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Research Article

Prevention of rocuronium injection pain in paediatrics: Ketamine versus midazolam? A prospective randomized double blind study

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KEYWORDS

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Abstract *Introduction:* Rocuronium bromide is a non-depolarizing muscle relaxant related to mono-quaternary steroid group which is used commonly in general anaesthesia for the facilitation of endotracheal intubation and for maintenance of muscle relaxation. Rocuronium injection pain is a significant drawback with an incidence ranging from 50% to 80% [1,2]. Separation of children from their parents and shifting them to the OT is an everyday problem to paediatric anaesthetists, in our centre; majority of anaesthetists use IV midazolam to solve this problem, some anaesthetists use IV ketamine hydrochloride instead. This randomized, double-blind study was designed to compare the effect of IV ketamine versus IV midazolam in reducing rocuronium injection-related withdrawal movements in paediatric patients.

Methods: Hundred and twenty paediatric patients aged 2–10 years subjected to urologic procedures under general anaesthesia were randomly classified into two groups: the ketamine group in which IV ketamine 1 mg kg^{-1} was given and the midazolam group in which IV midazolam 0.05 mg kg^{-1} was given before shifting the child to the operation room.

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Results: Ketamine showed a highly significant reduction in the incidence of rocuronium injection-related withdrawal movements in paediatric patients (*P*-value 0.000) compared to midazolam which was ineffective.

Conclusion: This study demonstrated that ketamine effectively reduced pain after injection of rocuronium in paediatric patients compared to midazolam which was ineffective, and both ketamine and midazolam resolved peacefully the problem of child-parent separation before shifting to the OR.

1. Introduction

Rocuronium bromide is a non-depolarizing muscle relaxant related to mono-quaternary steroid group which is used commonly in general anaesthesia for facilitation of endotracheal intubation and for maintenance of muscle relaxation. Rocuronium injection pain is a significant drawback with an incidence ranging from 50% to 80% [1,2]. This pain was manifested in conscious patients given a sub-paralysing dose by severe burning sensation and in unconscious patients by withdrawal movements of the injected limb. The underlying mechanism of such pain is unclear; however the significant increase in histamine and tryptase release from mast cells after rocuronium injection and the resultant activation of perivascular nociceptive nerve endings and poly-modal nociceptors in the wall of the peripheral veins may explain rocuronium injection pain [3,4].

Separation of children from their parents and shifting them to the OT is an every day problem to paediatric anaesthetists, in our centre; majority of anaesthetists use IV midazolam to solve this problem, some anaesthetists use IV ketamine hydrochloride instead. This randomized, double-blind study was designed to compare the effect of IV ketamine versus IV midazolam in reducing rocuronium injection-related withdrawal movements in paediatric patients subjected to elective urologic surgeries under general anaesthesia.

2. Methods

This study was conducted in the Urology and Nephrology center/Mansoura University Hospital/Egypt. Both institutional committee approval and an informed consent from each parent were taken. 120 children classified ASA1 and ASA2 (age range 2–10 years) admitted for elective urologic procedures under general anaesthesia were included. Children with known history of allergy to rocuronium bromide, midazoalm, ketamine, and those having either difficult cannulation (more than two trials) or suspected difficult intubation were excluded from the study. Eligible patients were randomly allocated to one of two equal groups (using computer generated-randomized test); ketamine group ($n = 60$) and midazolam group ($n = 60$). EMLA cream was applied for all children on the selected vein on the dorsum of the hand and covered with gauze about 1 h before shifting them to the main OT. In the waiting area of the main OT a 22 G IV cannula was secured followed by IV administration of glycopyrrolate (5 μg kg^{-1}) in addition to midazolam (0.05 mg kg^{-1}) in the midazolam group or ketamine hydrochloride (1 mg kg^{-1}) intravenously. The calculated dose of ketamine and midazolam was diluted with normal saline into 5 ml and given IV slowly by an anaesthetist while the child was being held by his or her parents and once the child was sedated he was placed supine on a trolley in accompaniment with both an anaesthetist and a nurse and shifted rapidly to the operating room (OR).

On arrival to the OR, children were immediately monitored with pulse oximetry, electrocardiograph, and non-invasive arterial blood pressure; meanwhile child was preoxygenated using a transparent face mask connected to Ayer T piece breathing circuit with 100% oxygen. Capnograph was connected after tracheal intubation. Oxygen desaturation defined by a first reading of SpO2 less than 92% was recorded.

Both groups were subjected to the same anaesthetic management; diluted thiopental (1.25%) 3 mg kg^{-1} was given intravenously then followed by an IV injection of rocuronium bromide 1 mg kg^{-1} in approximately 30 seconds to facilitate tracheal intubation. All children were intubated successfully after 90 seconds with an appropriate sized endotracheal tube followed by an IV administration of fentanyl (1 μg kg^{-1}). Children were mechanically ventilated with air enriched oxygen using a low-flow closed circuit. After induction of anaesthesia, the child was placed in lateral position and a lumbar epidural analgesia with a ''single shot'' injection of a mixture of isobaric bupivacaine 0.25% (0.8 mg kg^{-1}) and fentanyl (0.6 μg kg^{-1}) was injected into lumbar 4–5 or 3–4 epidural spaces in order to achieve both intraoperative and postoperative analgesia. Anaesthesia was maintained with isoflurane in a concentration of approximately 1% and air-enriched oxygen, increments of rocuronium were given to maintain muscle relaxation, at the end of surgery both atropine and neostigmine were administered for reversal of muscle relaxant and all children were extubated and shifted uneventfully to post-anaesthesia care unit.

To achieve study blindness, one of the anaesthetists (OR anaesthetist) gave premedication; glycopyrrolate and ketamine/midazolam according to group randomization kept with him, this anaesthetist prepared induction agents and rocuronium according to the study protocol. A second anaesthetist who was oblivious to group assignment injected both induction agent and rocuronium and assessed rocuronium injection pain objectively using the following withdrawal scale (Table 1).

Table 1 Grading of withdrawal response [5].

Degree of movement	Patient response
1	No response withdrawal
2	Movement at wrist only
3	Movement/ withdrawal involving arm only
4	Generalized response – withdrawal movement in more than one extremity, cough, or breath holding