

Research Article

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## Midazolam Enhances Ureter Visualization in Children Undergoing Magnetic Resonance Urography

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Sara Salarian<sup>1</sup>,  
Bahar Taherkhanchi<sup>2</sup>,  
Reza Seyyed Hossein Beigi<sup>3</sup>,  
Semiramis Salarian<sup>4</sup>,  
Bahador Bagheri<sup>5\*</sup>

1 Department of Anesthesiology, Mofid Children Hospital, Tehran, Iran.  
2 Department of Pediatrics, Arak University of Medical Sciences, Arak, Iran .  
3 Paytakht Medical Imaging Center, Tehran, Iran.  
4 School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.  
5 Department of Pharmacology, Semnan University of Medical Sciences, Semnan, Iran.

**\* Corresponding Author**

Bahador Bagheri, PhD  
Department of Pharmacology,  
Semnan University of Medical Sciences, Semnan,  
Iran  
Tel: 00982333448998  
Fax: 00982333448999  
Email: bahadordvm@yahoo.com

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### Introduction

Magnetic Resonance Urography (MRU) is used to examine physiologic or structural anomalies of the urinary tract even in neonates and infants [1]. The method is most commonly applied for the evaluation of hydronephrosis and provides valuable insight into a wide range of obstructive uropathies [2,3]. It is also beneficial in tumor characterization, in preoperative planning, and in the diagnosis of pyelonephritis and renal scarring where MRU has been shown to be superior to renal scintigraphy [4]. The use of MRU for the assessment of urolithiasis, vesicoureteral reflux,

**Introduction:** Magnetic Resonance Urography (MRU) is a popular method for identifying uropathies in children. Some children are not cooperative for such examinations and are sedated. We decided to evaluate the effects of midazolam as a sedative drug on ureter visualization in patients undergoing MRU.

**Materials and Methods:** The study was conducted in Paytakht Medical Imaging Center, Tehran, Iran. Two hundred and three children with urologic diseases were divided into 2 groups. Patients in the non-cooperative group received midazolam prior to MRU.

**Results:** Our findings showed that non-cooperative children had a better ureter visualization on MRU ( $P<0.01$ ).

**Conclusions:** Midazolam increased ureter visualization possibly by reduction in the ureter peristaltic motility. Therefore, its use could shorten the duration of MRU. It is beneficial to use midazolam in all children who undergo MRU.

**Keywords:** Diagnostic Imaging; MRI; Urography; Midazolam; Child; Ureter.

**Running Title:** Midazolam Enhances Ureter Visualization on MRU

renal trauma, and fetal urinary tract abnormalities is still partially limited [5]. In general, such examinations may frighten children and decrease their cooperation. Midazolam is one the most common sedative drugs both in adults and children. This drug acts through stimulation of GABA<sub>A</sub> receptors and causes a significant anxiolytic state [6]. In addition, various drug combinations have been proved to be useful for the sedation of children [7]. Midazolam alone or in combination with diphenhydramine is one the most popular sedative regimens for MRU [8]. It has been shown that midazolam can reduce the

peristaltic motion of the esophagus and is of value in endoscopy [9]. The aim of this study was to evaluate the effects of midazolam on ureter visualization in children undergoing MRU. We hypothesized that midazolam administration could increase ureter visualization.

**Materials and Methods**

**Study subjects**

The study population was children aged 4 to 8 with urinary disorders who required MRU. From 2009 to 2014, 203 children were studied in Paytakht Imaging Center, Tehran, Iran. Based on the children’s cooperation, they were allocated into 2 groups: patients who received midazolam as a sedative agent and patients who did not require sedation.

**MRU protocol**

All children were NPO for 8 hours. They were all hydrated with 10-15 cc/Kg normal saline. For sedation, patients received an IV dose of midazolam (0.15 to 0.3 mg/kg, Chemie pharmaceuticals, Iran). Furosemide (0.5 to 0.75 mg/kg) was given 20 minutes prior to administration of the contrast medium. Then, the patients underwent MRU by a 1.5T scanner (Magnetom Aera, Siemens, Erlangen, Germany) at 5-minute sequences. Three 5-minute sequences were taken.

**Statistical analysis**

Continuous data was analyzed using the Student’s t-test or the Mann–Whitney U test. P-values less than 0.05 were considered statistically significant.

**Results**

**Characteristics of the study subjects**

Clinical characteristics of the patients are presented in [Table 1](#). Both groups had similar range of age. About 60% of the patients in the cooperative group and 51% in the non-cooperative group were male. Vesicoureteral reflux was the most common indication for MRU in both groups.

**Ureter visualization**

From a total of 203 children, 127 patients were sedated and 76 patients were not. In the cooperative group, 10 (12.7 %) patients showed ureter visualization in the first sequence while in the non-cooperative group, 26 (34.2 %) patients had ureter visualization in the first sequence (P<0.01). Comparative visualization of the ureter is presented in [Table 2](#). In both groups, there were 3 patients with poor function and no ureter visualization.

**Table 1.** Clinical characteristics of the study groups [↑](#)

Characteristics	Cooperative group (no.127)	Non-Cooperative group (no.76)	P value
Age (years)	5 ± 1.4	6 ± 2.1	Non significant
Male	71	39	Non significant
<b>Urinary disorders</b>			
Urolithiasis	54	23	
VUR	70	52	
Trauma	5	2	
Malignancies	2	1	

Data are shown in number or mean ± SD

**Table 2.** Ureter visualization in different sequences in study groups [↑](#)

Sequence	Cooperative Group	Non-Cooperative Group	P value
1 <sup>st</sup> sequence	10 (12.7)	26 (34.2)	0.01
2 <sup>nd</sup> sequence	35 (27.5)	27 (35.5)	-
3 <sup>rd</sup> sequence	82 (64.5)	23 (30.2)	0.01

Data are shown in number or percent (%)

**Discussion**

In the present study, we showed that midazolam administration could increase ureter visualization and reduce artifacts in patients undergoing MRU. Sedation is very helpful in patients who are not cooperative. A considerable body of evidence supports the role of midazolam as an effective and safe drug in children. It has a rapid onset and short duration of action [8,10,11]. Midazolam alone or in combination with other drugs is routinely used for such examinations. However, some investigations have reported the untoward effects of midazolam even in short term use. It is believed that midazolam can rarely initiate

paradoxical effects in patients who use sedative medications for a long time [12]. Interestingly, a recent study by Hyun Tae showed that 2 mg midazolam caused paradoxical effects in adult patients who underwent endoscopy [13]. Even a single dose of midazolam could cause effects like excitement, restlessness, and loss of cooperation. In our study, we did not experience such problems. It is very well established that benzodiazepines bind to molecular components of the GABA<sub>A</sub> receptor in neuronal membranes in the central nervous system [6]. Electrophysiologic studies have shown that benzodiazepines potentiate GABAergic inhibition at all levels of the neuraxis, including the spinal cord, hypothalamus, hippocampus, substantia nigra, cerebellar cortex, and cerebral cortex. Benzodiazepines appear to increase the efficiency of GABAergic synaptic inhibition [6,7]. It is not known with certainty how midazolam can increase the visualization of ureter or how it is helpful in endoscopic procedures in some cases. Midazolam is obviously very lipid soluble and can promptly enter the CNS. On the other hand, Brown reported a Parkinsonian tremor affecting both hands and arms, as well as quite marked head titubation in a patient receiving the subcutaneous form of midazolam [14]. Taken together, the benefits of midazolam outweigh its rare side effects. It can shorten the duration of MRUI by increasing ureter visualization in the first sequences. To best of our knowledge, this is the first report of the effects of midazolam on the ureter peristaltic motility.

### Conclusions

Midazolam could increase ureter visualization. It is suggested that all patients receive midazolam for MRU, if not contradicted. Further investigations should provide more insight about the other off-label uses of midazolam and reveal that how this agent increases ureter visualization.

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### Conflict of Interest

None declared

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None declared

### References

1. Grattan-Smith, Little SB, Jones R. MR urography in children: how we do it. *Pediatr Radiol*, 2008;38:S3-17.
2. Leyendecker JR, Barnes CE, Zagoria RJ. MR urography: techniques and clinical applications. *Radiographics*, 2008;28(1):23-46.
3. Riccabona M. Feasibility of MR urography in neonates and infants with anomalies of the upper urinary tract. *Eur Radiol*. 2002;12(6):1442-50.
4. Nolte-Ernsting N. MR urography today. *Abdom Imaging*.2003;28(2):191-209.
5. Garcia-Valtuille R. Magnetic resonance urography: a pictorial overview. *Br J Radiol*.2006; 79(943):614-26.
6. Amin J, Weiss DS. GABA<sub>A</sub> receptor needs two homologous domains activation by GABA but not by pentobarbital. *Nature*.1993;366:565-569
7. Elder JS, Longenecker R. Premedication with oral midazolam for voiding cystourethrography in children: safety and efficacy. *American Journal of Roentgenology*. 1995;164:1229-32.
8. Lin TF. Antiemetic and analgesic-sparing effects of diphenhydramine added to morphine intravenous patient-controlled analgesia. *Br J Anaesth*. 2005;94(6):p. 835-9.
9. Cohen LB, Wechsler JS, Gaetano JN, et al. Endoscopic sedation in the United States: results from a nationwide survey. *American Journal of Gastroenterology*2006;101:967-74.
10. Mancuso CE, Tanzi MG, Gabay M. Paradoxical reactions to benzodiazepines: literature review and treatment options. *Pharmacotherapy*. 2004;24:1177-85.
11. Bahal-O'Mara N, Nahata MC, Murray RD, et al. Sedation with meperidine and midazolam in pediatric patients undergoing endoscopy. *European Journal of Clinical Pharmacology*. 1994;47:319-23.
12. Golparvar M, Saghaei M, Sajedi P, et al. Paradoxical reaction following intra-venous midazolam premedication in pediatric patients – a randomized placebo controlled trial of ketamine for rapid tranquilization. *Paediatric Anaesthesia*.2004;14:924-30.
13. Taea H, Kanga K, Mina Y, Ahn H B, et al. Paradoxical reaction to midazolam in patients undergoing endoscopy under sedation: Incidence, risk factors and the effect of flumazenil. *Digestive and Liver Disease*. 2014;46:710-715.
14. Brown D, Arthur D. Subcutaneous midazolam as a cause of extrapyramidal side effects in a patient with prostate cancer. *Jof Pain and Sympt Manage*. 2007;34:111-113.