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Ketamine procedural analgosedation before and after introducing nitrous oxide 70% in a paediatric emergency department

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Summary

AIMS OF THE STUDY: The spectrum of agents available for procedural analgosedation (PAS) in paediatric emergency departments (EDs) has increased over the last few decades, yet the pharmacological agents most used in our ED are ketamine and nitrous oxide (N_2O). The aim of this study was to assess which patient characteristics in an ambulatory setting were associated with physicians selecting N_2O 70% or ketamine as the sedating agent in our paediatric ED, after N_2O 70% was introduced.

METHODS: Patients aged 0 to 16 years who received PAS in a tertiary children's hospital ED in 2007 (before N_2O 70% implementation) and 2016 (after N_2O implementation) were included in this retrospective, single-centre cohort study. Data were collected by querying the outpatient ED database for N_2O 70% and ketamine. Obtained data included patient characteristics, procedure type and sedation medication.

RESULTS: 1168 patients were included; 59.8% (699) were male. The overall mean age was 6.3 (± 4.0) years; in the ketamine subgroup, 4.6 (± 4.0) years and in the N_2O subgroup, 7.8 (± 3.4) years. In 2016, N_2O was chosen in 86.7% of cases involving children aged 4 to 16 years, compared to 28.5% of cases involving children three years and younger. The most apparent shift from ketamine to N_2O occurred in patients with displaced upper extremity fractures, with an increase of N_2O 70% from 0% in 2007 to 90.8% in 2016.

CONCLUSIONS: The use of ketamine PAS shifted to N_2O PAS, especially in children older than three years and for the reduction of displaced upper extremity fractures.

Keywords: *paediatric emergency department, nitrous oxide, ketamine, procedural analgosedation*

Introduction

Procedural analgosedations (PAS) in paediatric emergency departments (EDs) are challenging. On the one hand, appropriate pain control is of paramount importance to avoid psychological trauma for a child and on the other, several other factors must also be considered: the child's characteristics, the planned procedure, and the ED's resources (manpower, bed space) [1–4]. Although the spectrum of agents available for PAS has increased over the last two decades, our ED mainly uses two pharmacologic agents, ketamine and nitrous oxide (N_2O) [5–13].

Ketamine, a nonbarbiturate anaesthetic with an onset within seconds when applied intravenously, is a noncompetitive N-methyl-D-aspartate (NMDA) and glutamate receptor antagonist with sedative, analgesic, and amnestic properties. It is mainly used for short-term procedures that do not require skeletal muscle relaxation. Ketamine is metabolised via the hepatic system, with a half-life of approximately 45 minutes [7, 8]. Since the 1990s, it has become one of the most often used sedatives in paediatric EDs because it allows spontaneous respiration due to the maintenance of laryngeal and pharyngeal reflexes and is also associated with respiratory and cardiovascular stimulation [2]. Potential serious side effects of ketamine are, amongst others, apnoea and laryngospasms, as well as cardiac and respiratory arrest. Therefore, both close monitoring and highly trained personnel who can manage these complications are essential. In our ED, this PAS is performed exclusively by anaesthesiologists [5, 9].

Nitrous oxide (N_2O), a colourless, tasteless and odourless gas with sedative, analgesic, anxiolytic and amnestic effects, has been used in dental-care settings for decades, but was introduced into paediatric EDs only in the 1990s, mainly for minor, painful procedures like placing an intravenous line or suturing a laceration in anxious children [5, 9, 11–13]. For procedures with a high pain score, the analgesic power of N_2O 50% combined with 50% oxygen is insufficient, so N_2O 70% was introduced into our ED a decade ago. N_2O 70% is an almost ideal agent for PAS in children because it is sufficient for most short, painful procedures, and neither an intravenous line nor fasting is required. Furthermore, its onset is rapid and recovery takes only three to five minutes once the gas is withdrawn [13]. Adverse events are mainly nausea, vertigo and vomiting. Hence, a trained ED consultant performs these PAS without an anaesthesiologist in our ED [13].

Ketamine and N_2O 70% are routinely used for sedation in paediatric EDs. However, studies have focused mainly

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on adverse events and sedation practices [14–16]. Our local policy, with anaesthesiologists performing ketamine sedations, may not be representative of most paediatric ED practices but, to the best of our knowledge, we are the first to analyse the changes of PAS practice caused by the implementation of N_2O 70% in a paediatric ED.

The aim of this study was to assess which patient characteristics were associated with physicians selecting N_2O 70% or ketamine as the sedating agent in our paediatric ED after the introduction of N_2O 70%.

Material and methods

Patient population

Patients aged 0 to 16 years who received PAS in the ED of the University Children's Hospital Zurich in 2007 (before N_2O 70% implementation) and in 2016 (after N_2O 70% implementation) were included in this retrospective, single-centre cohort study. The local ethics board approved this study.

Data collection

Data was collected by querying our outpatient ED database for N_2O and ketamine. The clinical records of all patients included were reviewed and the following data were collected: demographics (age and gender), indication for PAS, choice of N_2O or ketamine, whether ketamine had to be chosen because of the insufficiency of N_2O sedation, adverse events of N_2O PAS, and who performed the procedure (ED physician or other specialist).

Procedural analgosedation

N_2O was applied through a facemask covering the patient's nose and mouth with a demand valve system, using the Ventyo machine (LINDE Gas GmbH, 4651 Stadl-Paura, Austria). No fasting period or intravenous line was necessary, parents were allowed to be present during PAS, and discharge was possible immediately following the procedure.

In contrast, ketamine PAS required the child to fast and receive an intravenous line. An anaesthesiologist performed the ketamine PAS and monitored the patient during and after the procedure until discharge. The parents were sent out of the room as soon as the child was analgosedated, and then the intervention was performed by either an ED physician or, in potentially more severe cases, a paediatric surgeon.

Statistics

Categorical data were described as frequencies, while continuous variables were described as means with standard deviation (SD). Statistical analyses were performed with IBM® SPSS® statistics version 24.

Results

A total of 1168 children were treated with PAS during the study period and were included in this study, of which 59.8% (699/1,168) were boys. Overall, 53.7% of children received N_2O 70% and 46.3% ketamine, most frequently for orthopaedic interventions (29.9%), wound suturing (25.9%), burn debridement (15%) and removal of foreign bodies (13.3%) as detailed in table 1.

The overall mean age was 6.3 (± 4.0) years; in the ketamine subgroup, the mean age was 4.6 (± 4.0) years, while in the N_2O subgroup it was 7.8 (± 3.4) years. Figure 1 illustrates the variability of the PAS chosen in different age groups in 2016. The use of N_2O in the age group up to three years was low (28.5%; 63/221), in contrast to the other age groups (4-16 years) where it was chosen in 86.7% (561/647) of cases.

An increase in PAS with N_2O and a corresponding decrease in ketamine use was observed from 2007 to 2016 (table 2). The most apparent shifts from ketamine to N_2O over the study period occurred in the patient group with displaced upper extremity fractures and in patients with

Figure 1: Procedural analgosedation in different age groups in 2016.Ketamine-ED: Intervention was performed by an ED physician; Ketamine-OR: Intervention was performed in the operation room by a paediatric surgeon (potentially more severe cases).

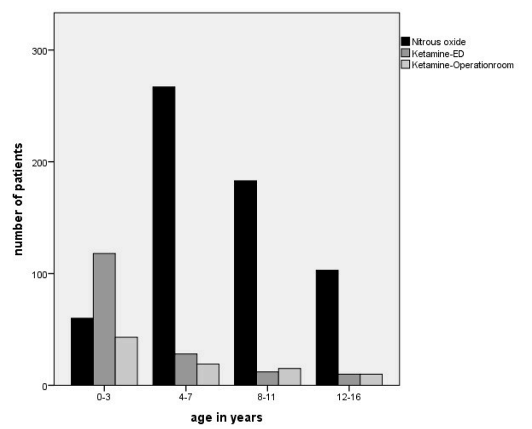

Table 1: Characteristics of patients who received nitrous oxide 70% (N_2O 70%) or ketamine

	Overall (n = 1168)	N_2O 70% (n = 627)	Ketamine (n = 541)
Mean age, y (SD)	6.3 (4.0)	7.8 (3.4)	4.6 (4.0)
Sex, male, n (%)	699 (59.8)	363 (57.9)	336 (62.1)
Procedures:			
Orthopaedic, n (%)	349 (29.9)	240 (38.3)	109 (20.1)
– Reduction upper extremity fracture, n	328	220	108
– Reduction lower extremity fracture, n	21	20	1
Wound suturing, n (%)	302 (25.9)	129 (20.6)	173 (32.0)
Burn debridement, n (%)	175 (15.0)	62 (9.9)	113 (20.9)
Removal of foreign body, n (%)	155 (13.3)	62 (9.9)	93 (17.2)
Abscess incision, n (%)	106 (9.1)	65 (10.4)	41 (7.6)
Other, n (%)	81 (6.9)	69 (11.0)	12 (2.2)

lacerations (table 3). The rate of N_2O for the reduction of upper extremity fractures increased from 0% to 90.8% (table 3). Suturing showed a less significant decrease in ketamine PAS; N_2O PAS increased from 0% to 61.1%, mainly in older children (mean age ± SD: with ketamine PAS, 3.3 ± 3.3 years compared to N_2O PAS, 6.6 ± 2.9 years) (table 4). Age and the affected localisations were decisive factors as to which PAS was chosen for suturing, as detailed in table 4. Similarly, a shift from ketamine PAS toward N_2O PAS occurred in burn debridement, but significant differences in mean age and amount of injured skin appeared between the two PAS groups. Children who received N_2O had a mean age of 5.8 (± 3.2) years compared to a mean age of 2.1 (± 2.3) years for children who received ketamine. Children who received N_2O had a mean affected body surface area of 1.6% (± 1.2), while children who received ketamine had a mean affected body surface area of 3.2% (± 2.4).

Adverse events, mostly nausea, vertigo and vomiting during and after N_2O PAS, occurred at a rate of 40%, although no serious adverse events occurred during N_2O PAS and the satisfaction rate among children and parents was over 95%. The N_2O PAS regime needed to be changed to ketamine in 1.8% (11/627) of all children who received N_2O, either because N_2O PAS was insufficient or because adverse events occurred. These children were mostly boys (81.8%) with a mean age of 7.8 ± 4.5 years. Indications for the PAS in these children were, amongst others, burn debridement (6.5%; 4/62), removal of foreign bodies (4.9%; 3/61), and reduction of upper extremity fractures (1.4%; 3/218).

The cost of treatment of a displaced upper-arm fracture with ketamine PAS were approximately twice as high as for N_2O 70% PAS (CHF 990 compared to CHF 470). Cost analysis showed that the main factor for the higher costs for ketamine PAS was the requirement of more medical personnel compared to N_2O PAS.

Discussion

This retrospective study analysed the change in PAS for children before and after introducing N_2O 70% in an ambulatory ED setting, with a shift from ketamine PAS to N_2O PAS, especially in children older than three years and most significantly for the reduction of displaced upper extremity fractures.

Choosing the best PAS for children in a paediatric ED depends on factors affecting the child, the planned procedure, the ED physician's experience, and the ED's and the institution's resources. First, N_2O PAS requires a cooperative child breathing strongly enough to open a demand valve system. In our study, this meant that N_2O PAS was only chosen for 28.5% of children three years and younger. An alternative to a demand valve system is a system with continuous flow, which might lower the possible age limit, but which brings with it the danger of increasing the concentration of N_2O in the room air above the legally set minimum alveolar concentration (MAC) values for N_2O [17]. Second, N_2O 70% is ideal for short, painful procedures and therefore it is mainly chosen for reduction of displaced fractures, small burn debridement, abscess incision and removal of foreign bodies, whereas ketamine is more suitable for longer and more painful procedures. It is noteworthy that in 2016, N_2O 70% PAS was chosen for fracture treatment in over 90% of cases of displaced forearm fractures. Ketamine PAS was chosen when a primary osteosynthesis was indicated, the child was too young for a demand

Table 2: Age groups and indications for sedations before (2007) and after (2016) introducing nitrous oxide 70% (N_2O 70%)

	2007 n = 298	2016 n = 870
N_2O 70%, n (%)	0	615 (70.7)
Ketamine – emergency department, n (%)	232 (77.9)	168 (19.3)
Ketamine – operating room*, n (%)	66 (22.1)	87 (10.0)
Age groups:		
– 0-3 years, n (%)	119 (39.9)	221 (25.4)
– 4–7 years, n (%)	104 (34.9)	314 (36.1)
– 8–11 years, n (%)	44 (14.8)	211 (24.3)
– 12–16 years, n (%)	31 (10.4)	124 (14.2)
Procedures:		
– Orthopaedic, n (%)	91 (30.5)	258 (29.7)
– Reduction upper extremity fracture, n	90	238
– Reduction lower extremity fracture, n	1	20
– Wound suturing, n (%)	94 (31.5)	208 (23.9)
– Burn debridement, n (%)	48 (16.1)	127 (14.6)
– Removal of foreign body, n (%)	36 (12.1)	119 (13.7)
– Abscess incision, n (%)	26 (8.7)	80 (9.2)
– Other, n (%)	3 (1.0)	78 (9.0)

* Intervention was performed by a paediatric surgeon (potentially more severe cases)

Table 3: Procedural analgosedation for reduction of upper extremity fractures and wound suturing in 2007 and 2016

	2007			2016		
	N_2O 70%*	Ketamine-ED**	Ketamine-OR***	N_2O 70%*	Ketamine-ED**	Ketamine-OR***
Reduction upper extremity fracture, n (%)	0	69 (76.7)	21 (23.3)	216 (90.8)	10 (4.2)	12 (5.0)
Wound suturing, n (%)	0	82 (87.2)	12 (12.8)	127 (61.1)	67 (32.2)	14 (6.7)

* nitrous oxide 70%; ** emergency department; *** operation room: intervention was performed by a paediatric surgeon (potentially more severe cases)

valve system, or was uncooperative about accepting a facemask. A less apparent shift from ketamine to N_2O 70% occurred in patients with lacerations. Ketamine PAS was administered in 80.6% of lip suturing cases in 2016, because it had been determined that local anaesthesia and anxiolytics were insufficient for this delicate repair. The vermilion border must be precisely repaired, even though lip lacerations are usually slight. However, these lacerations mostly occurred in children too young for N_2O PAS (2016 data: mean age 2.7 ± SD 2.6), which implies that age was the actual decisive factor for ketamine PAS. Similar results were found for burn debridement in 2016, where ketamine PAS was chosen for the younger children (mean age 2.1 years) and those with larger affected body surface areas (mean 3.2% ± SD 2.4). The third factor concerned the ED physician. An ED physician's experience with PAS as well as the planned procedure probably also influence the decision whether to choose N_2O or ketamine. This choice is determined by weighing benefits and risks in the context of the child's needs [18]. Fourth, the overall picture must be taken into consideration. In our ED, the following factors are considered: ED resources, crowding and the availability of the anaesthesiology team, which performs ketamine PAS. The fifth factor in choosing the best PAS concerns the institution's resources. A socioeconomic analysis tends towards N_2O PAS because less medication and fewer medical personnel are required, and there is a faster discharge and a lower risk of complication. In contrast, for ketamine PAS, children must be fasting and have an intravenous line placed. Anaesthesiologists are needed to perform the anaesthesia in our ED, and a place in the recovery ward must be organised. As a consequence, costs for ketamine PAS are approximately twice as high as for N_2O PAS.

Based on our data, we conclude that alternatives to N_2O are needed for children younger than three years and for procedures that require longer lasting effects of analgesia in order to improve efficacy and efficiency. For these cases, nasal application of ketamine might be an effective alternative to the intravenous route. Another alternative would be introducing newer pharmacologic agents like dexmedetomidine, which we are planning to include in our ED [19].

This study confirmed that N_2O 70% PAS is safe in that no serious adverse events occurred. A change from N_2O PAS to ketamine was documented in 1.8% of all children receiving N_2O, either because N_2O PAS was insufficient or because adverse events occurred.

Limitations

Several factors limit the interpretation and generalisation of these results. First, this was a retrospective and single-centre study. Second, patients and families were not asked by default about the pros and cons of the chosen PAS. Other potential limitations include the lack of data as to why a certain PAS was chosen and whether adverse events during ketamine PAS occurred.

Our local ED setting, which depended on the availability of the anaesthesiology team for ketamine PAS, differs from most ED settings.

Conclusions

The rate of ketamine PAS use shifted to N_2O PAS, especially in children older than three years and in the patient group with displaced upper extremity fractures. However, in children younger than three years and for interventions like wound suturing and debridement, ketamine PAS was chosen most frequently.

Disclosure statement

No financial support and no other potential conflict of interest relevant to this article was reported.

Table 4: Procedural analgosedation for wound suturing in 2016; age dependency and affected localisations

Localisations	Nitrous oxide	Ketamine	Total
Finger/Toe, n (%)	47 (64.4%)	26 (35.6%)	73
Age, years, mean (SD)	6.7 (± 2.4)	3.7 (± 2.9)	5.7 (± 3.8)
Lips, n (%)	6 (17.1%)	29 (82.9%)	35
Age, years, mean (SD)	5.3 (± 2.3)	2.2 (± 1.6)	2.7 (± 2.6)
Arm/Leg, n (%)	27 (90%)	3 (10%)	30
Age, years, mean (SD)	7.6 (± 2.4)	8.5 (± 5)	7.7 (± 3.3)
Chin, n (%)	18 (100%)	0	18
Age, years, mean (SD)	5.6 (± 2.5)		5.6 (± 2.5)
Nose/Ear	5 (29.4%)	12 (70.6%)	17
Age, years, mean (SD)	5.6 (± 1.3)	2 (± 0.6)	3.2 (± 1.9)
Cheek	8 (72.7%)	3 (27.3%)	11
Age, years, mean (SD)	4.1 (± 1.2)	2.7 (± 1.6)	3.7 (± 1.8)
Scalp	8 (88.9%)	1 (11.1%)	9
Age, years, mean (SD)	7.1 (± 1.8)	3	6.7 (± 2.5)
Eyebrow	4 (80%)	1 (20%)	5
Age, years, mean (SD)	8 (± 2)	3	7 (± 3)
Trunk	3 (75%)	1 (25%)	4
Age, years, mean (SD)	9.2 (± 1.9)	10	9.3 (± 2.1)
Genitals	1 (25%)	3 (75%)	4
Age, years, mean (SD)	6	7.7 (± 0.9)	7.3 (± 1.3)
Tongue	0	2 (100%)	2
Age, years, mean (SD)		1.5 (± 0.5)	1.5 (± 0.5)
All localisations	**127 (61.1%)**	**81 (38.9%)**	**208**
Age, years, mean (SD)	**6.6 (± 2.9)**	**3.3 (± 3.3)**	**5.3 (± 3.5)**

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