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ABSTRACT

INTRODUCTION: Sedation is often used to optimise renography in children < 3 years, but it requires continuous monitoring.

METHODS: We discontinued routine use of chloral hydrate sedation of patients undergoing renography, and introduced that children < 2 years were placed in a child immobiliser for nuclear examinations at the Department of Paediatrics before being transported for renography. In addition, children < 3 years were offered melatonin, which is not a sedative. Chloral hydrate was given only if parents wanted sedation. We analysed the results from a consecutive series of patients undergoing renography from August 2010 to December 2015 and compared data from those who had been administered choral hydrate sedation with those who had received no sedation.

RESULTS: Renography was unaccomplished in 10% (3/30) of the choral hydrated sedated children and in 11% (54/512) of the non-sedated children (p = 0.83). Uncooperative children resulted in failed renography in 0% (0/3) and 39% (21/54) of cases, respectively (p = 0.46). Patients placed in a child immobiliser at the Department of Paediatrics had the greatest probability of achieving successful renography (p = 0.0013), the shortest renography procedure duration irrespective of melatonin use (p = 0.0001) and the lowest risk of a procedure duration > 60 minutes (p = 0.0004).

CONCLUSIONS: Renography can be performed without sedation. We recommend that children < 2 years be placed in a child immobiliser at the Department of Paediatrics before being transported for renography. Additional studies are needed to investigate the effects of melatonin.

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TRIAL REGISTRATION: not relevant.

Renography is often indicated in prenatally diagnosed renal or urinary tract anomalies [1] and after pyelonephritis [2, 3]. Decisions regarding surgical intervention are often based on the renography results [1, 4].

A prerequisite to a successful renography is that patients do not move for the duration of the 20-minute examination [4]. In 2012, approximately 60% of all Danish departments of clinical physiology and nuclear medicine used regular pharmacological sedation (i.e., chloral hydrate) for renography in children < 3 years [5].

Previously, chloral hydrate was used for sedation of children < 3 years who underwent renography at our centre. However, it is mandatory that children treated with chloral hydrate be monitored constantly throughout the procedure [6, 7]. This proved to be quite a burden at our facility, where roughly two hours of observation by a trained nurse was required for chloral hydrate-sedated children before, during and after their renography.

5-methoxy-N-acetyltrypamine (melatonin) is a pineal hormone that is widely used to treat sleep disorders [8]. It has been successfully used to induce sleep in children undergoing electrocardiograms, including in children < 3 years [7, 9-12]. Melatonin has also been used to induce sleep during testing for auditory cerebral palsy response in children aged from 12 months to six years [13], in magnetic resonance imaging studies of children [14] and as premedication of paediatric patients [15]. An important advantage of melatonin is that it has no major side effects and it is not considered a sedative [7].

To save children from the potential risks of sedation and to reduce the amount of resources required for constant monitoring, we discontinued regular use of choral hydrate and introduced use of melatonin as part of a new policy to accomplish renography in children in the summer of 2010. Previously, the child was lifted from the bed to a child immobiliser immediately before being placed in the gamma camera for renography. Unfortunately, however, the child frequently woke up. As part of the new policy, children < 2 years were now placed in a child immobiliser used for nuclear medicine scans already at the Department of Paediatrics. All parents were informed of the new policy, and if they preferred sedation with choral hydrate, this was given to the child.

We hypothesise that sedation with chloral hydrate may be avoided in paediatric renography patients. For this purpose, we registered the number of unaccomplished renographies and the length of renography in non-sedated patients so that we would subsequently be able to compare these with data from children who had been sedated with choral hydrate.

METHODS

The present study was a prospective, non-randomised,

ORIGINAL ARTICLE

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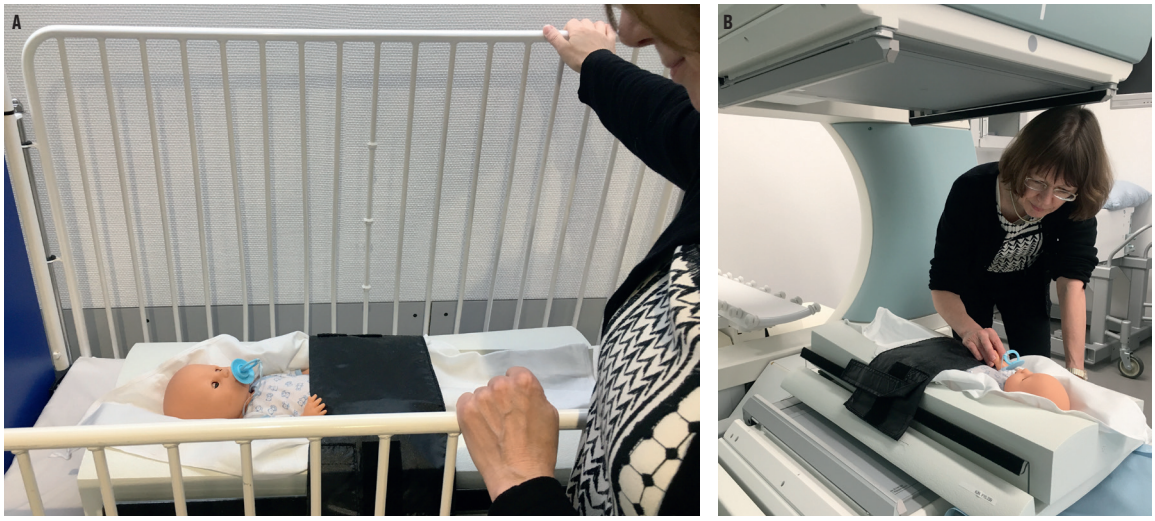
FIGURE 1

A. The mother brings the child to the Department of Clinical Physiology and Nuclear Medicine in the child immobiliser used for nuclear examinations. **B.** The mother is present throughout the procedure.
The "mother" in the photos is author Dina Cortes, the "child" is a doll.
Photos: authors Bente Ingvardsen and Pernille Lemvig.



observational study. It included a consecutive series of 542 patients < 3 years who underwent renography between 1 August 2010 and 31 December 2015 at Hvidovre Hospital, Denmark.

Parents were informed of the facility's change in policy with respect to renography without chloral hydrate sedation and informed consent was obtained for the treatment. Children could be placed in a child immobiliser at the Department of Paediatrics if they were < 2 years and if they had a crown-to-rump length < 71 cm. Furthermore, oral melatonin was offered to children < 3 years of age. When the study started, it had been published that the use of melatonin was safe in doses between 2 mg and 20 mg for children aged one year or more [9, 11, 14]. In adults, doses of 3-5 mg had been reported helpful to induce sleep in cases of jetlag [8]. Melatonin was dosed according to body weight, < 10 kg: 1.5 mg, 10-20 kg: 3 mg and > 20 kg: 6 mg, in accordance with the procedure for children who underwent electroencephalography at the department and in line with a Swedish report [10]. Patients who received melatonin did not have to fast before their renography.

Chloral hydrate sedation was given in cases where parents wanted sedation. An anaesthesiologist was contacted when there was any doubt if choral hydrate sedation was acceptable for that specific child.

To promote sleep, parents were encouraged to sleep-deprive their child prior to renography. Parents with children < 4 months were requested to feed their infant before renography, as infants generally sleep when satiated. All the time, the children were accompanied by their parents, so the child could be comforted as needed, **Figure 1**.

Renography was carried out using ^{99m}Tc-mercaptoacetyltriglycine, which was injected as a bolus at zero minutes. Furosemide 0.1 mg/kg was given if the tracer did not fill the kidneys sufficiently. Renography had a duration of 20 minutes [4].

At the Department of Clinical Physiology and Nuclear Medicine, the following variables were noted for each patient: age, if the patient arrived in the child immobiliser, melatonin administration, chloral hydrate administration, time of arrival at and departure from the department, time at start and end of renography, if renography was successful, and the reasons for unsuccessful renography. Start and end times were rounded up or down to the nearest five minutes. The procedure time for renography was defined as the time from arrival at the Department of Clinical Physiology and Nuclear Medicine to the end of the renography.

Data were registered continuously in most patients, but this failed in a few cases, which were consequently excluded. No patients were suspected of having liver diseases.

Patients were analysed in three age-groups: < 4 months, 4 months-1.9 years and 2.0-2.9 years. We compared the data of the patients who had choral hydrate sedation with the data of those who had no sedation to the rate of successful renography. The results of the non-sedated patients were analysed according to four different scenarios; arrival to renography in the child immobiliser and no melatonin administration, arrival in the child immobiliser and melatonin administration, arrival without the child immobiliser and melatonin administration, arrival without the child immobiliser and no melatonin administration.

Statistics

Descriptive statistics are given as numbers, medians and ranges. Continuous variables were compared using

the Mann-Whitney U or Kruskal-Wallis test, and categorical variables were compared using the Fisher's exact or Yates' corrected chi-squared test. In all cases, double-sided p-values were used. $p < 0.05$ was considered statistically significant. All analyses were carried out using Social Science Statistics [16] and OpenEpi [17].

Ethics

The study was conducted in accordance with the Helsinki II Declaration. Patient data were collected anonymously; it was not possible to connect the data to the person and therefore there was no need to apply for the approval from the Danish Data Protection Agency.

Trial registration: not relevant.

RESULTS

Renography was performed in 542 patients. The median age of the 30 patients who received chloral hydrate was 1.2 years (0.2-2.7 years). The median age of the 512 non-sedated patients was 0.7 years (0.1-2.9 years), ($p = 0.0002$).

The number of unsuccessful renographies was equal for chloral hydrate sedated and non-sedated patients; 10% (3/30) and 11% (54/512), respectively ($p = 0.83$). The primary reason for not completing a renography was a lack of a functioning intravenous access; 100% (3/3) in chloral hydrate-sedated patients and 61% (33/54) in non-sedated patients ($p = 0.46$). These chloral-hydrate sedated patients were 11, 12, and 17 months of age. Equivalently, the non-sedated patients aged from four months to 1.9 years had the highest risk of not having a functioning intravenous access ($p = 0.0005$), **Table 1**. Uncooperative children resulted in unaccomplished renography in 0% (0/3) of the sedated patients versus 39% (21/54) of the non-sedated patients ($p = 0.46$). The highest risk of uncooperative children appeared in non-sedated patients > 2 years ($p = 0.0037$), and in patients where only melatonin was used ($p = 0.0013$), Table 1.

The duration of the renography procedure was not significantly different for chloral hydrate-sedated and non-sedated patients; both had a median duration of 40 minutes and ranges of 25-75 minutes and 25-210 minutes, respectively, ($p = 0.36$). Without sedation, the duration of the renography procedure was shortest for children who arrived to renography in the child immobiliser, irrespective of melatonin use ($p = 0.0001$), **Table 2**. In patients > 2 years, the duration of the renography procedure was shortest for patients who did not arrive in the child immobiliser and had no melatonin to complete the examination ($p = 0.0093$), Table 2.

The frequency of a procedure duration > 60 minutes was not significantly different between chloral hydrate-sedated and non-sedated patients; 4% (1/27) and 14% (64/458), respectively, ($p = 0.22$). The non-sedated children who arrived in the child immobiliser to renography had the lowest risk of a renography procedure lasting > 60 minutes ($p = 0.0004$), **Table 3**.

DISCUSSION

Our study found that 90% of the renography proced-

TABLE 1

Renography in 512 non-sedated children stratified according to numbers and causes of the 54 unsuccessful renographies, shown as age-group frequencies. Unsuccessful renography in non-sedated children due to an uncooperative child.

	All patients		〈 4 mo.s		4 mo.s-1.9 yrs		2-2.9 yrs		
	% (n/N)	p-value[e]	% (n/N)	p-value[e]	% (n/N)	p-value[e]	% (n/N)	p-value[e]	p-value[f]
Renography									
Unsuccessful renography	11 (54/512)	-	3 (5/166)	-	14 (42/299)	-	15 (7/47)	-	0.0007[a]
Not functioning IV access	6 (33/512)	-	1 (2/166)	-	10 (30/299)	-	2 (1/47)	-	0.0005[a]
Uncoorperative child	4 (21/512)	-	2 (3/166)	-	4 (12/299)	-	13 (6/47)	-	0.0037[a]
Unsuccessful renography									
Arriving in child immobiliser only[a]	1 (1/121)		1 (1/77)		0 (0/44)		-		-
Arriving in child immobiliser and melatonin[b]	4 (5/140)	0.0013	0 (0/17)	0.0056	4 (5/123)	0.218	-	0.040	-
Melatonin only[c]	10 (12/118)		25 (1/4)		7 (6/84)		17 (5/30)		-
Arriving without child immobiliser and no melatonin[d]	2 (3/133)		1 (1/68)		2 (1/48)		6 (1/17)		-

IV = intravenous.
a) p-value between the 3 age groups: 〉 0.9999.
b) p-value between the 3 age groups: 〉 0.9999.
c) p-value between the 3 age groups = 0.2027.
d) p-value between the 3 age groups = 0.5449.
e) Between the 4 scenarios.
f) Between the 3 age groups.

TABLE 2

Duration of the renography procedure for 458 non-sedated children with a successful renography.

	Arriving in child immobiliser only		Arriving in child immobiliser and melatonin		Melatonin only		Arriving without child immobiliser and no melatonin		
Age-group	n	duration, median (range), min	n	duration, median (range), min	n	duration, median (range), min	n	duration, median (range), min	p-value
All patients	114	35 (25-130)	122	40 (25-110)	98	45 (30-210)	124	45 (25-150)	0.0001
⟨ 4 mo.s	74	35 (25-130)	17	35 (30-90)	3	60 (50-130)	67	45 (25-125)	⟨ 0.0001
4 mo.s-1.9 yrs	40	35 (25-120)	105	40 (25-110)	70	45 (30-210)	42	45 (25-150)	0.0052
2-2.9 yrs	-		-		25	45 (30-120)	15	35 (30-45)	0.0093

TABLE 3

The frequency of renography procedure duration ⟩ 60 minutes for 458 non-sedated children with a successful renography.

	Frequency, % (n/N)				
Age-group	arriving in child immobiliser only	arriving without child immobiliser and no melatonin	melatonin only	arriving in child immobiliser and melatonin	p-value
All patients	7 (8/114)	8 (10/122)	24 (24/98)	18 (22/124)	0.0004
⟨ 4 mo.s	7 (5/74)	12 (2/17)	33 (1/3)	18 (12/67)	0.1543
4 mo.s-1.9 yrs	8 (3/40)	8 (8/105)	24 (17/70)	24 (10/42)	0.0034
2-2.9 yrs	-	-	24 (6/25)	0 (0/15)	0.0396

ures were accomplished without chloral hydrate sedation, thus demonstrating that renography can be accomplished sedation-free. A previous study examining the use of melatonin versus chloral hydrate in auditory brainstem response testing in children aged 12 months to six years of age showed similar results [13]. The use of melatonin required adapted facilities to receive the child and its parents, including a quiet parent-child room [13]. We used a child immobiliser as an adapted facility. The use of a child immobiliser adheres to the guidelines for paediatric renography by the European Association of Nuclear Medicine, which recommends support of the child by either sandbags or Velcro straps or placement of the child in a vacuum cushion [4].

The present study found that children < 2 years who were placed in a child immobiliser before arriving at the Department of Clinical Physiology and Nuclear Medicine had the highest rate of successful renographies, the shortest procedure duration and the lowest risk of a procedure duration > 60 minutes. When the child was placed in the immobiliser at the Department of Paediatrics, it could arrive to renography in a state of sleep. Children aged > 2 years were too large to be placed in the child immobiliser, and in this group unsuccessful renographies were generally due to inability to immobilise the child during the procedure.

The most common reason why an unsuccessful renography was insufficient intravenous access, a problem occurring especially in children aged from four months to 1.9 years. Large skin folds are primarily seen in children aged from three months to about two years [18]. At this age, peripheral vessels are located relatively deep below the skin and can hinder the insertion of an intravenous line [19]. The frequency of successful renography can be increased if a functioning intravenous access is available when the patient arrives for renography.

This study did not reveal a specifically beneficial effect of melatonin, and the frequency of unsuccessful renography due to uncooperative children was highest if only melatonin was used. Recently, sequential administration of melatonin and hydroxyzine was reported to be effective in obtaining sleep during electrocardiogram recordings in children [7].

The strengths of our study include its prospective nature, the inclusion of many patients and the analysis of four alternatives to choral-hydrate sedation.

It is a limitation that our study was not a randomised case-control study. The choral-hydrate sedated children were older than those who did not receive sedation. There is a risk that the children who received chloral-hydrate sedation had more difficulty in laying still than those who had no sedation. Equivalently, we also found a shorter renography procedure duration for children aged two years who neither arrived in the child immobiliser nor received melatonin, compared with those who received melatonin. It is possible that more children who were expected to be uncooperative received melatonin. Another non-randomised study also reported that sedation with nitrous oxide resulted

in a higher voiding cystourethrography procedure time than in non-sedated patients [20]. After the study was initiated, it was reported that melatonin induces dose-dependent analgesic and sedative effects, and high doses of melatonin have been safely used even in newborns [15]. However, there is still no clear consensus as to which doses of melatonin should be administrated in children, but doses of 0.5 mg/kg [15] or 10 mg in all children [14] have been reported. Despite these limitations, we find that our results are important from a clinical point of view. We have shown that renography can be performed reliably and adequately without sedation in children < 3 years, which has been welcomed by families and staff alike while saving a substantial amount of staff resources.

CONCLUSIONS

Renogr aphy in children can be accomplished without sedation. Based on our findings, we recommend that children < 2 years be placed in a child immobiliser at the Department of Paediatrics before their arrival at the Department of Clinical Physiology and Nuclear Medicine for renography. This will shorten the duration of the procedure. A functioning intravenous access is mandatory. Further studies are needed to examine the effects of melatonin. The changed policy had the added benefit of saving substantial staff resources.

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