaviour during oral drug administration (P=0.0075). The two groups were similar in terms of behaviour during nasal drug administration (P=1.00). Six (5.6%) of 108 children from the chloral hydrate group and none from the dexmedetomidine group vomited after drug administration (P=0.0337). Two children and none in the respective groups experienced hypoxia required oxygen supplementation; the magnitude of hypotension and bradycardia was mild, and no child required medical intervention for haemodynamic disturbances (Table). None experienced bradycardia had hypotension. Overall, more children who received chloral hydrate had hypotension (P=0.0058) and hypoxia requiring oxygen therapy (P=0.048), and more children who received dexmedetomidine had bradycardia (P=0.0016).

The incidence of post-sedation adverse effects was low and did not significantly differ between groups except for motor imbalance (6.2% vs 0%).

Discussion

The rate of successful sedation was similar in children who received oral chloral hydrate (50 mg/kg) or intranasal dexmedetomidine (3 µg/kg). Chloral hydrate is the most common sedative for non-painful procedures in young children because of the low cost and high success rate. Nevertheless, chloral hydrate is bitter to taste with pungent odour and associated with spitting and vomiting. Intranasal dexmedetomidine has similar success rate and can be an alternative.

Although dexmedetomidine is a more expensive than chloral hydrate, it is easier to administer and is associated with less aversive behaviour during drug administration. It was difficult to elucidate the incidence of nausea associated with oral chloral hydrate; approximately 5% of the children vomited after its administration. Fewer than 2% of the children who received chloral hydrate experienced

oxygen desaturation and required oxygen therapy. The incidence is similar to that reported in previous study.[5] Incidence of desaturation is even lower with dexmedetomidine sedation.

Similar to previous reports, the most common complications associated with chloral hydrate after discharge is motor imbalance. The incidence of other adverse effects (restlessness, hyperactivity, agitation, and gastrointestinal disturbance) was low and similar between groups.

Although dexmedetomidine has a much shorter half-life with no active metabolites, the time to resume normal activities was similar between groups. This is a surprising finding; it is possible that the difference is small and our sample size is inadequate to detect such a small difference. It is also possible that young children are more sensitive to the effect of sedatives which in turn leads to prolonged recovery.

Conclusions

Intranasal dexmedetomidine 3 µg/kg and oral chloral hydrate 50 mg/kg are comparable in terms of the success rate for sedation in young children for imaging study. Although dexmedetomidine is associated with better behaviour and fewer gastrointestinal adverse effects during drug administration, the recovery profile of the two drugs is similar.

Acknowledgement

References

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