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SHORT COMMUNICATION

Use of ketamine by paediatricians in Italian paediatric emergency departments: a missed opportunity?

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Abstract

Procedural sedation and analgesia with ketamine are part of daily practice for children undergoing painful procedures in the paediatric emergency department (ED) of North America. A massive number of studies demonstrate ketamine's safety and efficacy in the hands of trained ED paediatricians, with few severe adverse events (SAEs) recorded. Since there are no data on ketamine's usage in Italian paediatric EDs, we created a survey to examine procedural sedation with ketamine in the EDs of the Italian PIPER (Pain in Paediatric Emergency Room) group, which includes 36 paediatric EDs providing 1.4 million paediatric visits each year. Results were reviewed using frequencies to describe responses. Thirty-two out of 36 centres replied to the questionnaire. In 6 (19%) out of 32 centres, ketamine is not used at all in the paediatric ED. In 6 centres (23%) of 26 which use ketamine, this drug is autonomously administered by the emergency paediatrician, whereas in 20 (77%) of them it is exclusively managed by the anaesthesiologist on call.

Conclusion: ketamine is autonomously administered only by a small percentage of Italian emergency paediatricians. There is an increasing need for implementation of procedural sedation training and use of ketamine in the everyday practice outside the operating room in paediatric EDs.

What is Known:
- *Ketamine is safely and efficaciously administered for children's procedural sedation and analgesia by trained emergency paediatricians in the everyday practice outside the operating room in North America.*
- *In the Italian setting, there are no data at all concerning ketamine's usage by the emergency paediatricians for procedural sedation and pain control.*

What is New:
- *In this study emerged that ketamine is poorly administered by Italian emergency paediatricians for procedural sedation and analgesia outside the operating room.*
- *A great deal of educational effort should be made to widen ketamine based procedural sedation availability in Italian emergency departments by spreading specific training tracks and guidelines.*

Keywords Ketamine · Procedural sedation · Emergency department · Analgesia · Children · Child

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Abbreviations

BP	Blood pressure
ED(s)	Emergency department(s)
ET-CO_2	End-tidal CO_2
HR	Heart rate
IM	Intramuscular
IN	Intranasal
IV	Intravenous
PIPER	Pain in Paediatric Emergency Room
RR	Respiratory rate
SAE(s)	Severe adverse event(s)
SIMEU	Italian Society of Emergency Physicians
SpO_2	Oxygen's saturation

Introduction

The awareness that children frequently require painful procedures in the emergency department (ED) has increased to the point that it is understood that procedural sedation and analgesia care for children has become standard of care [1–4].

Among different drugs available in the setting of procedural sedation and analgesia outside the operating room, ketamine shows the best safety record and the broadest available literature proving its efficacy and safety on a 3 decades experience. Strong evidence confirms that ketamine can be safely administered not only by anaesthesiologists but also by trained emergency physicians and paediatricians [4–6].

Ketamine is a unique dissociative agent which provides pain control and sedation without loss of protective airways reflexes and respiratory depression, maintaining both heart rate and blood pressure, and is efficaciously administered intravenously and intramuscularly [2, 7], the latter is particularly useful when vascular access is difficult to obtain [8, 9]. Despite strong literature on ketamine's efficacy and safety on a massive number of children in North America [3, 5], where this drug is part of daily practice outside the operating room, there are few studies on procedural sedation with ketamine in Europe [10], and no data at all concerning its use in Italian paediatric EDs. Therefore, this study aimed to take a picture of ketamine's usage in Italian paediatric EDs.

Materials and methods

This survey was conceived and carried out at the Institute for Maternal and Child Health IRCCS Burlo Garofolo of Trieste, Italy. Data collection took place between March and June 2018. Italian paediatric hospitals and general hospitals with a distinct paediatric ED were invited to participate in our study. All centres ($n = 36$) are part of the Italian PIPER group (Pain in Paediatric Emergency Room) and provide care to approximately 1.400.000 patients/year overall. For every centre, the survey was completed by the delegate paediatrician of the PIPER group.

Information about EDs policies regarding ketamine's use for procedural sedation was collected through a structured questionnaire, digitally formatted for easier compilation. The survey, shared through the PIPER network, investigated the following issues:

- Use of ketamine by the ED's paediatrician
- Use of ketamine by the anaesthesiologist in paediatric EDs
- Specific training before procedural sedation
- Routes of administration of ketamine
- Ketamine's dosage for each route of administration
- Premedication with atropine or ondansetron
- Specific procedures in which ketamine is administered
- Monitoring during ketamine's procedural sedation
- An estimation of severe complications (need for intubation, intensive care unit admission or death), observed during ketamine's administration, based on the review of local records and the personal experience of paediatricians who participate in the survey
- Years of ketamine's usage by ED's paediatricians

The primary study outcome was the prevalence of ketamine's use in the Italian paediatric EDs. Secondary outcomes were prevalence of ketamine's use by paediatricians and prevalence of specific training for its use.

Results

During the study period, we sent the survey to 36 centres, part of the PIPER network. Of these, 32 (88%) answered the questionnaire. Results were reviewed using frequencies to describe responses. In the 18.75% (6 out of 32 centres), ketamine is not used in the paediatric ED. Regarding the centres that use ketamine in the ED, in the 76.9% (20 out of 26 centres), the drug is exclusively administered by the anaesthesiologist on call when available and in 23% (6 out of 26 centres) is used by paediatricians.

We investigated training protocols in the 6 Italian paediatric EDs where ketamine is directly administered by the paediatrician outside the operating room. Formal specific training teaching ketamine's usage is implemented in 5 out of 6 centres (83.3%), consisting mainly of theoretical lessons, simulations, and training in EDs, procedural sedation units and operating room. No one centre routinely uses antiemetic premedication with ondansetron. One centre uses atropine premedication, but only in the presence of upper airway secretions.

Intravenous (IV) route of administration is used in all the 6 centres (100%), intramuscular (IM) in 5 out of 6 (83.3%) and intranasal (IN) in 2 out of 6 (33.3%). Procedures requiring analgesia and sedation with ketamine in the 6 paediatric EDs are shown in Table 1.

The dosage of ketamine, based on the route of administration, was found to comply with guidelines (0.5–2 mg/kg for IV route, 4–5 mg/kg for IM route) [7], and only a single case revealed an IM administration lower (1–2 mg/kg) than recommended dosages.

During procedural sedation with ketamine, all centres monitor heart rate (HR), respiratory rate (RR) and oxygen saturation as measured by pulse oximetry (SpO_2), one monitors blood pressure (BP), one electrocardiogram and two centres monitor end-tidal CO_2 (ET-CO_2).

Based on the personal experience of the survey respondents, who reviewed the local records, no severe adverse events (SAEs) such as the need for intubation, intensive care unit admission or death occurred during direct ketamine administration by the paediatrician in the ED.

Finally, from the questionnaire, we were able to determine that procedural sedation with ketamine is only recently performed in all the 6 centres.

Discussion

This study shows that ketamine is only rarely administered by Italian ED paediatricians autonomously.

While ketamine is used in 75% ($n = 26$) of the Italian paediatric EDs included in the study, in the majority of cases it is administered exclusively by on-call anaesthesiologists ($n = 20$), and only in 20% of cases by paediatricians ($n = 6$). Remarkably, in comparison to North America where ketamine is the most commonly administered sedative for children who require procedural sedation and analgesia for painful procedures in the ED setting, in 6 EDs, ketamine is not used at all.

By analysing the answers to our questionnaire, we determine that ketamine is administered by paediatricians only in those centres equipped with a paediatric intensive care unit, where probably there is both closer attention to procedural sedation management and facilities for procedural sedation training. In this survey, we did not investigate the airway management skills of paediatricians who have answered the survey. Even rarely, ketamine may cause laryngospasm or apnoea. Therefore, we want to highlight that before any implementation of the use of ketamine in the paediatric emergency setting, providers should have performed appropriate training in airway management.

Table 1 Procedures in which ketamine is used by the paediatrician for sedation and analgesia (6 centres)

Burns	4 of 6 centres
Difficult venous access	1 of 6 centres
Lumbar puncture	1 of 6 centres
Arthrocentesis	1 of 6 centres
Dislocation reduction	1 of 6 centres
Fracture reduction	4 of 6 centres
Medication/suture of wounds	5 of 6 centres

As already expected from several studies reporting an extremely low incidence of SAEs with ketamine [2–5], based on the questionnaire answers, survey respondents reported a low-perceived incidence of serious adverse events when paediatricians provide ketamine in the Italian setting.

From the questionnaire, different monitoring strategies emerged during ketamine's administration.

Basic continuous mechanical monitoring with pulse oximetry, capnography and cardiac monitoring associated with RR and HR assessment are required whereas, as reported in several studies, there is no need for continuous BP detection since ketamine releases catecholamines without depressing cardiovascular system [2]. Capnography, earlier than pulse oximetry, provides nearly real-time evaluation of the respiratory drive, therefore should be used in this setting.

Focusing on the centres in which ketamine is autonomously used by paediatricians, all these centres use IV ketamine, 5 of 6 IM ketamine and 2 of 6 the IN route. Efficacy of IM and IV sedation with ketamine is equivalent, with the IM route associated with a higher rate of emesis than the IV one [2, 9]. Remarkably, from limited evidence available from the literature, high IN dosages (9 mg/kg) are required to reach significant blood levels. The efficacy of IN ketamine is questionable and this route of administration should be considered only for analgesia and not for sedation [11, 12].

Despite in several countries (USA [3], Canada [5]) ketamine is administered by the emergency paediatrician in the everyday practice outside the operating room, with an excellent safety and efficacy profile underlined by years of strong literature, in Italy, only a few centres have met with this opportunity and there is no study at all on procedural sedation with ketamine. To our knowledge, in Europe, no survey is available on ketamine's usage in paediatric EDs, except for the UK's experience [9, 10].

These data suggest that a great deal of educational effort should be made to widen ketamine-based procedural sedation availability in Italian EDs by disseminating specific training tracks and guidelines for paediatric emergency physicians.

Remarkably, in Italy, no dedicated educational program in paediatric emergency medicine is available at the moment in the postgraduate schools, as it happens in other countries such as the USA. The development of such a track could be a major opportunity to develop and disseminate knowledge and skills in the sedation field.

Our study has some limitations. We did not quantitatively investigate ketamine's frequency of usage, side effects and the specific training protocols in Italian paediatric EDs, but this was not our aim. Considering data collection through a questionnaire, we could have missed some potential SAEs. Even if only a few centres included in the Italian PIPER, research

group did not answer our survey, the sample is not absolutely representative of all Italian paediatric emergency facilities. In many local hospitals, children are frequently managed in EDs by general physicians. While the Italian Society of Emergency Physicians (SIMEU) guidelines strongly encourage the use of ketamine in children by trained general ED physicians, no survey has been performed to investigate their impact on real life. Moreover, no official guideline on this topic has been issued by the Italian Society of Paediatrics.

Despite strong literature on ketamine's safety and efficacy in children, showing that its administration has predictable adverse event rates and an excellent safety profile when managed by specifically trained providers [1–3], this drug is hardly part of the Italian paediatric ED's daily practice outside the operating room.

In conclusion, our study documents the infrequent administration of ketamine by ED paediatricians in Italy. Given the growing need for appropriate procedural sedation for children and the common practice of ketamine administration by appropriately trained ED paediatricians in North America, we suggest the need for implementation of paediatrician's procedural sedation training and the use of ketamine in the everyday paediatric ED's practice.

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Compliance with ethical statements

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors. The study did not involve any collection or analysis of personal data regarding human participants but only hospitals and policies, according to Italian law requirements for informed consent, and approval by Ethics Committee was not applied. In Italy ethical review is mandatory only for clinical trials on pharmaceutical products (*http://www.agenziafarmaco.gov.it/sites/default/files/Decreto_Legislativo_n._211_del_24_giugno_2003.pdf*) and for observational studies on use of drugs by human participants (*http://www.agenziafarmaco.gov.it/sites/default/files/det_20marzo2008.pdf*).

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