Propofol-Based Procedural Sedation with or without Low-Dose Ketamine in Children

Sheikh Sohail Ahmed[1] Mara Nitu[1] Shawn Hicks[1] Lauren Hedlund[1] James E. Slaven[2] Mark R. Rigby[1]

[1] Department of Pediatric Critical Care, Riley Hospital for Children at Indiana University Health, Indiana University School of Medicine, Indianapolis, Indiana, United States
[2] Department of Biostatistics, Indiana University School of Medicine, Indiana University, Indianapolis, Indiana, United States

Address for correspondence Sheikh Sohail Ahmed, MD, Section of Pediatric Critical Care, Riley Hospital for Children at Indiana University Health, 705 Riley Hospital Drive, RI 4B 4909, Indianapolis, IN 46202, United States (e-mail: ssahmed@iupui.edu).

J Pediatr Intensive Care 2016;5:1–6.

Abstract

Objective Examine comparative dosing, efficacy, and safety of propofol alone or with an initial, subdissociative dose of ketamine approach for deep sedation.

Background Propofol is a sedative-hypnotic agent used increasingly in children for deep sedation. As a nonanalgesic agent, use in procedures (e.g., bone marrow biopsies/aspirations, renal biopsies) is debated. Our intensivist procedural sedation team sedates using one of two protocols: propofol-only (P-O) approach or age-adjusted dose of 0.25 or 0.5 mg/kg intravenous ketamine (K + P) prior to propofol. With either approach, an initial induction dose of 1 mg/kg propofol is recommended and then intermittent dosing throughout the procedure to achieve adequate sedation to safely and effectively perform the procedure. *Approach*: Retrospective evaluation of 754 patients receiving either the P-O or K + P approach to sedation.

Results A total of 372 P-O group patients and 382 K + P group. Mean age (7.3 ± 5.5 years for P-O; 7.3 ± 5.4 years for K + P) and weight (30.09 ± 23.18 kg for P-O; 30.14 ± 24.45 kg for K + P) were similar in both groups (p = NS). All patients successfully completed procedures with a 16% combined incidence of hypoxia (SPO2 < 90%). Procedure time was 3 minutes longer for K + P group than P-O group (18.68 ± 15.13 minutes for K + P; 15.11 ± 12.77 minutes for P-O; $p < 0.01$), yet recovery times were 5 minutes shorter (17.04 ± 9.36 minutes for K + P; 22.17 ± 12.84 minutes for P-O; $p < 0.01$). Mean total dose of propofol was significantly greater in P-O than in K + P group (0.28 ± 0.20 mg/kg/min for K + P; 0.40 ± 0.26 mg/kg/min for P-O; $p < 0.0001$), and might explain the shorter recovery time.

Conclusion Both sedation approaches proved to be well tolerated and equally effective. Addition of ketamine was associated with reduction in the recovery time, probably explained by the statistically significant decrease in the propofol dose.

Keywords
- propofol
- ketamine
- painful procedure

Introduction

Procedural sedation and analgesia are routinely provided to pediatric patients requiring painful procedures. In this context, propofol has gained popularity because of its rapid induction of deep sedation and brief duration of action. Propofol is thought to produce its sedative/anesthetic effects by the positive modulation of the inhibitory function of the neurotransmitter γ-aminobutyric acid (GABA) through the ligand-gated $GABA_A$ receptors. The onset of sedation is within 40 seconds and a single dose of propofol typically wears off within minutes.[1–4] Limitations of propofol include

received
November 17, 2014
accepted after revision
May 7, 2015
published online
November 18, 2015

DOI http://dx.doi.org/10.1055/s-0035-1568152.
ISSN 2146-4618.

pain at the injection site, as well as respiratory and hemodynamic instability. Because propofol lacks intrinsic analgesic properties, opioids may be co-administered during the procedures, which may add to the risk of cardiac and respiratory depression.[3,5–8] Ketamine is a unique sedative resulting in a lack of patient response to any stimuli caused by dissociation between the thalamic and limbic regions of the brain. This dissociative sedation resembles a trancelike cataleptic state with profound sedation, analgesia, and amnesia due to its action on *N*-methyl-D-aspartate (NMDA) and non-NMDA glutamate receptors, nicotinic and muscarinic cholinergic, and monoaminergic and opioid receptors. Its onset of action is within a few minutes of administration with an elimination half-life of 7 to 11 minutes.[9–11]

Ketamine preserves respiratory drive and maintains protective airway reflexes with minimal cardiovascular depression due to sympathomimetic properties.[10,11] Major side effects of ketamine are the incidence of emergent reactions at increasing doses, such as hallucination, nightmares, and excessive salivation in certain patients.[10,11]

Several synergies are apparent between these two agents. As a result, this combination is being increasingly used due to perceived advantages over propofol only for procedural sedation but few known direct comparisons exist. Our intensivist-led sedation team used a propofol-only protocol from 2006 to 2010 for all painful and nonpainful procedures.

In 2011, our group transitioned to the use of low-dose ketamine with propofol for all procedures. We hypothesized that the use of this combination is a safe and effective alternative, with the potential of less propofol requirements resulting in shorter recovery times.

Materials and Methods

Collection of quality assurance data includes: patient demographics, adverse events, physiologic variables, drug dosages, time required to sedate the patient, time needed to complete the procedure, and recovery time. After approval by the institutional review board, we conducted a retrospective analysis using the above-mentioned database of all patients who received deep sedation for procedures between October, 2010, and May, 2012.

Institutional sedation policies, based on guidelines developed by the Joint Commission on Accreditation of Health Care Organization and the American Academy of Pediatrics, were closely followed.[12,13] All patients were screened to make sure that they were appropriate sedation candidates (e.g., ASA I and III) and age 6 months to 18 years. The screening process includes a chart review, past medical history, and surgical and anesthetic histories. Patients were excluded from the study for: age < 6 months or > 18; ASA classification IV or greater; history of significant active cardiac, pulmonary, hepatic, or renal disease; weight > 130 kg; history of diagnosed obstructive sleep apnea; or history of allergy or sensitivity to any sedation medication. Parents are contacted directly by telephone to resolve any unclear medical issues. Vital signs including pulse oximetry, heart rate, noninvasive blood pressure monitoring, and nasal capnography were continuously monitored and documented every 5 minutes throughout sedation.

The propofol-only (P-O) sedation protocol consisted of an intravenous (IV) bolus of propofol 1 mg/kg over 1 to 2 minutes. Repeat boluses were used as needed to achieve and maintain the desired level of sedation until the procedure was over. In the ketamine + propofol (K + P) group, sedation was started with a single low dose of ketamine bolus (0.5/kg mg < 20 kg; 0.25/kg mg > 20 kg) followed with IV propofol titrated as above. The reason for choosing low dose in heavy weight and older patient was to avoid giving them higher cumulative doses and to avoid the side effects of emergence reaction and excessive salivation.

There was no maximum dose of propofol as long as the patient's respiratory and hemodynamic status remained stable. Supplemental oxygen was administered via nasal cannula if saturation dropped to less than 90% for more than 30 seconds. Peak onset of the sedation is the time from the start of the loading dose to achievement of a Ramsay score of 4. Procedure time is defined as the time from achieving the required Ramsay score to the end of the procedure (stoppage of drug administration). Recovery time was defined as the time from the end of the procedure to actual time the patient was back to baseline status. Discharge time is the time from recovery until the discharge of the child from the recovery room.

Data are presented as means and standard deviations, unless otherwise noted. Propofol-induced vital sign changes from baseline for the entire study cohort were compared using student's *t*-test and Wilcoxon nonparametric test, depending on the distribution of the data, for continuous data and with Fisher exact tests for categorical data. The two sedation groups were compared with respect to demographic, clinical, and time variables. We also performed a comparative subgroup analysis of the patients who received low- and high-dose ketamine based on their weight to assess if this was associated with any significant effect on the propofol dose and time variables among the groups. Data were analyzed using dedicated statistical software, SAS v9.3 (SAS Institute, Cary, NC). A p-value < 0.05 was considered statistically significant. Data analysis was performed by James E. Slaven, one of the authors of the manuscript, who works for Indiana University's School of Medicine's Department of Biostatistics.

Results

A total of 754 patients received procedural sedation for painful procedures: 372 patients in the P-O group and 382 in the K + P group. The most common procedures were lumbar puncture, central line placement, dental procedures, and bronchoscopies (►**Table 1**). There was no difference between the groups with respect to age, weight, and gender (►**Table 2**). Of the 754 procedures performed, 748 (99.2%) were completed successfully with 18 patients (2.3%) requiring adjunctive medications. Seven patients in the K + P group required fentanyl, while in the P-O group eight were given either fentanyl or midazolam to complete the

Table 1 Comparison of specific procedures

	Ketamine + propofol		Propofol		*p*-Value
	Number	Procedure time in minutes	Number	Procedure time in minutes	
Minor orthopedic procedures	10	14 (10)	7	12 (6)	0.845
Chest tubes	5	13 (5)	4	13 (12)	0.549
Bronchoscopies	39	12 (5)	46	10 (6)	0.038
Bone marrow	34	11 (6)	13	9 (6)	0.545
Lumbar punctures	113	10 (7)	113	10 (8)	0.843
Lumbar punctures + bone marrow	15	16 (8)	14	11 (5)	0.049
Dental procedures	16	48 (13)	10	31 (15)	0.018
Central line insertions	40	28 (13)	46	21 (12)	0.011
Auditory brainstem responses	15	40 (18)	7	39 (20)	0.972
Kidney biopsies	15	13 (6)	10	12 (4)	0.642
Liver biopsies	8	14 (6)	14	9 (3)	0.055
Burn/wound dressing changes	16	27 (13)	12	18 (9)	0.040
Bone scan	12	44 (16)	13	45 (20)	0.957
CT scan	12	11 (5)	38	11 (7)	0.981
Other	32	26 (17)	24	21 (16)	0.202

Note: Values are the number of procedures and the mean (standard deviation) of procedure time in minutes. *p*-Values are from Wilcoxon nonparametric tests due to the skewness of the data.

Table 2 Demographics and times

	Ketamine + propofol ($n = 382$)	Propofol group ($n = 372$)	*p*-Value
Age (y)	7.3 (5.4)	7.3 (5.5)	0.99
Weight (kg)	30.1 (24.5)	30.1 (23.2)	0.81
Male (%)	216 (56.5%)	212 (57.0%)	0.90
Propofol dose (mg/kg/min)	0.28 (0.20)	0.40 (0.26)	<0.0001
Procedure time (min)	18.68 (15.13)	15.11 (12.77)	<0.01
Recovery time (min)	17.04 (9.36)	22.17 (12.84)	<0.01
Overall time (min)	35.71 (17.46)	37.23 (17.88)	0.16

Note: Values are mean (standard deviation) for continuous variables and frequency (%) for categorical variables. *p*-Values are from Wilcoxon nonparametric test, due to skewness in data, and Fisher exact test for categorical variables.

procedure. Mean total dose of propofol was significantly different between groups (0.28 ± 0.20 mg/kg/min for K + P vs. 0.40 ± 0.26 mg/kg/min for P-O; $p < 0.0001$) (►**Fig. 1**). Median procedure time was longer in the K + P group with shorter recovery times compared with the P-O group (►**Table 2** and ►**Fig. 2**). The incidence of adverse events was comparable between the groups (16.5% for K + P vs. 15.6% for P-O) (►**Table 3**).

The 382 patients in K + P group were further divided into two groups (K + P 25 and K + P 50) based on the ketamine dose they received. There were 186 patients in K + P 50 group and 196 in K + P 25 group. Because their ketamine dose was based on weight, K + P 25 includes the section of patients who were older and heavier than the patients in the K + P 50 group but there was no gender difference among the groups. The propofol dose was significantly different among the groups (0.32 ± 0.21 mg/kg/min for K + P 50 vs. 0.28 ± 0.19 mg/kg/min for K + P25; $p < 0.0001$) . Median procedure time was longer by 8.27 minutes in K + P 50 group (22.92 ± 17 vs. 14.65 ± 11.82; $p < 0.0001$). Similarly, recovery time also was longer by 1.36 minutes in K + P 50 groups (17.75 ± 9.36 vs. 16.36 ± 9.33; $p < 0.001$). The incidence of adverse events was comparable between the groups.

All the patients were NPO for 8 hours prior to procedure and no one has hypersecretion or was given prophylactic anticholinergic to prevent this. There was no episode of aspiration in any of the patients. The most common adverse event in both groups was desaturation, and all of the patients responded to airway positioning or supplemental oxygen. Five (1.3%) patients in the K + P group and three (0.8%) in the P-O group required bag-valve-mask ventilation but no one in either group required tracheal intubation.

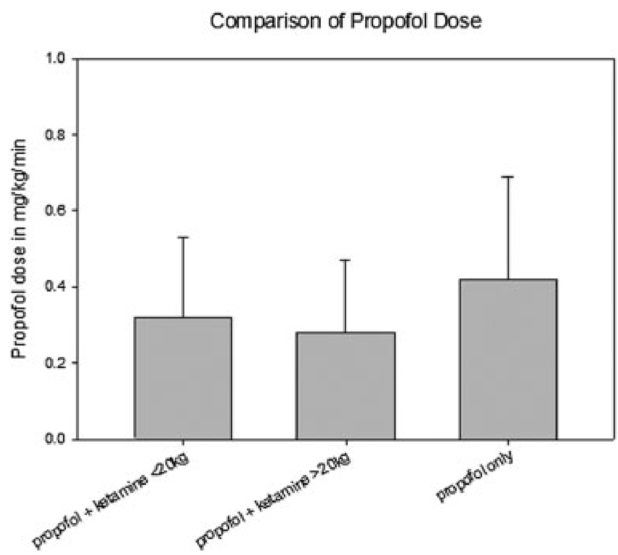

Fig. 1 Mean propofol dose.

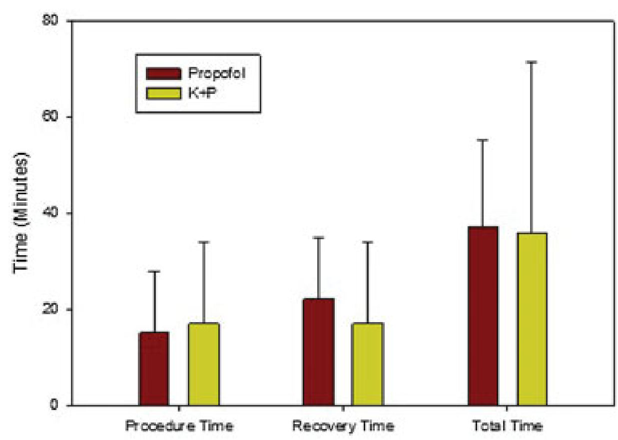

Fig. 2 Procedure time, recovery time, and total time.

Hypotension was defined as one blood pressure recording below the age-based normal range.[5] The incidence of hypotension between the groups was not statistically significant ($p = 0.56$). Although a drop in blood pressure was commonly observed, medical intervention was not needed.

Table 3 Complications and adjunctive therapy

Complication or adjunctive therapy	Ketamine + propofol	Propofol only	*p*-Value
Desaturation	63 (16.5)	58 (15.7)	0.767
Bag-valve-mask ventilation	5 (1.3)	3 (0.8)	0.725
Hypotension	16 (4.2)	12 (3.2)	0.565
Unable to complete procedure	2 (0.5)	4 (1.0)	0.526
narcotic	7 (1.8)	6 (1.6)	1.000
Benzodiazepine	0 (0)	2 (0.5)	0.151
Ondansetron	3 (0.8)	17 (4.6)	0.001

Discussion

Many children require procedures for diagnosis and management.[14] Some procedures are brief but can be painful and anxiety provoking. Children undergoing painful diagnostic and therapeutic interventions in outpatient and inpatient settings are routinely managed with sedatives. Amnesia and analgesia with a predictable depth of sedation, a short duration of action, and rapid, uneventful recovery are the important aspects of ideal sedation regimen.

Propofol does exhibit numerous exceptionally desirable characteristics as a procedural sedation agent. First of all, it has an essentially immediate effect after IV administration. It also has a marked potency of reliably producing effective sedation even for very painful procedures at higher doses. Propofol, itself, does not have analgesic properties. Furthermore, the recovery after sedation is exceptionally short, typically 5 to 15 minutes. Finally, patient satisfaction is high because propofol has amnesic and apparent euphoric properties. No doubt this agent is very popular despite its potential for respiratory depression and hypotension.[10] Many studies have suggested that adding ketamine to propofol might enhance hemodynamic stability, decrease respiratory depression, stabilize respiratory drive, and add analgesia even at small doses.[11,15–20] In the dose range between 0.1 and 0.5 mg/kg, well below those used to induce dissociative sedation, ketamine has well-documented analgesic effects. In our study, we used higher doses for children <20 kg and lower doses in children with > 20 kg to avoid the side effects of emergence reaction and excessive salivation but still within the range of dosage described in the literature to produce adequate analgesia for procedural sedation.[21–23]

Peak level of sedation was achieved almost immediately in the P-O group and required up to 3 minutes in K + P group. This delay in onset of peak sedation in the K + P group is attributed to the waiting time required for ketamine to take effect and to switch the syringes prior to propofol (►**Fig. 3**). All procedures were completed comfortably with a failure

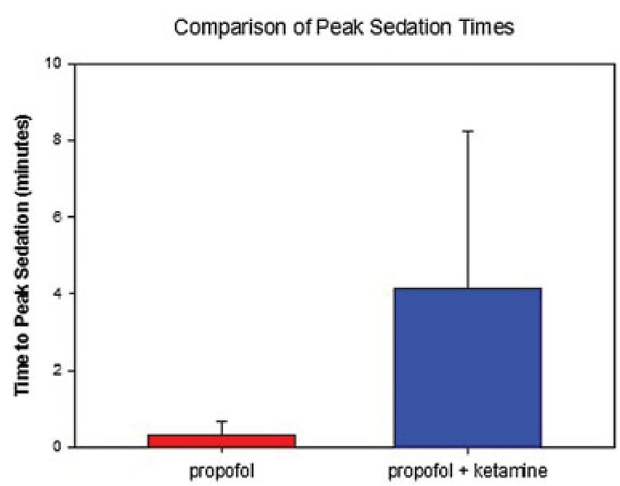

Fig. 3 Time to peak sedation: values displayed are medians with interquartile ranges.

rate of only 0.8%. Seven in the K + P and eight in the P-O group required protocol deviation by adding either fentanyl/versed. Like other studies, use of ketamine resulted in statistically significant decrease in the propofol dose requir ment and resulted in rapid recovery in this group of patients[24] (►**Fig. 3**).

Bradycardia has been described as a possible adverse effect of propofol when administered alone or in combination with opioids.[25,26] In our study, the incidence of bradycardia was zero (defined as a decrease in heart rate >20% from baseline). Propofol has also been shown to cause transient decrease in blood pressure when administered as a bolus or prolonged infusion.[25,26] No patient in this study experienced hypotension (defined as >20% decrease in blood pressure from baseline) (►**Table 3**).

Respiratory events constitute a large proportion (5.5–31.7%) of sedation complications in children.[27,28] We observed similar levels of hypoxemia (16% of patients). The occurrence of apnea appears to depend on the dose and the rate of administration, with a high incidence of apnea reported with the larger doses. No one in our study had apneic episodes.[29,30] The majority of the patients simply required airway positioning and use of supplemental oxygen. Potentially, serious airway complications occurred in 1% of the patients overall; all such events were quickly identified and easily dealt with the use of brief bag-valve-mask ventilation by the pediatric intensivist. In our study, the addition of low-dose ketamine was not associated with any decrease incidence of desaturation between the groups.

Of note, no prophylactic supplemental oxygen was administered unless the oxygen saturation fell below 90%. This likely contributed significantly to the frequency and rapidity of oxygen desaturation. The use of routine supplemental oxygen administration during procedural sedation of selected low-risk patients is debatable.[31] Published trials have not identified a standardized approach to its use.[1,32] It can be asserted that oxygen desaturation in patients breathing room air is an early and rapidly detected sign of respiratory depression, helping the sedating physician to recognize an otherwise subtle event. Additionally, room air desaturation typically responds quickly to administration of oxygen,patient stimulation, or interruption of propofol administration.

ETC02 was monitored throughout the procedure, yet the recordings were often unreliable as most of the procedures were brief and in some procedures the oral cavity had to be maintained wide open or was being manipulated, thus decreasing the value of continuous capnography as a monitoring tool for this type of procedure. A previous study found that for low-risk patients breathing room air, oxygen desaturation usually precedes changes in capnography during procedural sedation with propofol and is readily reversible.[33]

No patient experienced nausea, vomiting, shivering, or perspiration with any of the two groups. All the patients at the time of discharge were given verbal and printed instruction and provided with a 24-hour callback contact number if any complication happened or any assistance was needed. No emergence phenomenon was observed, which is not surprising given our low-dose ketamine. In a previous study using a medium dose of 0.75 mg/kg ketamine co-administered with propofol, 3 of 114 patients experienced emergent reaction and 1 required treatment.[34]

The time required for patients to reach full recovery could be seen as a significant benefit. Patients in the K + P group reached their presedation level of consciousness prior to patients in the P-O group within minutes of completion of the procedure. It is also important to mention that mean procedure time in the K + P group was longer than P-O group by 3 minutes; however, this is likely influenced by the procedure itself rather than the procedural sedation approach.

In the subgroup analysis of K + P group, the interesting finding was the need for a high propofol dose in patients with high-dose ketamine. Even though the K + P 50 group has higher per kg ketamine dose, their cumulative dose was still much lower than the K + P 25 group due to significant weight difference among the groups (13.5 ± 3.4 for K + P 50 vs. 46 ± 25 for K + P 25; $p < 0.01$). This is the best explanation that could be given for a high propofol dose requirement in K + P 50 group. The longer procedure time in K + P5 0 group is due to higher numbers of noninvasive procedures (35 vs. 4). These noninvasive procedures mostly include auditory brainstem responses and bone scans, and the average time for each of this procedure is 40 to 50 minutes. The recovery time was only slightly longer in K + P 50 groups and did reach to a statistically significant difference but may not be of significant clinical effect.

The limitations of our study include its retrospective nature and single-center experience. The current study presents a 99% success rate of sedation for procedures using either approach. It could be asserted that the reported efficacy is due to the use of an intensivist-based specialized sedation team rather than to the medicines itself. This is reasonably true to some extent as specialization and experience should increase both success and efficiency. In spite of that, this can be stated with confidence: much of the reported success is specifically a function of the drug used alone or in combination. This is a descriptive study and few, if any, conclusions can be drawn about safety. Addressing safety is more of a secondary issue because the occurrence of serious sedation-related side effects is, fortunately, rare.[35] Additional prospective studies of the procedural sedation using propofol only versus propofol + ketamine in a greater number of pediatric patients are warranted to provide a true idea of safety. Postoperative nausea and vomiting may occur with 24 hours of sedation or anesthesia. This side effect, even if to be expected a rare one, may be underreported because of short follow-up.

Conclusion

In conclusion, both the propofol-only approach and one that includes a single initial low dose of I/V ketamine proved to be well tolerated and equally effective for procedural sedation. Addition of ketamine was associated with reduction in recovery times, probably explained by the decrease in the propofol dose. Both appear to be viable options for procedural sedation.

References

1 Miner JR, Biros M, Krieg S, Johnson C, Heegaard W, Plummer D. Randomized clinical trial of propofol versus methohexital for procedural sedation during fracture and dislocation reduction in the emergency department. Acad Emerg Med 2003;10(9):931–937
2 Burton JH, Miner JR, Shipley ER, Strout TD, Becker C, Thode HC Jr. Propofol for emergency department procedural sedation and analgesia: a tale of three centers. Acad Emerg Med 2006;13(1):24–30
3 Frazee BW, Park RS, Lowery D, Baire M. Propofol for deep procedural sedation in the ED. Am J Emerg Med 2005;23(2):190–195
4 Miner JR, Danahy M, Moch A, Biros M. Randomized clinical trial of etomidate versus propofol for procedural sedation in the emergency department. Ann Emerg Med 2007;49(1):15–22
5 Zed PJ, Abu-Laban RB, Chan WW, Harrison DW. Efficacy, safety and patient satisfaction of propofol for procedural sedation and analgesia in the emergency department: a prospective study. CJEM 2007;9(6):421–427
6 Godambe SA, Elliot V, Matheny D, Pershad J. Comparison of propofol/fentanyl versus ketamine/midazolam for brief orthopedic procedural sedation in a pediatric emergency department. Pediatrics 2003;112(1, Pt 1):116–123
7 Loh G, Dalen D. Low-dose ketamine in addition to propofol for procedural sedation and analgesia in the emergency department. Ann Pharmacother 2007;41(3):485–492
8 Campbell SG, Magee KD, Kovacs GJ, et al. Procedural sedation and analgesia in a Canadian adult tertiary care emergency department: a case series. CJEM 2006;8(2):85–93
9 Innes G, Murphy M, Nijssen-Jordan C, Ducharme J, Drummond A. Procedural sedation and analgesia in the emergency department. Canadian Consensus Guidelines. J Emerg Med 1999;17(1):145–156
10 Krauss B, Green SM. Procedural sedation and analgesia in children. Lancet 2006;367(9512):766–780
11 Guldner GT, Petinaux B, Clemens P, Foster S, Antoine S. Ketamine for procedural sedation and analgesia by nonanesthesiologists in the field: a review for military health care providers. Mil Med 2006;171(6):484–490
12 American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologistss. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology 2002;96(4):1004–1017
13 Coté CJ, Wilson S; American Academy of Pediatrics; American Academy of Pediatric Dentistry; Work Group on Sedation. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: an update. Pediatrics 2006;118(6):2587–2602
14 Zeltzer LK, Altman A, Cohen D, LeBaron S, Munuksela EL, Schechter NL. American Academy of Pediatrics Report of the Subcommittee on the Management of Pain Associated with Procedures in Children with Cancer. Pediatrics 1990;86(5, Pt 2):826–831
15 Hui TW, Short TG, Hong W, Suen T, Gin T, Plummer J. Additive interactions between propofol and ketamine when used for anesthesia induction in female patients. Anesthesiology 1995;82(3):641–648
16 Morse Z, Sano K, Kanri T. Effects of a propofol—ketamine admixture in human volunteers. Pac Health Dialog 2003;10(1):51–54
17 Akin A, Esmaoglu A, Guler G, Demircioglu R, Narin N, Boyaci A. Propofol and propofol-ketamine in pediatric patients undergoing cardiac catheterization. Pediatr Cardiol 2005;26(5):553–557
18 Akin A, Esmaoglu A, Tosun Z, Gulcu N, Aydogan H, Boyaci A. Comparison of propofol with propofol-ketamine combination in pediatric patients undergoing auditory brainstem response testing. Int J Pediatr Otorhinolaryngol 2005;69(11):1541–1545
19 Tomatir E, Atalay H, Gurses E, Erbay H, Bozkurt P. Effects of low dose ketamine before induction on propofol anesthesia for pediatric magnetic resonance imaging. Paediatr Anaesth 2004;14(10):845–850
20 Suzuki M, Tsueda K, Lansing PS, et al. Small-dose ketamine enhances morphine-induced analgesia after outpatient surgery. Anesth Analg 1999;89(1):98–103
21 Tverskoy M, Oz Y, Isakson A, Finger J, Bradley EL Jr, Kissin I. Preemptive effect of fentanyl and ketamine on postoperative pain and wound hyperalgesia. Anesth Analg 1994;78(2):205–209
22 Choe H, Choi YS, Kim YH, et al. Epidural morphine plus ketamine for upper abdominal surgery: improved analgesia from preincisional versus postincisional administration. Anesth Analg 1997;84(3):560–563
23 Wong CS, Liaw WJ, Tung CS, Su YF, Ho ST. Ketamine potentiates analgesic effect of morphine in postoperative epidural pain control. Reg Anesth 1996;21(6):534–541
24 David H, Shipp J. A randomized controlled trial of ketamine/propofol versus propofol alone for emergency department procedural sedation. Ann Emerg Med 2011;57(5):435–441
25 Short SM, Aun CS. Haemodynamic effects of propofol in children. Anaesthesia 1991;46(9):783–785
26 Newson C, Joshi GP, Victory R, White PF. Comparison of propofol administration techniques for sedation during monitored anesthesia care. Anesth Analg 1995;81(3):486–491
27 Hasan RA, Shayevitz JR, Patel V. Deep sedation with propofol for children undergoing ambulatory magnetic resonance imaging of the brain: experience from a pediatric intensive care unit. Pediatr Crit Care Med 2003;4(4):454–458
28 Burton JH, Harrah JD, Germann CA, Dillon DC. Does end-tidal carbon dioxide monitoring detect respiratory events prior to current sedation monitoring practices? Acad Emerg Med 2006;13(5):500–504
29 Bryson HM, Fulton BR, Faulds D. Propofol. An update of its use in anaesthesia and conscious sedation. Drugs 1995;50(3):513–559
30 Smith I, White PF, Nathanson M, Gouldson R. Propofol. An update on its clinical use. Anesthesiology 1994;81(4):1005–1043
31 Deitch K, Chudnofsky CR, Dominici P. The utility of supplemental oxygen during emergency department procedural sedation and analgesia with midazolam and fentanyl: a randomized, controlled trial. Ann Emerg Med 2007;49(1):1–8
32 Burton JH, Bock AJ, Strout TD, Marcolini EG. Etomidate and midazolam for reduction of anterior shoulder dislocation: a randomized, controlled trial. Ann Emerg Med 2002;40(5):496–504
33 Messenger DW, Sivilotti ML, van Vlymen J, Dungey PE, Murray HE. Which alarms first during procedural sedation: the pulse oximeter or the capnograph? Can J Emerg Med 2007;9:186
34 Willman EV, Andolfatto G. A prospective evaluation of "ketofol" (ketamine/propofol combination) for procedural sedation and analgesia in the emergency department. Ann Emerg Med 2007;49(1):23–30
35 Cravero JP, Blike GT, Beach M, et al; Pediatric Sedation Research Consortium. Incidence and nature of adverse events during pediatric sedation/anesthesia for procedures outside the operating room: report from the Pediatric Sedation Research Consortium. Pediatrics 2006;118(3):1087–1096