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Research Article

Procedural Analgosedation with Ketamine and Nitrous Oxide 70% in a Pediatric Emergency Department - from 2007 to 2016

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Abstract

Procedural analgosedation (PAS) in pediatric emergency departments (EDs) have experienced a considerable development over the last years, nevertheless the pharmacologic agents most used in our ED are ketamine and nitrous oxide (N_2O). The aim of this study was to assess the change of the PAS regimes in our pediatric ED from 2007- when N_2O 70% was introduced - to 2016. Patients aged 0 to 16 years who received PAS in a tertiary Children's Hospital ED between 1 January 2007 and 31 December 2016 were included in this retrospective, single-center cohort study. Data collection was performed by reviewing the clinical records of all included patients for N_2O and ketamine. The following data were collected: patient characteristics, procedure type, and sedation medication. A total of 6497 patients were included; 57.3% (3726) were boys. The overall mean age was 6.5 (± 4.1) years; in the ketamine group, 4.2 (± 3.6) years and in the N_2O group, 8.3 (± 3.5) years. N_2O was chosen in 73.2% of cases involving children aged 4 to 16 years, compared to 6.4% of cases involving children younger than three years. The patient subgroup with displaced upper extremity fractures accounted for the most apparent increase of N_2O 70% with a rate of 90.7% in 2016.

The implementation of N_2O PAS in our ED resulted in a decrease in ketamine PAS, especially in children older than three years with displaced upper extremity fractures requiring closed reduction.

Keywords: Pediatric Emergency Department; Emergency Department; Nitrous Oxide; Ketamine; Procedural Analgosedation

Abbreviations

PAS: Procedural Analgosedation; ED: Emergency Department; N_2O: Nitrous Oxide.

Introduction

Procedural analgosedations (PAS) in pediatric emergency departments (EDs) have experienced a considerable development over the last years. Intravenous ketamine used to be the drug of choice for PAS but as the number of ED consultation rose steadily, PAS regimes had to be optimized. Selecting the most suitable PAS for children depends on factors affecting the patient, the planned procedure, the ED physician's experience, and the institutional resources [1-3]. The spectrum of potential agents for PAS has increased over the last years, yet our ED primarily uses ketamine and nitrous oxide (N_2O) [4-13].

Ketamine is an anesthetic with analgesic, sedative, and amnestic properties with an onset within seconds if applied intravenously and a half-life of approximately 45 minutes [6,7]. Its main benefit lies in allowing spontaneous respiration and respiratory and cardiovascular stimulation [2]. Potential serious side effects of ketamine are, amongst others, apnea 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 anesthesiologists [4,8].

Nitrous oxide (N_2O) is a gas with analgesic, sedative, anxiolytic, and amnestic effects and pediatric EDs use it primarily for distressing and minor painful procedures like placing an intravenous line or suturing lacerations [4,8,10-13]. N_2O 70% was introduced into our ED a decade ago as an alternative for ketamine PAS for procedures with a high pain score. N_2O 70% is an excellent agent for PAS in children, because neither intravenous lines nor nil per os are required; its onset is fast and its effect is sufficient for most short-lasting painful procedures. Recovery only takes a few minutes once the gas is withdrawn [12,13]. Adverse events are mainly nausea, vertigo and vomiting; hence, a trained ED consultant without an anesthesiologist performs these PAS in our ED [12,13].

Ketamine and N_2O 70% are the pharmacologic agents most routinely used for PAS in pediatric EDs, yet studies focused primarily on adverse events and sedation practices [14-16]. Our local practice with anesthesiologist control over ketamine sedations may not be representative of most pediatric ED practices, however, to the best of our knowledge, we are the first to analyze the changes of PAS practice caused by the implementation of N_2O 70% in a pediatric ED.

The aim of this study was to assess the change of the PAS regimes in our pediatric ED from 2007- when N_2O 70% was introduced - to 2016.

Materials and Methods

Patients up to 16 years of age who received PAS in the ED of the University Children's Hospital Zurich between 1 January 2007 and 31 December 2016 were included in this retrospective, single-center cohort study without any exclusion criteria. This study was approved by the local ethics board.

Data collection was performed by reviewing the clinical records of all included patients for N_2O and ketamine. The subsequent data were collected: patient's age and gender, procedure type, sedation medication, and who performed the procedure (ED physician or other specialist).

N_2O was applied via a demand valve system with a facemask covering the patient's nose and mouth, 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, for ketamine PAS an intravenous line and nil per os were mandatory. Ketamine PAS was exclusively performed by anesthesiologists who monitored the patient until discharge. Parents were not allowed to be present during the PAS; the intervention was usually performed by an ED physician or sometimes by a pediatric surgeon, indicating a potentially more severe case.

Data were described as frequencies or means with standard deviation (SD). Statistical analyses were performed with the IBM® SPSS® statistics version 24.

Results and Discussion

A total of 6497 patients were included in this study; 57.3% (3726/6497) were boys. Overall, N_2O 70% PAS was chosen in 54% and ketamine PAS in 46%, mostly for wound suturing (30.6%), orthopedic interventions (27.2%), burn debridement (13.9%), and removal of foreign bodies (12.8%) as detailed in Table 1.

	Overall (n= 6497)	N_2O 70% (n=3534)	Ketamine (n=2963)	p
Mean age, y (SD)	6.5 (4.1)	8.3 (3.5)	4.2 (3.6)	< .001
Sex, male, n (%)	3726 (57.3%)	1997 (56.5%)	1729 (58.4%)	.131
Procedures:				
Orthopedic, n (%)	1770 (27.2)	1303 (36.9)	467 (15.8)	< .001
Reduction upper extremity fracture, n	1619	1183	436	< .001
Reduction lower extremity fracture, n	151	120	31	< .001
Wound suturing, n (%)	1990 (30.6)	848 (24.0)	1142 (38.5)	< .001
Burn debridement, n (%)	905 (13.9)	277 (7.8%)	628 (21.2)	< .001
Removal of foreign body, n (%)	830 (12.8)	367 (10.4)	463 (15.6)	< .001
Abscess incision, n (%)	525 (8.1)	346 (9.8)	179 (6.0)	< .001
Other, n (%)	477 (7.3)	393 (11.1)	78 (2.7)	< .001

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

The overall mean age was 6.5 (± 4.1) years; in the ketamine group, the mean age was 4.2 (± 3.6) years, while in the N_2O group, it was 8.3 (± 3.5) years. The PAS chosen in different age groups is illustrated in figure 1. The use of N_2O in the youngest children was the lowest compared to the other age groups. N_2O was chosen in 73.2% in children aged 4 to 16 years (3258/4448), compared to 6.4% in children younger than three years (92/1447) (Figure 1).

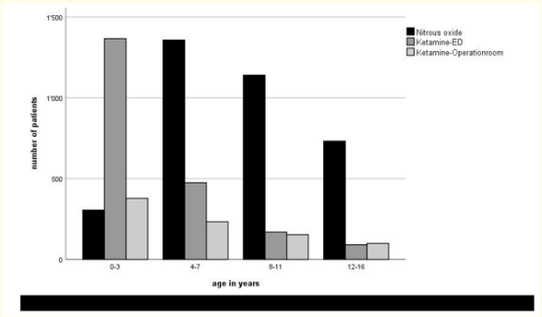

Figure 1: Procedural analgosedation in different age groups.

Ketamin-ED: Intervention was performed by an ED physician.

Ketamin-Operationroom: Intervention was performed by a pediatric surgeon (potentially more severe cases).

A steady increase of PAS with N_2O could be observed and a corresponding decrease in ketamine use over the years (Figure 2). The patient subgroups with displaced upper extremity fractures and patients with lacerations accounted for the most apparent increase of N_2O 70% (Figure 3). N_2O PAS was chosen for reduction of upper extremity fractures with a rate of 90.7% in 2016 (Table 2). Suturing showed a less significant decrease in ketamine PAS; N_2O PAS increased from 0 to 55.7%, mainly in older children (mean age ± SD: with ketamine PAS, 3.2 ± 3.3 years compared to N_2O PAS, 6.6 ± 2.9 years) (Table 2). Decisive factors for PAS selection for suturing were age and the affected localizations (Table 3). Similarly, a shift from ketamine PAS toward N_2O PAS occurred in burn debridement, yet significant differences in mean age and amount of injured skin appeared between the two PAS groups: Children with a mean age of 5.8 (± 3.2) years received N_2O compared to children with a mean age of 2.1 (± 2.3) years received ketamine; children with a mean affected body surface of 1.6% (± 1.2) received N_2O compared to children with a mean affected body surface of 3.1% (± 1.9) received ketamine.

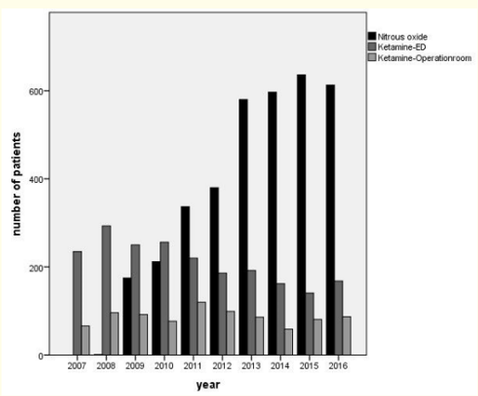

Figure 2: Procedural analgosedation over time in a pediatric Emergency department (ambulatory setting).

Ketamin-ED: Intervention was performed by an ED physician

Ketamin-Operationroom: Intervention was performed by a pediatric surgeon (potentially more severe cases).

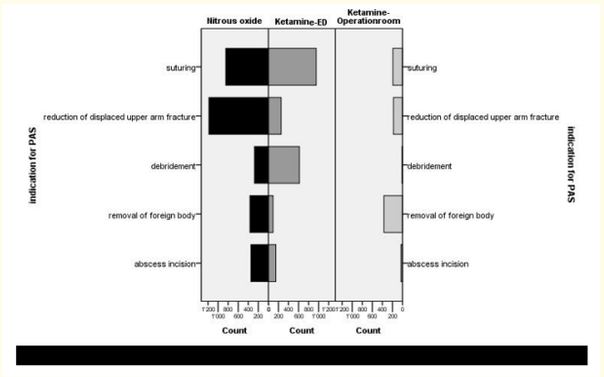

Figure 3: The most frequent indications for nitrous oxide and ketamine procedural analgosedations

Ketamin-ED: Intervention was performed by an ED physician

Ketamin-Operationroom: Intervention was performed by a pediatric surgeon (potentially more severe cases).

Table 2: Procedural analgosedation for reduction of upper extremity fractures. (A) and wound suturing over time (B).

A: Reduction of upper extremity fractures

B: Wound suturing

Table 2: (A)

Year	Nitrous oxide n (%)	Ketamine-ED n (%)	Ketamine-Operationroom n (%)	Total (n)
2007	0 (0%)	71 (77.2%)	21 (22.8%)	92
2008	0 (0%)	38 (53.5)	33 (46.5%)	71
2009	81 (68.1%)	21 (17.6%)	17 (14.3%)	119
2010	100 (70.4%)	23 (16.2%)	19 (13.4%)	142
2011	124 (67%)	26 (14.1%)	35 (18.9%)	185
2012	117 (66.1%)	41 (23.2%)	19 (10.7%)	177
2013	171 (89.1%)	11 (5.7%)	10 (5.2%)	192
2014	168 (93.3%)	7 (3.9%)	5 (2.8%)	180
2015	206 (91.6%)	10 (4.4%)	9 (4%)	225
2016	214 (90.7%)	10 (4.2%)	12 (5.1%)	236

Table 2: (B)

Year	Nitrous oxide n (%)	Ketamine-ED n (%)	Ketamine-Operationroom n (%)	Total (n)
2007	0 (0%)	82 (87.2%)	12 (12.8%)	94
2008	0 (0%)	146 (86.4)	23 (13.6%)	169
2009	37 (19.7%)	128 (68.1%)	23 (12.2%)	188
2010	39 (20.9%)	131 (70%)	17 (9.1%)	187
2011	80 (37.6%)	98 (46%)	35 (16.4%)	213
2012	82 (45.6%)	74 (41.1%)	24 (13.3%)	180
2013	136 (57.9%)	88 (37.4%)	11 (4.7%)	235
2014	194 (66.2%)	84 (28.7%)	15 (5.1%)	293
2015	153 (68.6%)	54 (24.2%)	16 (7.2%)	223
2016	127 (55.7%)	67 (32.2%)	14 (6.7%)	208

Localizations	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, n (%)	5 (29.4%)	12 (70.6%)	17
Age, years, mean (SD)	5.6 (± 1.3)	2 (± 0.6)	3.2 (± 1.9)
Cheek, n (%)	8 (72.7%)	3 (27.3%)	11
Age, years, mean (SD)	4.1 (± 1.2)	2.7 (± 1.6)	3.7 (± 1.8)
Scalp, n (%)	8 (88.9%)	1 (11.1%)	9
Age, years, mean (SD)	7.1 (± 1.8)	3	6.7 (± 2.5)
Eyebrow, n (%)	4 (80%)	1 (20%)	5
Age, years, mean (SD)	8 (± 2)	3	7 (± 3)
Trunk, n (%)	3 (75%)	1 (25%)	4
Age, years, mean (SD)	9.2 (± 1.9)	10	9.3 (± 2.1)
Genitals, n (%)	1 (25%)	3 (75%)	4
Age, years, mean (SD)	6	7.7 (± 0.9)	7.3 (± 1.3)
Tongue, n (%)	0	2 (100%)	2
Age, years, mean (SD)		1.5 (± 0.5)	1.5 (± 0.5)
All localizations, n (%)	127 (61.1%)	81 (38.9%)	208
Age, years, mean (SD)	6.6 (± 2.9)	3.3 (± 3.3)	5.3 (± 3.5)

Table 3: Procedural analgosedation for wound suturing in 2016; age dependency and affected localizations.

The N_2O PAS regime needed to be changed to ketamine in 1% of all children receiving N_2O (37/3571) because either N_2O PAS was insufficient or adverse events occurred. These children were mostly boys (67.6%) with a mean age of 7.5 ± 4.2 years; indications for the change in PAS were, amongst others, removal of foreign bodies (2.7%; 10/378), burn debridement (1.4%; 4/279) and reduction of upper extremity fractures (0.9%; 11/1190).

This retrospective study analyzed the change of the PAS regimes in our pediatric ED from 2007- when N_2O 70% was introduced - to 2016. The implementation of N_2O PAS resulted in a decrease in ketamine PAS, especially in children older than three years with displaced upper extremity fractures requiring closed reduction.

Selecting the most suitable PAS for children depends on factors affecting the patient, the planned procedure, the ED physician's experience, and the institutional resources [1-3].

First, for N_2O PAS a child has to be cooperative, has to tolerate a facemask, and has be able to breathe strongly enough to open a demand valve system; in our study, N_2O PAS was only chosen in 6.4% of children younger than three years. Another type of application for N_2O is a system with continuous flow, which might be a possibility for younger children; however, this application bears the risk of exceeding the acceptable concentration in the room air above the legally set minimum alveolar concentration (MAC) values for N_2O [17]. Second, N_2O 70% is ideal for brief painful procedures such as reduction of displaced fractures, small burn debridement, abscess incision and removal of foreign bodies. In contrast, the preferable choice for PAS for longer and more painful procedures is ketamine PAS. Lip lacerations were mostly treated with ketamine PAS, probably because this repair is delicate, but also because most of the patients were too young for N_2O PAS (2016 data: mean age 2.7 ± SD 2.6). Comparable results were assessed for burn debridement, where ketamine PAS was chosen for children with a mean age of 2.1 years (SD± 2.3) and affected body surfaces of 3.1 (SD± 1.9). Third, the ED physician's know-how with PAS along with the planned procedure presumably also affect the choice for N_2O or ketamine. Additionally, the child's needs as well as benefits and risks influence this decision [18]. Fourth, the institutional resources like crowding and the availability of the anesthesiology team must be considered. Fifth, N_2O PAS is about half as expensive as ketamine PAS because less medication and medical personnel are needed and children can be discharged sooner. Unlike N_20 PAS, for ketamine PAS, an intravenous line and nil per os is mandatory; anesthesiologists are needed to carry out the anesthesia, and a place in the recovery ward has to be arranged.

An increase in our ED's efficacy and efficiency might be achieved by working as autonomously as possible; thus, changing our current intravenous ketamine PAS routine might be necessary. Instead of depending on the availability of the anesthesiologists, trained ED physicians could assume responsibility for ketamine PAS. This training can today be expected of pediatric ED physicians, as already demonstrated in North America [19]. Bhatt., *et al*. analyzed adverse events from PAS performed by pediatric ED physicians and concluded it to be safe with an overall incidence of 11.7% adverse events and a low rate of SAEs (1.1%) [20]. To enhance our efficacy and efficiency, alternatives such as nasal application of ketamine or implementation of newer pharmacologic agents like dexmedetomidine might be a possibility for children younger than three years and longer lasting procedures [21].

Limitation of this study are its retrospective design and our local ED setting where ketamine PAS is solely performed by anesthesiologists. No data were available to assess if the children and par-

ents were pleased with the chosen PAS. Other missing data were the rate of adverse events during PAS and why a certain PAS was chosen.

Conclusion

The implementation of N_2O PAS in our ED resulted in a decrease in ketamine PAS, especially in children older than three years with displaced upper extremity fractures requiring closed reduction.

Conflict of Interest

The author has no financial interest or any conflicts of interest to disclose.

The author states that this manuscript is a republication of a manuscript by the same author, which was published in Swiss Medical weekly (Seiler M, Staubli G. Ketamine procedural analgosedation before and after introducing nitrous oxide 70% in a paediatric emergency department. Swiss Med Wkly. 2019;149: w20027). In contrast to the previously published article, which focused on the years 2007 and 2016, this manuscript contains all data from 2007 to 2016 during the implementation of nitrous oxide 70%.

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