Dexmedetomidine improves success of paediatric MRI sedation.

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What is known about this topic?

- Sedation is often necessary for young children undergoing diagnostic imaging, especially MRI.
- Oral midazolam is usually ineffective, despite being recommended by NICE
- Dexmedetomidine has been used for paediatric sedation internationally for over a decade but is not widely used in the UK.

What this study adds

- Intranasal dexmedetomidine is a well tolerated and effective alternative to oral midazolam for children >15kg and in children where chloral has previously been unsuccessful.

Abstract

Objective

To improve success rates of children requiring sedation for MRI.

Methods

Audits of sedation success for children attending for planned MRI using three different approaches: 1) NICE guidance (Chloral hydrate if <15kg and oral midazolam if ≥15kg) 2) Chloral hydrate for all patients 3) Chloral hydrate +/- intranasal dexmedetomidine if <15kg and intranasal dexmedetomidine alone if ≥15kg.

Results

74 patients had 85 MRI scan attempts. Overall success rates were significantly higher when using intranasal dexmedetomidine compared to following NICE guidance (81% vs 52% p = 0.017). Dexmedetomidine performed better than oral midazolam for the same indication (76% vs 33% p = 0.026). The side effect profile for dexmedetomidine was as reported in larger studies.

Conclusions

Intranasal dexmedetomidine is an effective alternative to oral midazolam for sedation for MRI and as a rescue medication where chloral hydrate has been ineffective.

Introduction

Sedation is frequently required for children undergoing MRI to avoid motion artefacts. NICE guidelines recommend oral chloral hydrate for children under 15 kg and oral midazolam for those over 15kg[1]. Sedation failure results in patient and parental distress, inefficient use of scanner time, multiple subsequent sedation attempts and/or having to perform scans under general anaesthesia. The latter involves additional risks, requires a specialist anaesthetic service and costs almost double that of a sedation-based service[2].

Dexmedetomidine is a colourless and odourless α2-agonist that can be painlessly administered intranasally to achieve serum concentrations equivalent to intravenous sedation doses. It has been used as a monotherapy at 1-4 micrograms/kg for sedation for a range of non-painful procedures including acoustic brainstem responses, EEG, CT and MRI[3]. It is also effective as a rescue/top-up sedative when 50mg/kg chloral hydrate has been ineffective[4]. Common side effects include a relative bradycardia and hypotension, which are rarely clinically significant requiring intervention[5]. The incidence of respiratory depression is considerably lower than that reported with midazolam[6].

We sought to assess the efficacy of three different protocols for paediatric sedation in our district general hospital.

Methods

We performed one retrospective and two prospective audits of the sedation success for patients attending the paediatric day assessment unit (PDAU) at North Middlesex Hospital. The retrospective audit covered an 11-month period from 28/2/2019-29/1/2020, when the NICE guidance was being followed with 50mg/kg p.o. chloral hydrate for children <15kg or 0.5mg/kg p.o. midazolam if ≥15kg ("epoch one"). Subsequently the local guideline was changed to recommend that only chloral hydrate was used, up to a maximal dose of 1g, and prospective audit performed from 4/2/2020-15/10/2020 ("epoch two"). In the third epoch (15/10/2020-21/5/2021) it was recommended to use chloral hydrate for children <15kg, with a top up dose of 2 micrograms/kg i.n. dexmedetomidine if

Ramsay Sedation score <4 and 4 micrograms/kg i.n. dexmedetomidine for children ≥15kg or any child who had failed sedation with another agent previously. Dexmedetomidine 100micrograms/ml was administered using a mucosal atomiser device. In all epochs children were fasted prior to sedation (minimum 6 hours for solids, 4 hours milk and 2 hours clear fluids). Sedation was contraindicated if the child was not fasted, acutely unwell, had a history of difficult airway, cardiac arrhythmia, neuromuscular disease, severe renal or hepatic impairment, or was using of digoxin (dexmedetomidine only). All children had continuous peripheral oxygen saturation monitoring and were escorted from the PDAU to the radiology department by a nurse trained in paediatric life support. In the 3rd epoch blood pressure monitoring was recommended pre-sedation and every 15-30mins after administration. Scans were considered successful if the images were sufficient for a paediatric radiologist to provide a diagnostic opinion.

Data collected during epoch one and two were age, scan type, agent used, weight, dose and scan success. During epoch three the baseline and lowest recorded HR and BP were also obtained.

Fisher's exact test was used to assess for differences between success rates the 1st and 3rd epoch and between midazolam and intranasal dexmedetomidine. Violations of normality were assessed with Shapiro-Wilk's test and consequently Kruskall-Wallis test used to assess for differences in age and weight between epochs.

Data were collected by the treating team as a quality improvement project so neither ethical nor research approvals were required.

Results

Study population

In total 74 children underwent 85 scan attempts. There were 33 scan attempts in epoch one, 20 in epoch two and 32 in epoch three. Two children had scans in 2 different epochs. All scans were MRIs, 81 of the head, 3 spine and 1 forearm. Median age was 3.25 years (IQR 2.1-4.5, minimum 0.25

maximum) and median weight 15.4kg (IQR 13.2-18.3) with no significant differences between epochs (Kruskall Wallis test p = 0.960 and 0.968 respectively).

Overall success by epoch

Sedation success rates were 17/33 (51.5%), 11/20 (55.0%) and 26/32 (81.2%) for epochs 1 to 3 respectively (Table 1). Success rates were significantly higher in epoch 3 than epoch 1 (Fisher's exact test p = 0.017).

Success by sedation method

There were 12 attempts using midazolam, 49 using chloral hydrate, 21 using dexmedetomidine, 2 using chloral and dexmedetomidine rescue and 1 using midazolam and chloral (Table 2).
The success rate of midazolam was 33.3% (4/12) and 76.2% (16/21) for dexmedetomidine (Fisher's exact test p = 0.026). The overall success for chloral hydrate was 65.3% (32/49). This was lower for patients ≥15kg (58.8%, 10/17) compared to those <15kg (67.9% 19/28) but did not meet statistical significance (Fisher's exact test p = 0.749).

Outcomes for children requiring multiple attempts at sedation

Ten children had multiple scan attempts using sedation (Table 3). Using the same sedation medication on a different day was never successful irrespective of medication used.

Side effect profile for children receiving dexmedetomidine

The observations of 18/21 children having 4 microgram/kg dexmedetomidine were available for review. During sedation 13/18 (72%) had a HR lower than the APLS normal range (defined as the 5th centile for age), but only 2 (11%) had a HR >20% lower than normal range. The median change in HR from baseline was 19% (IQR 15-24%). Two patients (11%) had a systolic blood pressure below APLS normal range. No patient required any interventions after review by a clinician. No grade 2 or higher adverse events were recorded.

Discussion

The long duration and noise of MRI scans often necessitates the use of sedation in both pre-school children and those with behavioural or learning difficulties. Although recommended by NICE, oral midazolam is often ineffective. We found replacing this with chloral hydrate did improve success rates slightly, but intranasal dexmedetomidine was the most effective agent. Intranasal dexmedetomidine is easy to administer even to non-compliant children unlike unpalatable chloral hydrate. Improving sedation success rates in a district general setting is important to reduce both the number of patients requiring repeat attempts either with sedation or under general anaesthesia (often in other hospitals).

Like published randomised controlled trials, we found that 2 microgram/kg intranasal dexmedetomidine is an excellent rescue medication where 50mg/kg chloral hydrate has been ineffective, avoiding having to reschedule the scan. Giving additional doses of chloral hydrate may also be effective, but as reported success rates are >95% with dexmedetomidine rescue we favour this approach.

We found the haemodynamic changes associated with dexmedetomidine similar to those reported in other larger series, with none requiring any intervention.

Although the cohorts in each epoch were similar in age and weight, other differences in patients or in the non-pharmacological approaches (e.g. use of earplugs in epoch three) could have confounded our results.

Despite these limitations we conclude that intranasal dexmedetomidine is effective as an alternative to oral midazolam and as a rescue medication after failed chloral hydrate. Larger comparative observational studies and randomised trials will be important to determine whether our new approach should be adopted more widely.

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Patient consent: Not required

Table 1 Patient demographics and success rates by epoch

	Epoch 1 (11 months)		Epoch 2 (8 months)	Epoch 3 (7 Months)		All Epochs
Drugs	<15kg: Chloral	≥15kg: Midaz	All patients: Chloral	<15kg: Chloral +/- 2mcg/kg Dexmed	≥15kg: 4mcg/kg Dexmed	
Patients*	30		18	30		74
Scan attempts	33		20	32		85
Age in months (Median+ IQR)	33 (29-59)		42 (26-53)	40 (23-49)		39 (26-54)
Weight in kg (Median +IQR)	14.6 (12.5-21.3)		15.1 (14.1-19.3)	15.7 (14.1-17.1)		15.4 (13.2-18.3)
Success per scan	52%		55%	81% Per protocol (n=29): 86%		
Chloral: Chloral hydrate 50mg/kg PO Max 1 g; Midaz: Midazolam 0.5mg/kg PO max 20mg Dexmed: Dexmedetomidine intranasal 2 or 4 microgram/kg max dose 200micrograms *Some patients had scans in multiple epochs						

Table 2 Success rates by medication used

	Patients	Success rate per scan
Midazolam	11	33% (4/12)
Chloral	43	65% (32/49)†
Dexmedetomidine	20	76% (16/21)*
Chloral + Dexmedetomidine	2	100% (2/2)
Chloral +Midazolam	1	0% (0/0)
** p<0.05 compared with midazolam, Fisher's exact test* *† If ≥15kg success was 58% (n=17) <15kg 69% (n=28), (weight unknown n = 4)*		

Table 3 Outcomes of multiple attempts on different dates

	1st	2nd	3rd
1	C	M	
2	M	M	
3	C	C	
4	C	D	
5	C	C	D
6	C	C	
7	C	D	
8	D	D	
9	D	C+D	
10	M	C	

C=Chloral, M=Midaz,
D=Dexmed
Red= failure
Green = success