doi: 10.5505/sakaryamj.2013.39306
Sakarya Medical Journal
Derleme
Article

Evaluation of Clinical Properties of Dexmedetomidine in Terms of Procedural Sedation and Analgesia

Prosedüral Sedasyon ve Analjezi Açısından Dexmedetomidinin Klinik Özelliklerinin Değerlendirilmesi

Recai Kaya[1], Mehmet Dokur[2]

[1] Department of Anesthesiology, Kilis State Hospital, Kilis, Turkey

[2] Department of Emergency Medicine, Kilis State Hospital, Kilis, Turkey

Abstract

Sedation for the short-term but potentially painful procedures is of often used in emergency service. In addition to its ability to provide an ideal sedative regime analgesia and anxiolytics, it must create minimal side effects, protect arterial reflexes, must not cause cardiorespiratory depression and must allow rapid recovery subsequent to the procedure. Objective in sedation is to ensure the conditions in which the patient can conveniently tolerate the process throughout the process. In this study, we efforted to demonstrate that clinical properties of dexmedetomidine an alpha-2 agonist agent which- is used for procedural sedation and analgesia in the light of current literature.

Keywords: dexmedetomidine, clinical properties, procedural sedation, analgesia

Aplication: 05.09.2011 **Accepted:** 12.01.2013

Özet

Kısa süreli fakat potansiyel olarak ağrılı prosedürler için sedasyon, sıklıkla acil serviste uygulanmaktadır. İdeal bir sedatif rejimi analjezi ve anksiyoliz sağlaması yanısıra minimal yan etki oluşturmalı, havayolu reflekslerini korumalı, kardiyorespiratuvar depresyona yol açmamalı ve prosedür sonrası hızlı derlenmeye olanak vermelidir. Sedasyondaki amaç, hastanın işlem boyunca işlemi rahat tolere edebileceği şartları sağlamaktır. Biz bu çalışmada, prosedüral sedasyon ve analjezi için kullanılan bir alfa-2 agonist ajan olan dexmedetomidinin klinik özelliklerini güncel literatür ışığında açıklamaya çalıştık.

Anahtar Kelimeler: deksmedetomidin, klinik özellikler, prosedüral sedasyon, analjezi

Başvuru Tarihi: 05.09.2011 **Kabul Tarihi:** 12.01.2013

Giriş

In order to provide procedural sedation and analgesia many drugs were used alone or in combination with others. An ideal drug for a physician should be effective, safe, cheap, titretable and rapidly acting that has sedative and analgesic properties as well as minimizing anxiety.

Use of dexmedetomidine which is an selective alfa-2 agonist and active dextroisomer of medetomidine to provide sedation and analgesia has started to increase during the recent years. The agonistic action of dexmedetomidine on the alfa-2-adrenergic receptors in the sympathetic ganglia modulates the release of catecholamines, resulting in a sympatholytic effect and there have been reports of bradycardia and hypotension. On the other hand dexmedetomidine has little effect on ventilation. So, dexmedetomidine may be indicated for the sedation of mechanically ventilated adult patients in an

Yazışma Adresi/Corresponding to: Dr. Recai Kaya, 1Department Of Anesthesiology, Kilis State Hospital, Kilis, Turkey
GSM: 05055272120, e-mail: drrecai@hotmail.com

intensive care setting and in non-intubated adult patients prior to and/or during surgical and other procedures[1,2].

As the loading dose of dexmedetomidine, 1 mcg/kg (10-20 min) and as the maintenance dose, 0,2-0,7 mcg/kg/hour use interval and no more than 24 hours of use are recommended. However, in the new 2 studies conducted dexmedetomidine was used in intensive care unit for more than 7 days in the form of infusion, no myocardial depression was observed in the patients and no rebound effect was developed during the discontinuation of the medication. Dexmedetomidin's biggest advantage when compared to the other sedatives is the respiration stability. Dexmedetomidin's characteristic effect is to correct anxiety, to reduce the opioid requirement and simplify the conscious sedation[3,4].

In spite of the fact that the opiates provide an effective analgesia, their anxiolytic effects remain limited and the opiates' combination in the benzodiazepine depresses the respiration. At this point, dexmedetomidin comes to the foreground by creating an in-depth sedation analgesia and anxiolytics without causing respiratory depression. One of the most important features of Dexmedetomidin sedation is that the patient who seems to be sleeping is easily responsive to the impulses and able to cooperate with the surrounds. In addition, reduced sympathetic effect and increased parasympathetic effect, reduced rate of metabolism, reduced heart rate, reduced myocardial contractility and vascular resistance take place and finally myocardial oxygen requirement is reduced.In the patients with severe trauma, in the tracheal intubation is generally considered to be the golden standard in the airborne method. Although tracheal intubation has such prime importance, it is sometimes difficult to conduct such process in the agitated patients or in various facial scares. In many of the cases, the most reliable technique to protect the airborne is to conduct awaken intubation with fibrotic bronchoscopy. In such cases, there become problems due to the fact that the medication selected in order to perform the sedation causes respiratory depression[5,6].

Agitation, delirium and withdrawal create difficulties to the providers of healthcare. The patients who are in the state of agitation, delirium and withdrawal may cause self-injuries and/or prevent others to help end treat them. Trauma patients are specifically under risk due to the worsening of their wounds and to the formation of new ones. Dexmedetomidin prevents and treats the agitation, delirium and withdrawal findings, and it is also an important weapon of the clinician to ensure that the patients stay stable. Dexmedetomidin reduces the sympathetic and noradrenergic activity and creates an effect that is opposite the effects during the withdrawal. One of the problems encountered in the intensive care is that a state of addiction was already developed during the termination of the use of narcotic and benzodiazepine. Hypertension, anxiety, agitation, tachycardia and temperature can be observed during the benzodiazepine and opioid withdrawal and dexmedetomidine eases them[7,8].

Dexmedetomidine is confirmed to be more successful than Midazolam at procedural processes such as MRI in children. However dexmedetomidine, alone, is not sufficient for very painful and invasive processes[9].

Dexmedetomidine is a novel agent with a wide safety margin and excellent sedative and moderate analgesic properties. Though its broadest use is currently in surgical and nonsurgical intensive care unit patients, dexmedetomidine appears to have promising future applications in the areas of neuroprotection, cardioprotection and renoprotection[10].

CLINICAL USES of DEXMEDETOMIDINE

As procedural sedatitive and analgesic dexmedetomidine, have a great range of clinical use from operating room to emergency department. Especially for recent 10 years, the clinical usage of dexmedetomidine, alone or along with the other sedative analgesics, has increased. With this aim, many studies on different clinical usages of dexmedetomidine have been performed. In this study, we have analyzed several major studies most of which have been done recently.

Riker et al., in the SEDCOM Study (Safety and Efficacy

of Dexmedetomidine Compared with Midazolam) compared the effects of midazolam and dexmedetomidin on the patients who are in the intensive care and connected to a ventilator. This study suggested that there was no difference between dexmedetomidine and midazolam in time at targeted sedation level in mechanically ventilated ICU patients. In addition, at comparable sedation levels, dexmedetomidine-treated patients spent less time on the ventilator, experienced less delirium, and developed less tachycardia and hypertension. According to SEDCOM study the most notable adverse effect of dexmedetomidine was bradycardia[11].

Multz reported that a patient who was a multiple-substance abuser admitted to the intensive care unit with acute respiratory distress syndrome (ARDS), subsequently complicated by ventilator-associated pneumonia, required long-term sedation. In his case described here, Multz concluded that dexmedetomidine facilitated withdrawal from lorazepam and fentanyl, and with no risk of respiratory depression, conscious sedation was maintained throughout weaning and extubation; the symptoms of withdrawal were relieved without delaying weaning[7].

Mato et al., implied that dexmedetomidine diminishes the need for other anesthetics and sympathicolytics, and it reduces catecholamine release and controlled clinical trials have looked at the use of dexmedetomidine in patients who require sedation and analgesia in postoperative intensive care units. In addition, some other researches as well show that dexmedetomidine lowers the need both for other sedatives, such as propofol or midazolam, and for analgesic morphine. Moreover, its effect on ventilation is scarce. Mato et al., suggested that dexmedetomidine may be promising drug if it is used as analgesic, hypnotic and sedative[12].

Hall et al., performed a study on healthy young volunteers. In this study one group of patient was administered at a rate of 0,2 mcg/kg/hour, other group was administered at a rate of 0,6 mcg/kg/hour for 10 minutes and then dexmedetomidine was infused for 50 minutes at a rate of 0,6mcg/kg/hour; during and after infusion sedation,analgesia, mild instantaneous memory and psychomotor performance impairment were observed, on pro-rata basis.Hemodynamics, SpO2, ETCO2 and respiratoryrate were well preserved throughout the infusion and recovery periods. Both small-dose and moderate-dose dexmedetomidine infusion provided effective sedation. 2 hours after from terminating infusion, sedated patients were awake.Shorter half-life of dexmedetomidine provides an important advantage for maintaining cardiorespiratory functions as well as sedation and analgesia. According to Hall et al. it seems that dexmedetomidine can be used safely and efficiently at postoperative intensive care units due to its mentioned features. But there is no sufficient data about using dexmedetomidine at the emergency service. Hall et al. also pointed out that on the other hand there is no data proving that using dexmedetomidine is unfavorable at the emergency department[13].

In their study Venn et Grounds observed that 20 postoperative patients who will require minimum 8-hour ventilation were administered either propofol or dexmedetomidine, and if required, alfentanil infusion was performed for analgesia. At the end of the study, although sedation rates were confirmed to be similar, propofol group received 3 times more alfentanil. No any significant difference was marked between blood pressures, however Heart Rate was apparently lower at dexmedetomidine group. In addition to those findings, extubation periods were similar and no adverse effects were observed at both groups. Furthermore the patients in dexmedetomidine group awaked more easily and became easily cooperative with environment. Venn et Ground concluded in this study that dexmedetomidine is an agent that can be regarded as safe and its properties don't show an increasing effect for coronary artery disease and blood pressure may provide a preventive effect for myocardial ischemia and dexmedetomidine significantly decreased need of opioid analgesic[14].

Taiji indicated in his study that dexmedetomidine is promptly eliminated from blood: In the phase II/III multi-center placebo-controlled double blind bridging study conducted in Japan, efficacy and safety were examined in patients brought to the ICU. As regards sedative ac-

tion, the ratio of patients who did not require additional propofol medication (>50 mg) while intubated was taken as the effective rate. According to results of this study the drug group showed a significantly high effective rate (90.9%; placebo group, 44.6%). Similarly, with analgesic action, the ratio of patients who did not require additional morphine medication during intubation was taken as the effective rate. The effective rate for the drug group was significantly high (87.3%; placebo group, 75.0%). Finally, the main adverse events observed in the drug group were hypertension and hypotension[15].

Jorden et al. reported that hemodynamic parameters were stable at the 3 patients who were administered with high dosage dexmedetomidine by mistake and a more significant sedation was not observed. All 3 patients were awakened 1 one hour after last drug administration. In addition Jorden et al. pointed out while hemodynamic alterations may be seen with dexmedetomidine use, hypertension from high dexmedetomidine plasma concentrations is not a consistent response. Jorden et al. suggested that practitioners using dexmedetomidine should carefully note that dosing for this agent is described by the manufacturer in microg/kg/h, not microg/kg/min[16].

In a relevant study Tobias made a computerized bibliographic search of the literature regarding dexmedetomidine and ketamine for procedural sedation. Tobias infered that dexmedetomidine povided limited analgesic effects and it does not appear to be the ideal agent for painful procedures. However, anecdotal experience and a few large series from the literature demonstrate the utility of a combination of dexmedetomidine with ketamine for procedural sedation17. Moreover, in this study Tobias demonstrate that -when used together- dexmedetomidine may limit the tachycardia, hypertension, salivation, and emergence phenomena from ketamine, whereas ketamine may prevent the bradycardia and hypotension that has been reported with dexmedetomidine. In additional the available literature except for one trial is favorable regarding the utility of a combination of ketamine and dexmedetomidine for procedural sedation. Tobias suggested that future studies with direct comparisons to other regimens appear warranted for both invasive and noninvasive procedures [18,19,20].

Jewett et Phillips pointed out in their study that although dexmedetomidine is used at intensive care unit and under preoperative conditions by infusion up to now; there is no information about its usage at procedural processes in the emergency room with bolus bolus method. However, dexmedetomidine is used at children and adults for short term sedation. In this study they drew attention that dexmedetomidine showed its impact with presynaptic alfa-2 agonism and decreases sympathetic nerve system activity; besides analgesia, it also provides deep sedation and half-life of dexmedetomidine is approximately 6 minutes and dexmedetomidine is administered primarily with a rate of 0,3-1 mcg/kg/minute through infusion. So, Jewett et Phillips suggested that dexmedetomidine is the only medicine that provides sedation and analgesia without causing respiratory depression[21].

Gerlach et al. demonstrated in their study that dexmedetomidine is an alternative for procedural sedation and can be used long-term (>24 h) in critically ill patients, in dosages up to 1.5 microg/kg/hour. More studies are needed to better define the role of dexmedetomidine in preventing and treating delirium[22].

Mason et al. in their study regarding pediatric CT sedation compared dexmedetomidine with pentobarbital. This study suggested that dexmedetomidine is a safe and effective alternative to pentobarbital for pediatric CT, being associated with a much shorter recovery time and less need for adjuvant sedatives[23].

Koroglu et al. evaluated in a similar study that the sedative, haemodynamic and respiratory effects of dexmedetomidine dexmedetomidine and compared them with those of midazolam in children undergoing magnetic resonance imaging(MRI) procedures. Preliminary results of this study showed that dexmedetomidine provided adequate sedation at 1 μg kg□1 loading and 0.5–0.7 μg kg□1 h□1 infusion doses in most of the children (aged between 1–7 yr) without affecting haemodynamics and respiration. Consequently Koroglu et al. suggested that

dexmedetomidine may be a suitable agent for MRI sedation in children[24].

Kaygusuz et al. in their study compared of sedation with dexmedetomidine or propofol during shockwave lithotripsy. This randomized, double-blind, clinical study was designed to compare the hemodynamic, analgesic, sedative, and respiratory effects of dexmedetomidine and propofol in combination with fentanyl during ESWL. According to conclusions of this study, although infusion of dexmedetomidine and propofol provided safe and adequate analgesia, sedation and patient comfort in the ESWL procedure, analgesic and respiratory variables were better with dexmedetomidine than propofol. Kaygusuz et al. suggested that dexmedetomidine in combination with small dose fentanyl can be useful during ESWL and it may be a valuable alternative to propofol[25].

Yuen et al., in their a double-blind study that made crossover assessment of the sedative and analgesic effects of intranasal dexmedetomidine. According to conclusions of this study, Nonparenteral administration of dexmedetomidine is a convenient and safe alternative to parenteral administration. In this study, we have demonstrated that 1 and 1.5 μg/kg of intranasally administered dexmedetomidine produced clinically significant sedation and hemodynamic changes in healthy volunteers. This study suggests that intranasal administration is effective with a smooth and predictable onset and with high patient acceptability. Dexmedetomidine could be particularly helpful in pediatrics. Besides the sedation produced may actually even be sufficient for some local anesthetic procedures, and this will be an interesting area for further study. Furhermore stressesed in this study that future studies are warranted to define the optimal dose and the role of this route of administration in clinical settings[26].

Cheung et al., in other a study evaluated that analgesic and sedative effects of intranasal dexmedetomidine in third molar surgery under local anaesthesia. In this study was demonstrated that intranasal dexmedetomidine appears to confer perioperative clinical sedation with improved postoperative analgesia for unilateral third molar surgery under local anaesthesia. In addition, no increase in complications or delay in psychomotor recovery was found. Cheung et al. stressed in this study further dose-finding studies using intranasal dexmedetomidine alone in surgical procedures should be explored[27].

Calver et Isbister assessed in their study that safety and effectiveness in difficult-to-sedate acute behavioural disturbance. They are suggested that intravenous dexmedetomidine for difficult-to-sedate patients with acute behavioural disturbance is not safe in the emergency department setting[28].

Phan et Nahata evaluated in their study which clinical uses of dexmedetomidine in pediatric patients. they drew attention that adverse hemodynamic and respiratory effects of dexmedetomidine were minimal; the agent was well tolerated in most patients. In this study the efficacy of dexmedetomidine varied depending on the clinical situation: efficacy was greatest during non-invasive procedures, such as MRI, and lowest during invasive procedures, such as cardiac catheterization. Moreover, they are pointed out that dexmedetomidine may be useful in pediatric patients for sedation in a variety of clinical situations. The literature suggests potential use of dexmedetomidine as an adjunctive agent to other sedatives during mechanical ventilation and opioid/benzodiazepine withdrawal. In addition, because of its minimal respiratory effects, dexmedetomidine has also been used as a single agent for sedation during non-invasive procedures such as MRI. However, Phan et Nahata concluded that additional studies in pediatric patients are warranted to further evaluate its safety and efficacy in all age ranges[29].

Su et Hammer, evaluated in their study that clinical uses and safety of dexmedetomidine in term of pediatric pharmacology. In this study they are pointed out that dexmedetomidine is a useful sedative and anxiolytic drug in the pediatric intensive care unit as well as during diagnostic and therapeutic procedures and deleterious effects of dexmedetomidine include hypotension and bradycardia. Additionally, hypertension may occur during the "loading dose" or with high infusion rates. Few

studies have been performed to evaluate the safety of dexmedetomidine in pediatrics. The development of tolerance and withdrawal has not been studied in children. Despite its favorable respiratory profile, dexmedetomidine may cause deleterious cardiovascular effects. In this study was pointed out that close monitoring of circulatory dynamics and judicious titration is recommended. Hence, Su et Hammer suggested that further studies are needed to better define adverse effects following long-term infusions as well as in special populations such as pre-term infants[30].

Darrouj et al. reported that a case of delirium tremens in which intravenous dexmedetomidine was used successfully as adjunctive treatment for withdrawal symptoms; we also describe the pharmacologic basis for its use. According to this study that is the only case report of a patient treated successfully with dexmedetomidine for acute delirium tremens. A patient demonstrated a significant decrease in agitation, improvement of mental status, and return of appropriateness of response after initiation of dexmedetomidine therapy. Consequently, Darrouj et al. pointed out while the use of dexmedetomidine in the treatment of acute delirium tremens has not been extensively studied thus far, the success in this case suggests that further research on the topic may be warranted[31].

McMorrow et Abramo reviewed that dexmedetomidine uses in pediatric procedural sedation outside the operating room. They pointed out that dexmedetomidine a drug approved for use in the adult intensive care setting and its role in pediatrics has varied in its use from sedation in ventilated children in the intensive care unit to treatment for emergence reactions from general anesthesia and in sedation needed for radiographic imaging studies, electroencephalography, and invasive procedures. McMorrow et Abramo concluded that reviewing of the many articles have been published thus far regarding dexmedetomidate in the non-ventilated, spontaneously breathing patient and identifies those patients where the use of this agent may not be indicated[32].

Mason et al. researched in a large series of children who received dexmedetomidine that incidence and predictors of hypertension during high-dose dexmedetomidine sedation for pediatric MRI. They concluded that when high-dose dexmedetomidine is used for pediatric sedation for MR imaging, the incidence of hypertension is low. Hypertension is most likely to occur in children <1 year of age during the continuous infusion, after they have received more than one bolus of dexmedetomidine[33].

Hoy et Keating reviwed of dexmedetomidine use for sedation in mechanically ventilated patients in an intensive care setting and for procedural sedation. In this study, they evaluated the pharmacological properties, therapeutic efficacy and tolerability of dexmedetomidine in randomized, double-blind, placebo-controlled, multicentre studies in these indications. Their study suggests that dexmedetomidine is associated with a lower rate of postoperative delirium than midazolam or propofol; it is not associated with respiratory depression. While dexmedetomidine is associated with hypotension and bradycardia, both usually resolve without intervention. Thus, Hoy et Keating concluded that intravenous dexmedetomidine provides a further option as a short-term (<24 hours) primary sedative in mechanically ventilated adult patients in an intensive care setting and in non-intubated adult patients prior to and/or during surgical and other procedures[34].

Arnold et al. focusing on safety (güvenlik üzerine odaklanarak) researched that optimizing sustained use of sedation in mechanically ventilated patients. They pointed out in their study that clinicians should closely monitor patients receiving dexmedetomidine for hemodynamic-altering bradycardia and strategies that promote frequent patient assessment with corresponding sedative dose minimization have demonstrated the benefits of limiting oversedation. This study suggested that implementation of a sedation protocol requires careful consideration of intensive care unit resources and staffing such that efforts made are sustainable and will be safe and effective for the patient population affected[35].

Jakob et al. researched in their study, two randomized controlled trial that dexmedetomidine, midazolam or

propofol for sedation during prolonged mechanical ventilation. This study was two phase 3 multicenter, randomized, double-blind trials carried out from 2007 to 2010. Jakob et al. suggested that among ICU patients receiving prolonged mechanical ventilation, dexmedetomidine was not inferior to midazolam and propofol in maintaining light to moderate sedation. In addition dexmedetomidine reduced duration of mechanical ventilation compared with midazolam and improved patients' ability to communicate pain compared with midazolam and propofol. More adverse effects were associated with dexmedetomidine[36].

Conclusions

These studies show that dexmedetomidine is a good option that can be used for short, urgent procedural processes. Despite the lack of studies with regard to the utilization of dexmedetomidine in the emergency service for procedural sedation and analgesia, the number of few studies conducted seems to conclude positive results.

Dexmedetomidine seems to be a proper agent for invasive or non-invasive operations in emergency service hence it provides early recovery, does not depress respiration, provides efficient sedation and analgesic features. However there are no significant studies on this topic. Despite Calver et al.[28] indicated that it was not safe to be used in emergency service, there were few cases about the topic. This study reports insufficient sedation, need of intubation in 2 patients, bradicardia and atrial fibrillation in another patient. Whereas use of propofol causes the similar problems as well. In addition mostly successful cases of sedation and analgesia outside the emergency care unit makes dexmedetomidine considerable for use in emergency service. In case dexmedetomidine is analgesically insufficient when it is solely used, it can be combined with any benzodiazepine, opioid or cetamine.

Just as the other medicines used with the aim of procedural sedation and analgesia, dexmedetomidine has predominant and insufficient, even unfavourable, effects. However, dexmedetomidine is generally a proper medicine for procedural sedation and analgesia. For this reason closely monitoring of vital parameters while use of dexmedetomidine can prevent potential problems and it is remarkably important to select the right group of patients for use of this agent.

References

1. Scheinin B, Lindgren L, Randell T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and perioperative fentanyl. Br J Anaesth 1992;68:126–131.
2. Hoy SM, Keating GM. Dexmedetomidine: a review of its use for sedation in mechanically ventilated patients in an intensive care setting and for procedural sedation. Drugs. 2011;71(11):1481-1501.
3. Symington L, Thakore S. A review of the use of propofol for procedural sedation in the emergency department. Emerg Med J. 2006;23(2):89-93.
4. Shehabi Y, Ruettimann U, Adamson H, Innes R, Ickeringill M. Dexmedetomidine infusion for more than 24 hours in critically ill patients: sedative and cardiovascular effects. Intensive Care Med. 2004;30(12):2188-2196.
5. Avitsian R, Lin J, Lotto M, Ebrahim Z. Dexmedetomidine and awake fiberoptic intubation for possible cervical spine myelopathy: a clinical series. J Neurosurg Anesthesiol. 2005 ;17(2):97-99.
6. Bergese SD, Khabiri B, Roberts WD, Howie MB, McSweeney TD, Gerhardt MA. Dexmedetomidine for conscious sedation in difficult awake fiberoptic intubation cases. J Clin Anesth. 2007;19(2):141-144.
7. Multz AS. Prolonged dexmedetomidine infusion as an adjunct in treating sedation-induced withdrawal. Anesth Analg. 2003;96(4):1054-1055.
8. Shukry M, Clyde MC, Kalarickal PL, Ramadhyani U.Does dexmedetomidine prevent emergence delirium in children after sevoflurane-based general anesthesia? Paediatr Anaesth. 2005 ;15(12):1098-1104.
9. Leroy PL, Gorzeman MP, Sury MR. Procedural sedation and analgesia in children by non-anesthesiologists in an emergency department. Minerva Pediatr. 2009;61:193-215.

10. Chrysostomou C, Schmitt CG. Dexmedetomidine: sedation, analgesia and beyond. Expert Opin Drug Metab Toxicol. 2008;4(5):619-627.
11. Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, Whitten P, Margolis BD, Byrne DW, Ely EW, Rocha MG; SEDCOM (Safety and Efficacy of Dexmedetomidine Compared With Midazolam) Study Group. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. JAMA. 2009;301(5):489-499.
12. Mato M, Pérez A, Otero J, Torres LM. Dexmedetomidine, a promising drug. Rev Esp Anestesiol Reanim. 2002;49(8):407-420.
13. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg. 2000;90(3):699-705.
14. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perceptions. Br J Anaesth. 2001;87(5):684-690.
15. Taiji K. Dexmedetomidine hydrochloride (Precedex), a new sedative in intensive care, its pharmacological characteristics and clinical study result. Nippon Yakurigaku Zasshi. 2004;124 (3):171-179.
16. Jorden VS, Pousman RM, Sanford MM, Thorborg PA, Hutchens MP. Dexmedetomidine overdose in the perioperative setting. Ann Pharmacother. 2004;38(5):803-807.
17. Tobias JD. Dexmedetomidine and ketamine: An effective alternative for procedural sedation? Pediatr Crit Care Med 2012;13:423–427.
18. Zor F, Ozturk S, Bilgin F, et al: Pain relief during dressing changes of major adult burns: Ideal analgesia combination with ketamine. Burns 2010; 36:501–505.
19. Levänen J, Mäkelä ML, Scheinin H: Dexmedetomidine premedication attenuates ketamine-induced cardiostimulatory effects and postanesthetic delirium. Anesthesiology 1995; 82:1117–1125.
20. Dilek O, Yasemin G, Atci M: Preliminary experience with dexmedetomidine in neonatal anesthesia. J Anesth Clin Pharm 2011; 27:17–22.
21. Jewett J, Phillips WJ. Dexmedetomidine for procedural sedation in the emergency department. Eur J Emerg Med. 2010;17(1):60.
22. Gerlach AT, Murphy CV, Dasta JF. An updated focused review of dexmedetomidine in adults. Ann Pharmacother. 2009;43(12):2064-2074.
23. Mason KP, Prescilla R, Fontaine PJ, Zurakowski D. Pediatric CT sedation: comparison of dexmedetomidine and pentobarbital. AJR Am J Roentgenol. 2011;196(2):W194-198.
24. Koroglu A, Demirbilek S, Teksan H, Sagir O, But AK, Ersoy MO. Sedative, haemodynamic and respiratory effects of dexmedetomidine in children undergoing magnetic resonance imaging examination: preliminary results. Br J Anaesth. 2005;94(6):821-824.
25. Kaygusuz K, Gokce G, Gursoy S,Ayan S,Mimaroglu C, Gultekin Y. A comparison of sedation with dexmedetomidine or propofol during shockwave lithotripsy: a randomized controlled trial. Anesth Analg 2008;106:114 –119.
26. Yuen VM, Irwin MG, Hui TW, Yuen MK, Lee LH. A double-blind, crossover assessment of the sedative and analgesic effects of intranasal dexmedetomidine. Anesth Analg. 2007;105(2):374-380.
27. Cheung CW, Ng KF, Liu J, Yuen MY, Ho MH, Irwin MG. Analgesic and sedative effects of intranasal dexmedetomidine in third molar surgery under local anaesthesia. Br J Anaesth. 2011; 107(3):430-437.
28. Calver L, Isbister GK. Dexmedetomidine in the emergency department: assessing safety and effectiveness in difficult-to-sedate acute behavioural disturbance. Emerg Med J. 2012;29(11):915-918.
29. Phan H, Nahata MC. Clinical uses of dexmedetomidine in pediatric patients. Paediatr Drugs. 2008;10(1):49-69.
30. Su F, Hammer GB. Dexmedetomidine: pediatric pharmacology, clinical uses and safety. Expert Opin Drug Saf. 2011;10(1):55-66.
31. Darrouj J, Puri N, Prince E, Lomonaco A, Spevetz A, Gerber DR. Dexmedetomidine infusion as adjunctive therapy to benzodiazepines for acute alcohol withdrawal. Ann Pharmacother 2008 ;42(11):1703-1705.
32. McMorrow SP, Abramo TJ. Dexmedetomidine sedation: uses in pediatric procedural sedation outside the operating room. Pediatr Emerg Care. 2012;28(3):292-296.
33. Mason KP, Zurakowski D, Zgleszewski S, et al. Incidence and predictors of hypertension during high-dose dexmedetomidine sedation for pediatric MRI. Paediatr Anaesth. 2010;20:516-523.
34. Hoy SM, Keating GM. Dexmedetomidine: a review of its use for sedation in mechanically ventilated patients in an intensive care setting and for procedural sedation. Drugs. 2011 ;71(11):1481-1501.
35. Arnold HM, Hollands JM, Skrupky LP, Mice ST. Optimizing sustained use of sedation in mechanically ventilated patients: focus on safety. Curr Drug Saf. 2010;5(1):6-12.
36. Jakob SM, Ruokonen E, Grounds RM, Sarapohja T, Garratt C, Pocock SJ, Bratty JR, Takala J.Dexmedetomidine for Long-Term Sedation Investigators. Dexmedetomidine vs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials. JAMA 2012;307(11):1151-1160.