

A pilot experience of the use of intramuscular ketamine for paediatric sedation in an Accident and Emergency department

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A prospective uncontrolled clinical trial was conducted to study the effectiveness and safety of using intramuscular ketamine in Accident & Emergency department in Hong Kong. Initial dose of 4 mg/kg (followed by a supplemental dose of 2-4 mg/kg if required) intramuscular ketamine was given to 35 children (between the ages of one to fourteen) to facilitate the carrying out of painful but necessary procedures. Satisfactory or acceptable sedation was obtained in more than 97% of these children without adjuvant physical restraint or local anaesthesia. The mean onset time was 6.78 minutes and mean time to regain consciousness was 94.97 minutes. Mean length of hospital stay was 186.65 minutes. None of these children developed laryngospasm, respiratory depression or cardiovascular instability. Trivial oxygen desaturation was observed in one child secondary to hypersecretion of saliva but he responded to suction and oxygen with no adverse sequel. The incidence of hypersalivation was 8.6%. Other side effects such as emesis (23.5%), muscle spasm (11.85%) were self-limiting. There was no case of upsetting reaction observed. Ketamine by intramuscular route provides a better option to facilitate painful procedures in children in Accident & Emergency department as compared with the application of physical restraint. Yet expertise and equipment for advanced airway management is necessary for the uncommon risk of airway complications. (*Hong Kong j.emerg.med.* 2000;7:141-147)

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Introduction

Physicians working in Accident and Emergency department are frequently required to perform painful procedures on children. They are often faced with the problem of how to reduce anxiety, pain and combative behaviour in these children, who must undergo painful procedures such as laceration repair, fracture reduction. Appropriate relief of pain and anxiety is essential for the optimal management of paediatric patients. Local anaesthesia and a calm, reassuring environment often attenuate their fears, but there is a certain subset of children in whom these techniques alone do not suffice. Moreover, some procedures may need certain degree of

immobilisation for optimal repair, for example, facial laceration. Therefore pharmacological sedation is indicated in these circumstances.

Ideally, a single pharmacological agent or combination of pharmacological agents should provide ease of administration, rapid onset of action, effective and predictable analgesia, adequate immobilisation, broad margin of safety over wide spectrum of clinical situations, rapid and smooth recovery and avoid causing airway and cardiopulmonary compromise. None of the currently available pharmacological agent satisfies all these requirements. Ketamine probably comes closest to representing the ideal sedative agent in Emergency Medical practice.

The bulk of clinical experience with ketamine comes from the developing world, where it is routinely and safely administered thousand of times daily by non-anaesthetists operating in area with limited resources. Despite its many advantages as an emergency sedative agent, widespread acceptance

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of ketamine in Hong Kong and other developed countries has been hesitant, due to factors like inexperience with the drug, apprehension about "emergence reactions", and the rare occurrence of adverse airway or breathing effects. In many circumstances, physical restraint was one of the main stays when immobilising children, producing psychological trauma and scarring to the children for life.

We have conducted a study to determine whether the combination of intramuscular administration of ketamine and atropine is a safe, effective and acceptable method of analgesic and sedation when carrying out painful procedures in Chinese children in the Emergency department setting in Hong Kong. Intramuscular route was chosen because of its simplicity, economy, and causing minimal upset to the children compared to intravenous route.

Materials and methods

The study was carried out in our Accident & Emergency department from February 1999 to September 1999. Chinese children aged 6 months to 15 years who underwent painful procedures were enrolled. Full informed consents were obtained from parents or guardians. The procedures were those expected to be completed within 15 minutes and which caused unpleasant feelings, emotional disturbance or excessive or severe pain to children especially in circumstances in which immobilisation was critical for procedure success.

We excluded children with contraindications to ketamine sedation as listed out in the Table 1 and children who had taken a full meal within 3 hours preceding the procedure.

Based on previous study,¹ the first dose of ketamine given to these children was 4 mg/kg intramuscularly over the gluteal region. Preparation of ketamine of 100 mg/ml was used in order to reduce the volume of drug required to be injected. Atropine at the dosage of 0.01 mg/kg was added in the same syringe for injection so as to reduce hypersalivation. If sedation were inadequate 10-15 min after injection, a second dose of ketamine of 2-4 mg/kg would be

injected as decided by the attending physician. Further supplemental physical restraint will be offered if indicated.

Sedated children would be put under close observation in our Accident and Emergency department. Oxygen supply, suction devices and instruments for advanced airway management would be available if and when required.

After completion of the procedure, close monitoring of the children were carried out by experienced nursing staff in our Observation room through clinical observation and continuous monitoring of SpO₂ and pulse by portable pulse oximeter until the children had fully recovered from the drug effects. Chest and neck were exposed for continuous inspection of the breathing effects. Minimal stimulation were given and emergency physician experienced in paediatric resuscitation was available if needed.

Children would be discharged only if certain discharge criteria were met. The criteria comprised of return to pre-sedation conscious level, purposeful movement with normal awareness and verbalisation appropriate for age and ability to walk with good balance appropriate for age.

Table 1. Contraindications to the use of ketamine.

Contraindications:

- Age of 3 months or less
 - Procedures involving stimulation of posterior pharynx
 - Active pulmonary disease or infection
 - History of airway instability, tracheal surgery, or tracheal stenosis
 - Cardiovascular disease, including angina, heart failure, aneurysm, or uncontrolled hypertension
 - Head injury associated with loss of consciousness or altered mental status
 - CNS mass lesion, hydrocephalus, or other conditions associated with intracranial hypertension
 - Glaucoma or acute globe injury
 - Prior adverse reaction to ketamine
 - Psychosis
 - Thyroid disorder
 - Porphyria
-

A discharge leaflet was given to parents or caretaker with the following instructions:

- Nil by mouth for 2 hours after discharge
- No independent ambulation for 2 hours
- Child may have mild vomiting
- Record any sleep disturbance or night screaming
- Come back if there is any abnormal behaviour or repeated vomiting

The degree of sedation were assessed by the attending doctors responsible for performing the procedures and consisted of 3 grading - satisfactory sedation, acceptable sedation and failed sedation. Any complications that occurred, for example, laryngospasm, aspiration, excessive salivation, emesis, seizures, apnoea, respiration depression and the corresponding intervention offered were recorded.

Results

Thirty-five children with a mean age of 5.94 years (range 1.08-13.67 years) were entered into the study. Twenty-three (65.7%) were boys and 12 (34.3%) were girls. Data of one child was omitted as he was admitted into the ward for failed close reduction of fracture distal radius and ulna. The procedures performed were as shown in Table 2.

Twenty-eight (80.0%) and 6 (17.1%) children had satisfactory and adequate sedation respectively, making up a total of 34 children (97.1% with 95% C.I. of 91.5%-100%). Only one (2.9%) child had failed sedation. The mean time of onset was 6.78 minutes with 95% C.I. of 5.47-8.09 minutes. The mean duration of sedation (from the time of injection until the children awoke) was 94.97 minutes (95% C.I. 79.42-110.52 minutes) and this was comparable to previous study in other countries. The mean time of hospital stay was 186.65 minutes (95% C.I. is 151.55-221.74 minutes). It was longer than the discharge time in previous studies because of the different discharge criteria.

The side effect of ketamine injection was uncommon. We had no patient with complication of laryngospasm or respiratory depression during this study. One patient with oxygen desaturation

was documented. He was an 11-year-old boy who sustained fracture of distal radius. Close reduction was performed under ketamine sedation. He developed significant hypersecretion of saliva causing transient desaturation with SpO₂ below 90% for less than 10 seconds and required suction and oxygen therapy. He was discharged less than 3 hours after ketamine sedation without any neurological sequel. The overall incidence of hypersalivation in our study was around 8.6% (95% C.I. 0%-18.0%).

Transient clonus and muscle spasm were present in 11.8% (95% C.I. 1%-22.6%) of these children. Emesis (23.5% with 95% C.I. of 9.2%-37.8%) was the most common side effect. None of the children developed emergence phenomena but 5.7% (95% C.I. 0%-13.5%) complained of nightmare on the same day of ketamine administration. Transient flushing of face occurred in one child (2.9% with 95% C.I. of 0%-8.5%). The side effects are summarised in Table 3.

There was a significant increase in pulse rate in one child. The maximum pulse rate was attained about 30 minutes after ketamine injection. The underlying

Table 2. Type of procedures.

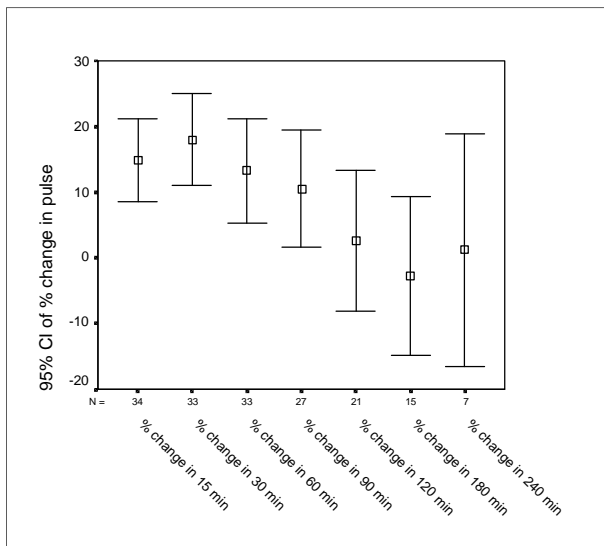
Procedures		Incidence
Suturing of laceration		20
Facial e.g. eyelid, lip, etc.	16	
Genitalia	2	
Limbs	2	
Incision & drainage of abscess		9
Pre-auricular abscess	3	
Paronychia	2	
Scalp	1	
Trunk and limb	3	
Fracture reduction		5
Fracture distal radius	3	
Fracture distal radius and ulna	2	
Foreign body removal i.e. fish hook over finger		1

Table 3. Incidence of side effects of ketamine.

Side effects recorded	Incident
Hypersalivation	8.6%
Transient clonus	11.8%
Emesis	23.5%
Nightmare	5.7%
Transient flushing of face	2.9%

reason was probably due to the combined pharmacological effects of these two drugs - ketamine is a sympathomimetic agent² and atropine is an anticholinergic agent. Both of them would cause an increase in pulse rate.

Percentage change in pulse after ketamine injection



Discussion

Ketamine hydrochloride (Ketalar[®]), structurally derived from the street drug phencyclidine in 1963,³ is a unique combination of sedative, amnesia and analgesic simultaneously. It suppresses the reticular activating system and generates a functional and electro-physiological dissociation between the

cortical and limbic systems which first described as "dissociative anaesthesia" by Corssen and Domino in 1966,⁴ during which laryngeal reflexes and independent airway were maintained and not impaired.

Many clinicians unfamiliar with ketamine have mistakenly categorised it as a general anaesthetic and in so doing have blocked its use for patient care in Emergency departments. Determination of appropriate standard for monitoring after administration of ketamine is difficult, as the unique features of this drug prevent it from being appropriately classified according to existing anaesthetic monitoring protocols. As patients receiving ketamine can maintain spontaneous breathing and protective airway reflexes without intubation, this drug violates the standard definition of general anaesthesia. (Table 4) Similarly, ketamine does not meet the definitions for either conscious sedation (which requires responsiveness) or deep sedation (which requires depressed airway reflexes or inability to maintain an independent airway). The sedated state caused by ketamine is fundamentally unique both pharmacologically and therefore clinically a fourth distinct category is appropriate.⁵⁻⁸

Ketamine produces dissociation, a trance state unique to anaesthesia. Patients sedated with ketamine would appear to be awake and have little higher cortical depression. But the cortical awareness is blocked from external stimuli, including

Table 4. Definition of terms of anaesthesia and sedation.

General anaesthesia

- Medical controlled state of unconscious
- Partial or complete loss of protective reflex
- Including the inability to maintain a patent airway independently

Conscious sedation

- Medical controlled state of unconscious
- Allow protective reflex to be maintained
- Retain ability for independent airway protection
- Permits appropriate response to physical stimuli

Deep sedation

- Medical controlled state of depressed consciousness or unconsciousness
- Patient is not easily aroused
- Partial or complete loss of protective reflexes
- Inability to maintain a patent airway independently
- Respond purposefully to physical stimulation or verbal command

visual, auditory, or painful inputs. Brainstem functions remain intact, and processes for maintaining essential cardiac and respiratory functions are preserved. The muscle tones are uninhibited and the eyes remain open with a "dissociated" stare.

Ketamine has excellent water and lipid solubility, thus allowing it to be conveniently administered by a variety of routes while still able to cross blood-brain barrier rapidly. It can be given by intranasal,⁹ rectal,¹⁰ oral, intravenous¹¹ and intramuscular routes. It does not cause any pain and is non-irritating after IV or IM injection.

Mechanisms for its pharmacological actions are still largely unknown. Ketamine binds to N-methyl-D-aspartate (NMDA) receptors located on central neurons and it was suggested that it might act via these receptors.¹²

The half-life of ketamine is 2-3 hours in adults¹³ and about 1-2 hours in children.¹⁴ After intramuscular injection, peak drug concentration is attained over 5 minutes together with the onset of effects (versus almost immediate effects in intravenous injection). Dissociation typically persist for 15-30 minutes with coherence and purposeful neuromuscular activities returning in around 30-120 minutes. Recovery time after intramuscular injection is more prolonged and variable compared to IV injection (average 15 minutes).¹

Effect on airway and respiration is the major concern when using ketamine. Spontaneous respiration and muscular tone of tongue and larynx are preserved. Protective reflexes like coughing, sneezing and swallowing are not depressed and may be slightly exaggerated.¹ Respiratory depression^{15,16} caused by intramuscular injection of ketamine is extremely rare and occurs more commonly after rapid intravenous injection with very high dose¹⁷ and in patients with CNS lesion^{18,19} or ill neonates.²⁰

Laryngospasm is frequently cited as a side effect but it is only rarely observed. Sonorous respiration is often mistaken for laryngospasm but is in fact due to airway positioning. True laryngospasm during ketamine sedation is usually caused by stimulation

of vocal cords by instrumentation or secretions. In a recent paediatric series, the risk of laryngospasm with intramuscular injection of ketamine was around 0.29% and none of these cases were associated with adverse sequelae.²¹ Despite its rarity, equipment should be available for timely intubation if required when ketamine was used.

Ketamine also stimulates salivary and tracheobronchial secretions. Therefore co-administration of anti-cholinergic agent such as atropine will be helpful to reduce airway secretions. Aspiration was documented in contrast study^{22,23} and clinical aspiration of non-neonate was reported only in two cases in which one patient has a brain tumour²⁰ (a relative contraindication of ketamine) and the other has a full stomach.²⁴

Ketamine has some beneficial actions towards the respiratory system. It causes bronchodilatation, making it a favoured induction agent for rapid-sequence intubation during status asthmaticus.^{25,26}

Ketamine is a sympathomimetic agent which would cause mild to moderate increase in blood pressure, heart rate and cardiac output.²⁷ These properties make it a favoured sedative agent for patients in shock. But the effect was minimal in children after intramuscular ketamine injection.

There is a report of two patients on levo-thyroxine who developed hypertension and supraventricular tachycardia after intravenous ketamine injection²⁸ (That is the reason for thyroid disease being one of the relative contraindications for ketamine). Otherwise, its effect on cardiac rhythms is controversial. No arrhythmia is documented in patients who underwent cardiac catheterisation²⁹ under ketamine sedation.

A summary of 97 reports in 1990 involving 17,550 administrations of ketamine, and in at least 11,589 paediatric patients, identified no associated major cardiorespiratory complications or death.¹

Hypertonicity and rigidity over skeletal muscles are often seen when ketamine is used. There is also random movement of head and extremity unrelated to painful stimuli. Sometimes intense myoclonus and twitching may be confused with seizure activity

but it is not associated with EEG changes. And actually ketamine may be a useful agent in the treatment of status epilepticus,^{30,31} though its net effect on seizure disorder is unclear.

Ketamine elevates intracranial pressure in patients with known intracranial cerebrospinal fluid (CSF) obstruction, but such increase was not observed in patients who had intracranial pathology without obstruction.^{32,33} Interestingly, ketamine exhibits neuroprotective effect in animal model.³⁴ It also demonstrated such an effect in a prospective study on head injured patients. However, its use in head injured patients is still considered controversial.³⁵

Emergence phenomena are well reported but the incidence is less than 1% in many studies. Because of the unique dissociation effect of ketamine, a sense of semi-conscious bodily detachment stimuli is often experienced by patients. Partially conducted stimuli may be interpreted as pleasant or distressful. Upsetting reaction are much less common in children and extremely rare in those less than 10 years of age^{2,36} as evidenced by the rare incidence of crying and agitation in the recovery period. Thus the fear of the adverse ketamine recovery experience should not preclude its use in children.

Emesis is a relatively common but self-limiting side effect with an incidence of 0-43%.¹ It always occurs late in the recovery period and the airway can be cleared without assistance because patient is alert at that time.

Other side effects such as nystagmus prevent the performance of eye procedures and transient rash may also occur.

Ketamine has many attractive pharmacological properties that makes it a useful sedative agent in emergency departments, namely, ease of administration, rapid onset and effective analgesia, adequate immobilisation, relative low cost, and smooth recovery.

Despite the above advantages, ketamine is not popular with Emergency physicians in Hong Kong. Traditionally, painful procedures in Emergency departments are performed by forcibly restraining the frightened child and quickly attending and

completing the procedure at hand. This is definitely a painful experience to all parties, especially to children and may produce significant psychological trauma and scarring.

Many traditional sedative agents previously utilised in Emergency departments are far more dangerous than their modern counterparts. For example, meperidine-promethazine-thorazine (lytic cocktail) and chloral hydrate were previously widely accepted as safe and effective agents for paediatric sedation, despite having long half-life, difficulty in titrating to the desired sedation levels, and more importantly, death have occurred from respiratory arrest.^{37,38} Morphine and diazepam, because of their long half-life, may cause severe and prolonged post-procedure respiratory depression, or even death from respiratory arrest. Shorter acting fentanyl-midazolam combination would be safer in such patient, but requires much closer observation.

In our study, it was clearly demonstrated that intramuscular ketamine facilitate the carrying out of painful procedure in children in emergency departments. More than 97% of these children receiving ketamine sedation under our protocol achieve satisfactory or acceptable level of sedation. There is also a wide margin of safety with only self limiting, easily rectifiable side effects.

Conclusion

In our prospective study, a high success rate of more than 97% was obtained under the protocol. Complications were uncommon and most were self-limiting. We suggested that intramuscular ketamine should be used whenever a painful, distressful procedure is going to be performed in Accident & Emergency departments on children aged 1 year to 15 years in order to alleviate fear and improve comfort. Nevertheless, close monitoring is needed and expertise and equipment for emergency airway management should be easily available when ketamine is being used.

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