American Journal of Emergency Medicine (2010) **28**, 820–827

ELSEVIER

The American Journal of Emergency Medicine

www.elsevier.com/locate/ajem

Brief Report

Low-dose ketamine for analgesia in the ED: a retrospective case series☆,☆☆

Laeben Lester MD[a,*], Darren A. Braude MD[a], Christopher Niles MD[b], Cameron S. Crandall MD[a]

[a]*Department of Emergency Medicine, University of New Mexico, Albuquerque, NM 87131-0001, USA*
[b]*Department of Emergency Medicine, Maimonides Medical Center, Brooklyn, NY 11219, USA*

Received 5 January 2009; revised 30 July 2009; accepted 30 July 2009

Abstract

Objectives: The aim of this study was to describe the use and effect of low-dose ketamine (LDK) for analgesia in the emergency department (ED).

Methods: A chart review was performed to identify all adult patients who received LDK for analgesia in our ED. Cases were identified by pharmacy record of ketamine administration. Low-dose ketamine was defined as the administration of 0.1 to 0.6 mg/kg of ketamine for pain control. Use of ketamine during procedural sedation was excluded. Data were analyzed descriptively.

Results: Thirty-five cases in which patients received LDK in the ED for a 2-year period were identified. Doses ranged from 5 to 35 mg. Administration was intravenous in 30 (86%) of 35 cases and intramuscular in 5 (14%) of 35 cases. Opioids were administered before or coadministered with LDK in 32 (91%) of 35 cases, and in the remaining 3 cases, opioids were used before the patient came to the ED. Improvement in pain was observed in 19 (54%) of 35 cases in which patients received LDK. Pain scores did not improve in 8 (23%) of 35 cases. Insufficient data were available to determine LDK effect for 8 (23%) of 35 cases. No significant adverse events were identified in any of the 35 cases.

Conclusions: The administration of LDK in the ED may be a safe and effective adjunct for analgesia in some patients. However, prospective randomized controlled trials are needed before widespread use of LDK for analgesia in the ED can be recommended.

1. Introduction

Pain is a common complaint in the emergency department (ED). Pharmacological agents used for the systemic treatment of pain in the ED generally fall into 1 of 3 categories: (1) opioids, (2) nonsteroidal anti-inflammatory drugs and acetaminophen, and (3) combinations of opioids such as hydrocodone or oxycodone with acetaminophen. Many studies have shown that pain is often undertreated in the ED [1-5]. Physician fear of oversedation and respiratory depression due to the administration of opioid medications has been cited as one contributing factor for the so-called oligoanalgesia in the ED [3,6,7].

The *N*-methyl-D-aspartate receptor blocker ketamine is a dissociative anesthetic with a proven safety record for anesthesia and procedural sedation in adults and children and has minimal respiratory depressant effect [8-11]. Although

☆ Computer funding provided by the Department of Emergency Medicine, University of New Mexico.

☆☆ Abstract presented at the SAEM Western Regional Research Forum, March 2007, Portland, OR.

* Corresponding author.

E-mail address: llester@salud.unm.edu (L. Lester).

0735-6757/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.ajem.2009.07.023

Table 1 Demographics and results for all subjects identified in the series

ID	Age (y)	Sex	Medication	IDU	ETOH use	ED CC/Dx	Pain before ketamine	Pain medications before ketamine	Dose and route of ketamine	Pain after ketamine	Additional pain medications in ED	Dispo	Comments
A. Improvement after LDK													
1	46	M	–	–	Yes	Assault with orbital wall Fx	10/10	Morphine 8 mg, Dilaudid 8 mg	15 mg IV	2-3/10	None	DC 45 min after ketamine	"Brief dysphoria" per physician
2	25	F	–	Heroin	–	Abscess	10/10	Vicodin × 2, fentanyl 250 mg, Dilaudid 2 mg	10 mg IV	0/10	None	Observation unit	I & D abscess before ketamine administration
3	54	M	Methadone	Heroin	–	Tibia fx with compartment syndrome	10/10	Morphine 4 mg	10 mg IV, 5 mg IV	"Marked relief of Sx" after LDK per physician note	None	Admit	OR
4	21	M	–	Heroin	–	Chemical cellulitis	10/10	Morphine 10 mg	10 mg IV	"Rests in bed, pt with pain improved"	None	DC 1 h 40 min after ketamine	
7	35	M	Oxycodone	–	–	CP with h/o leukemia	8/10	Morphine 16 mg	10 mg IV ×2	5/10	Morphine 4 mg (4 h 15 min after ketamine)	Admit	
8	43	F	Percocet	–	–	Kidney stones	8/10	Morphine 16 mg, Toradol 30 mg	10 mg IV	3/10	None	DC 2 h after ketamine	
8	43	F	Percocet	–	–	Kidney stones	8/10	Morphine 24 mg, Toradol 30 mg	5 mg IV ×2	4/10, "Ketamine with better relief of pain"	None	DC 41 min after ketamine	
10	37	M	–	–	–	Abscess	10/10	Morphine 26 mg	7 mg IV	"Resting comfortably, no complaints at this time" per physician	Morphine 10 mg (after OR)	Admit	OR
11	24	M	–	–	–	Pilonidal cyst	7/10	Morphine 18 mg	10 mg IV	2/10	None	DC 45 min after ketamine	I & D abscess

(*continued on next page*)

Table 1 (*continued*)

ID	Age (y)	Sex	Medication	IDU	ETOH use	ED CC/Dx	Pain before ketamine	Pain medications before ketamine	Dose and route of ketamine	Pain after ketamine	Additional pain medications in ED	Dispo	Comments
14	34	F	Methadone	Heroin	–	Abscess	10/10	None	10 mg IV ×2	2/10, "with good results"	None	Admit	OR
15	23	M	Oxycodone	–	–	Abdominal pain	10/10	Morphine 4 mg	8 mg IV	0/10	None	DC 1 h 45 min after ketamine	
22	37	M	Methadone	Heroin	–	Lower extremity cellulitis	10/10	Morphine 10 mg	20 mg IV	0/10	None	DC 2 h 5 min after ketamine	
28	55	M	–	Heroin	–	Triquetral fx	"Appeared in discomfort" per physician	None	10 mg IM ×2	"Marked but not complete resolution of pain" per MD	None	DC 5 min after ketamine	Splinting
32	21	M	Fentanyl, Demerol, Percocet	–	–	Back pain	10/10	Fentanyl 200 mg, Dilaudid 2 mg	5 mg IV ×2	"Pt feeling much better status post s/p ketamine"	None	DC 1 h 5 min	
33	51	M	–	Heroin	–	Abscess, HIV+	10/10	None	20 mg IM ×3	0/10	None	Admit	I & D abscess
35	32	M	Morphine	Heroin	–	Cellulitis/ abscess	10/10	Fentanyl 500 mg (concurrent with ketamine)	10 mg IV ×4	"Pt sleeping, ketamine with excellent results, pain was well controlled" between doses	None	DC 1 h 15 min after ketamine	Fentanyl given as 100-mg doses × 5; ketamine as 10 mg IV ×4 every 2-5 h for 13 h
36	35	M	Percocet, methadone	Heroin	–	Cellulitis	8/10	Morphine 10 mg, Dilaudid 22 mg	20 mg IV, 10 mg IV	0/10	Dilaudid 4 mg ×2	Admit	
38	42	M	Librium	Polysubstance	–	Hemorrhoids	8/10	Morphine 4 mg	10 mg IV	5/10	None	DC 1 h 15 min after ketamine	
39	45	F	–	–	–	Kidney stones	10/10	Fentanyl 100 mg, Morphine 12 mg, Toradol 20 mg	5 mg IV	5/10	None	DC 2 h 50 min after ketamine	

B. No improvement after LDK													
5	27	F	Morphine, oxycodone	–	–	Abdominal pain, constipation, UTI	10/10	Dilaudid 6 mg	5 mg IV	10/10	Dilaudid 10 mg, PCA	Admit	Phenergan before and after ketamine
13	34	M	–	–	–	Abscess, metacarpal fx	10/10	Fentanyl 300 mg	20 mg IV	10/10	None	DC	Ketamine also with reduction
16	44	F	–	Heroin	–	Abscess	10/10	Morphine 4 mg	20 mg IM	8/10	None	DC	I&D then 0/10
19	27	F	–	–	–	Elbow dislocation	10/10	Morphine 8 mg	10 mg IV	10/10	Morphine 8 mg	DC	Elbow reduced then 2/10
23	36	M	–	Heroin	–	Abscess	Unknown	Morphine 5 mg	10 mg IV	Unknown	Morphine 16 mg (4 mg ×2, 8 mg ×1, 15 and 45 min after ketamine)	DC	No pain levels noted
25	50	F	–	Heroin	–	Back pain, bacteremia	10/10	Vicodin, Percocet ×2	7 mg IV, 5 mg IV	"No relief," 10/10	Dilaudid 9 mg	Admit	
29	46	M	–	Heroin	–	Osteomylitis, abscess	10/10	Fentanyl 75 mg	7 mg IV	Unknown	Oxycodone 20 mg PO	Admit	No pain level noted after ketamine, 5/10 after oxycodone
31	57	M	Fentanyl, Vicodin, Neurontin	–	–	CP	8/10	Morphine 28 mg	10 mg IV	7/10	None	DC	
C. Insufficient data													
12	36	M	–	Heroin	–	Abscess	10/10	Morphine 8 mg (concurrent)	7 mg IM	Unknown	None	DC 50 min after ketamine	I&D
20	31	M	–	Heroin	–	Abscess	Unknown	None	10 mg IM	Unknown	Vicodin ×2	DC to mental health center 1 h 50 min after ketamine	I&D
24	44	M	–	Heroin	–	Abscess	10/10	Morphine 12 mg	35 mg IV	Unknown	None	DC 1 h 30 min after ketamine	I&D

(*continued on next page*)

Table 1 (*continued*)

ID	Age (y)	Sex	Medication	IDU	ETOH use	ED CC/Dx	Pain before ketamine	Pain medications before ketamine	Dose and route of ketamine	Pain after ketamine	Additional pain medications in ED	Dispo	Comments
26	37	M	–	–	Yes	Motorcycle accident, multiple fx	7/10	Fentanyl 300 mg	10 mg IV 30 mg IV	Unknown	Fentanyl 100 mg concurrent then Fentanyl 200 mg, Morphine 18 mg, Percocet ×6	Admit	
27	33	F	Methadone	IV Cocaine	–	Abscess	10/10	None	10 mg IV	Unknown	Unknown	Unknown	Paucity of information surrounding procedure
30	29	F	–	Crack	Yes	Cellulitis, abscess	10/10	Roxicet ×2	5 mg IV ×2, 10 mg IV	Unknown	Morphine 10 mg	Admit	I&D
34	40	M	–	Heroin	–	Abscess	10/10	Morphine 8 mg (concurrent)	10 mg IV	Unknown	Unknown	DC 5 h 20 min after ketamine	I&D
37	27	F	Morphine, Neurontin	–	Yes	N/V, abdominal pain	10/10	None	5 mg IV	Unknown	None	Left AMA 2 h after ketamine	

IV indicates intravenous; IM, intramuscular; UTI, urinary tract infection; PO, per os: IDU, Illicit Drug Use; ETOH, alcohol; CC/Dx, chief complaint/Diagnosis; Dispo, disposition, fx, fracture; DC, discharge; I&D, Incision and Drainage; sx, symptoms; OR, operating room; PCA, patient controlled analgesia; AMA, against medical advice; UTI, urinary tract infection; PO, by mouth.

the use of ketamine in the ED was once highly controversial, a large number of studies published in the last 2 decades have confirmed its safety and have made ketamine available in most EDs [12-14]. Many studies of subanesthetic administration of ketamine, termed *low-dose ketamine* (LDK), suggest that it provides effective analgesia with minimum adverse effects when administered alone or as an adjunct to opioids [15-19]. Likewise, LDK has been reported to decrease tolerance to opioids and to have an opioid-sparing effect [20-23]. The use of LDK for analgesia has been reported in the anesthesia and surgical literature for treatment of postoperative or cancer-associated pain [15-19,23]. Likewise, nonclinical experimental studies in the gastroenterology, anesthesia, and emergency medicine literature have shown the efficacy of LDK for analgesia alone and as an adjunctive medication with opioids [24-27]. A recent study performed in ED-affiliated mobile intensive care units in France showed that LDK had an opioid-sparing effect in trauma patients with acute pain [20]. To our knowledge, no reports of LDK administration in the ED for the treatment of pain have been published in the medical literature.

In this article, we present a retrospective case series of patients receiving LDK for analgesia in the ED to describe the efficacy and safety of the agent in that setting.

2. Methods

We performed a retrospective review of cases in which LDK was administered in our ED. The study received approval from the institutional review board at our university, and informed consent was waived.

The study site is an urban level I trauma center and university teaching hospital that also serves as the local county hospital. The ED sees approximately 75,000 adult patients per year.

All patients 18 years or older who received ketamine in the ED within a 2-year period (from July 1, 2004, to June 30, 2006) were identified by pharmacy records. The electronic medical record was then reviewed by one of the primary authors to identify which of these patients had received LDK for analgesia. Low-dose ketamine was defined as the administration of less than 0.6 mg/kg of ketamine for pain control, excluding patients receiving ketamine during procedural sedation. This cutoff was chosen because 0.5 mg/kg is the maximum single bolus analgesic dose described in most studies in the literature, although some include doses as high as 1 mg/kg [28]. Once subjects were identified, the chart was further reviewed by the authors to identify the dose, route, and effect of LDK administration. Data were extracted onto a standardized collection sheet; data collection was not blinded. Use of narcotics and other pain medications before and/or after LDK as well as demographic data (including sex; age; medical history; use of pain medications, illicit drugs, or alcohol; chief complaint; disposition; and time to discharge) were also assessed. The data were analyzed and are presented descriptively.

3. Results

Thirty-five cases in which LDK was administered for pain control during the 2-year period, representing 34 different patients, were identified (Table 1). The mean age of the patients in this study was 37 years; 66% were men, and 34% were female. The most common chief complaint was abscess, representing 16 (46%) of 35 cases. Chronic pain medication use or illicit drug abuse was specifically recorded in 28 (80%) of 35 cases.

Each ketamine dose ranged between 5 and 35 mg. The median dose was 10 mg, and the mean dose was 15.7 mg. Repeat dosing occurred in 12 (34%) of 35 cases, and the maximum total dose was 60 mg, delivered as 3 separate 20-mg intramuscular doses. The drug was administered intravenously in 30 (86%) of 35 cases and intramuscularly in 5 (14%) of 35 cases. Opioids were administered before or concurrent with LDK in 32 (91%) of 35 cases. The remaining 3 patients were on long-acting opioids or had used heroin near their visit.

Low-dose ketamine seemed to improve pain in 19 (54%) of 35 cases by a documented 3-point decrease in pain score on a 10-point scale or physician or nurse description of marked improvement in pain (Fig. 1, Table 1A). In 8 (23%) of 35 cases, no benefit was seen (Table 1B). For an additional 8 (23%) of 35 cases, no post–drug administration pain scale or description of pain was available in the medical record (Table 1C).

In subjects with improved pain scores after LDK, only 3 (16%) of 19 received additional opioid pain medications in the ED, whereas 5 (63%) of 8 subjects in the group who did not have improved pain scores received additional pain medications. In the group with insufficient data, 3 (38%) of 8 subjects received additional pain medications.

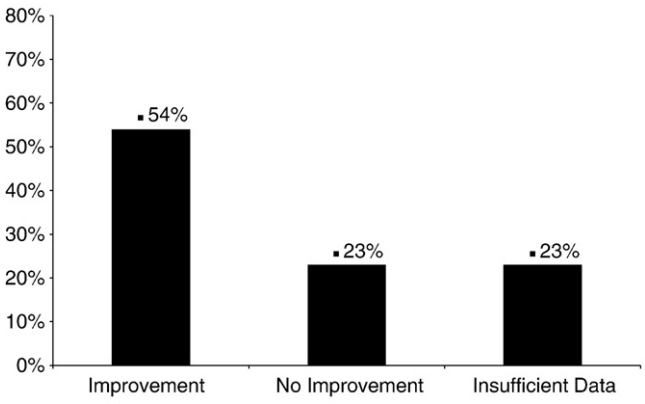

Fig. 1 Response after LDK: improvement, no improvement, or insufficient data.

No dangerous adverse events associated with the administration of LDK were identified in this retrospective case series. In 1 patient, "brief mild dysphoria" was noted, but the patient also had improvement in his pain.

4. Discussion

In this retrospective case series, we provide the first description of LDK for analgesia in the ED. Our series suggests that LDK may be an effective adjunct to opioid pain medication in patients with pain that is difficult to treat. Low-dose ketamine was primarily administered to patients with high tolerance to narcotics, a group in which pain is often difficult to treat with the doses of narcotics that many physicians and nurses are comfortable using [6,7]. The few patients who did not receive narcotics in the ED were reported to use opioids regularly and were very likely to have drugs of this class in their system, further suggesting that use of LDK in this series was primarily adjunctive and was being selected by the treating physicians to target this patient population.

A clinically significant reduction in pain was observed in 19 (54%) of 35 cases after the administration of LDK, suggesting that LDK may be an efficacious analgesic in the ED. This response rate is in range with those reported in studies evaluating the analgesic efficacy of other nonopioid agents [29-31]. However, this is less than the 80% response rate reported by Sadove et al in the original study introducing LDK for analgesia [19]. If any of the patients in whom a post-LDK pain score was not recorded in fact had benefit, the response rate in our series might have been higher. Three of these patients were discharged without receiving further parenteral narcotics, suggesting a high likelihood of efficacy in up to 22 (63%) of 35 cases. Likewise, we chose 3 points on a 10-point scale as the minimal clinically significant difference (MCSD) [32], whereas others have suggested a 2-point MCSD [33]. Had we used 2 points for the MCSD, 1 additional patient would have shown to have a positive response (23/35 cases, 66%).

Our results suggest a possible opioid-sparing effect in patients responding to LDK. This is consistent with the findings of Galinski et al [20], who found a 26% decrease in opiate use when adjunctive LDK was administered to trauma patients in the field. Several previous studies also show an opioid-sparing effect, including 2 meta-analyses of perioperative LDK [21,22]. Improved analgesia with LDK in the perioperative period has also been found in multiple studies and has also been found by meta-analysis [22,28]. In patients with cancer pain, studies also suggest an improved analgesia and decreased tolerance [23]. Conversely, 2 recent studies of perioperative pain show no benefit of LDK [34,35].

No dangerous adverse events were noted after the administration of LDK in this series. Although this is reassuring, this is a retrospective case series, and this study was not designed nor powered to assess for safety. The single minor adverse effect reported was "brief mild dysphoria." In our anecdotal experience, it is very important to instruct the nurse that medication be administered slowly over at least 60 seconds and to warn the patient about the possibility of a brief unpleasant "rush."

There are several limitations to this study. It is a retrospective case series and not randomized or placebo controlled. The case series is small, and incomplete data were found in nearly a quarter of the identified cases (8/35 cases). Without randomization, the case series is more subject to bias, and there is no way to control for other interventions that may have affected outcomes. Prospective, randomized, placebo-controlled trials of LDK in the ED are warranted.

In conclusion, this case series describes the use of LDK for analgesia in our ED and suggests that it may be a safe and effective analgesic adjunct in some ED patients, particularly those with high narcotic tolerance.

References

[1] Todd KH, Ducharme J, Choiniere M, Crandall CS, Fosnocht DE, Homel P, et al. Pain in the emergency department: results of the Pain and Emergency Medicine Initiative (PEMI) multicenter study. J Pain 2007;8(6):460-6.
[2] Pines JM, Perron AD. Oligoanalgesia in ED patients with isolated extremity injury without documented fracture. Am J Emerg Med 2005; 23(4):580.
[3] Ngai B, Ducharme J. Documented use of analgesics in the emergency department and upon release of patients with extremity fractures. Acad Emerg Med 1997;4(12):1176-8.
[4] Wilson JE, Pendleton JM. Oligoanalgesia in the emergency department. Am J Emerg Med 1989;7(6):620-3.
[5] Reichl M, Bodiwala GG. Use of analgesia in severe pain in the accident and emergency department. Arch Emerg Med 1987;4(1):25-31.
[6] Haller G, Waeber JL, Infante NK, Clergue FK. Ketamine combined with morphine for the management of pain in an opioid addict. Anesthesiology 2002;96(5):1265-6.
[7] Rapp SE, Wild LM, Egan KJ, et al. Acute pain management of the chronic pain patient on opiates: a survey of caregivers at University of Washington Medical Center. Clin J Pain 1994;10(2):133-8.
[8] Green SM, Sherwin TS. Incidence and severity of recovery agitation after ketamine sedation in young adults. Am J Emerg Med 2005;23(2):142-4.
[9] Ellis DY, Husain HM, Saetta JP, Walker T. Procedural sedation in paediatric minor procedures: a prospective audit on ketamine use in the emergency department. Emerg Med J 2004;21(3):286-9.
[10] Green SM. Ketamine in adults: what emergency physicians need to know about patient selection and emergence reactions. Acad Emerg Med 2000;7:278-81.
[11] Green SM, Rothrock SG, Lynch, et al. Intramuscular ketamine for pediatric sedation in the emergency department: safety profile with 1,022 cases. Ann Emerg Med 1998;31(6):688-97.
[12] Pruitt JW, Goldwasser MS, Sabol SR, Campbell RL, et al. Intramuscular ketamine, midazolam, and glycopyrrolate for pediatric sedation in the emergency department. J Oral Maxillofac Surg 1995;53 (1):13-7 [discussion 18].
[13] Green SM. The safety of ketamine for emergency department pediatric sedation. J Oral Maxillofac Surg 1995;53(10):1232-3.
[14] Green SM, Krauss B. Ketamine is safe, effective, and appropriate technique for emergency department paediatric procedural sedation. Emerg Med J 2004;21(3):271-2.
[15] Dal D, Celebi N, Elvan EG, et al. The efficacy of intravenous or peritonsilar infiltration of ketamine for postoperative pain relief in children following adenotonsillectomy. Paediatr Anaesth 2007;17(3): 263-9.

[16] Mitchell AC, Fallon MT. A single infusion of intravenous ketamine improves pain relief in patients with critical limb ischemia: results of a double blind randomized controlled trial. Pain 2002;97(3):275-81.
[17] Aida S, Yamakura T, Baba H, Taga K, Fukuda S, Shimoji K. Preemptive analgesia by intravenous low-dose ketamine and epidural morphine in gastrectomy: a randomized double-blind study. Anesthesiology 2000;92(6):1624-30.
[18] Janeczko GF, el-Etr AA, Younes S. Low-dose ketamine anesthesia for obstetrical delivery. Anesth Analg 1974;53(6):828-31.
[19] Sadove MS, Shulman M, Hatano S, Fevoid N. Analgesic effects of ketamine administered in subdissociative doses. Anesth Analg 1971; 50(3):452-7.
[20] Galinski M, Dolveck F, Combes X, et al. Management of severe acute pain in emergency settings: ketamine reduces morphine consumption. Am J Emerg Med 2007;25(4):385-90.
[21] Bell RF, Dahl JB, Moore RA, et al. Peri-operative ketamine for acute post-operative pain: a quantitative and qualitative systematic review (Cochrane review). Acta Anaesthesiol Scand 2005;49(10):1405-12.
[22] Elia N, Tramer MR. Ketamine and postoperative pain—a quantitative systemic review of randomized trials. Pain 2005;113:61-70.
[23] Mercadante S, Arcuri E, Tirelli W, et al. Analgesic effect of intravenous ketamine in cancer patients on morphine therapy: a randomized, controlled, double-blind, crossover, double-dose study. J Pain Symptom Manage 2000;20(4):246-52.
[24] Strigo IA, Duncan GH, Bushnell MC, et al. The effects of racemic ketamine on painful stimulation of skin and viscera in human subjects. Pain 2005;113:255-64.
[25] Takada M, Fukusaki M, Terao Y, et al. Preadministration of low-dose ketamine reduces tourniquet pain in healthy volunteers. J Anesth 2005; 19(2):180-2.
[26] Tucker PT, Kim YK, Nadeson R, Goodschild CS. Investigation of the potentiation of the analgesic effects of fentanyl by ketamine in humans: a double-blinded, randomized, placebo controlled, crossover study of experimental pain. BMC Anesthesiol 2005;5(1).
[27] Smith DC, Mader TJ, Smithline HA. Low dose intravenous ketamine as an analgesic: a pilot study using an experimental model of acute pain. Am J Emerg Med 2001;19(6):531-2.
[28] Subramaniam K, Subramaniam B, Steinbrook RA. Ketamine as adjuvant analgesic to opioids: a quantitative and qualitative systematic review. Anesth Analg 2004;99(2):482-95.
[29] Mellegers MA, Furlan AD, Mailis A. Gabapentin for neuropathic pain: systemic review of controlled and uncontrolled literature. Clin J Pain 2001;17(4):284-95.
[30] Lipton RB, Goldstein J, Baggish JS, et al. Aspirin is efficacious for the treatment of acute migraine. Headache 2005;45(4):283-92.
[31] Lewis DW, Winner P, Hershey AD, et al. Efficacy of zolmitriptan nasal spray in adolescent migraine. Pediatrics 2007;120(2):390-6.
[32] Bird SB, Dickson EW. Clinically significant changes in pain along the visual analog scale. Ann Emerg Med 2001;38:639-43.
[33] Todd KH, Funk JP. The minimum clinically important difference in physician-assigned visual analog pain scores. Acad Emerg Med 1995; 3:142-6.
[34] Katz J, Schmid R, Snijdelaar DG, et al. Pre-emptive analgesia using intravenous fentanyl plus low-dose ketamine for radical prostatectomy under general anesthesia does not produce short-term or long-term reductions in pain or analgesic use. Pain 2004;110(3):707-18.
[35] Aubrun F, Gaillat C, Rosenthal D, et al. Effect of a low-dose ketamine regimen on pain, mood, cognitive function and memory after major gynaecological surgery, a randomized, double-blind, placebo-controlled trial. Eur J Anaesthesiol 2008;25(2):97-105.