The use of Dexmedetomidine in patients with Spinal Cord Injury

Afrati S[1], Vlamis J[2], Pneumaticos S[3].

Afrati S. Anesthesiologist, Academic Fellow, 3rd Department of Orthopedic Surgery, University of Athens, KAT Hospital, Athens, Greece

As.Professor of Orthopedics, 3rd Department of Orthopedic Surgery, University of Athens, KAT Hospital, Athens, Greece

Professor of Orthopedics, 3rd Department of Orthopedic Surgery, University of Athens, KAT Hospital, Athens, Greece

ABSTRACT

Traumatic Spinal Cord Injury (SCI) may often lead to significant disability in affected individuals and reduce quality of life.

Over 70% of SCI patients suffer from multiple injuries, concomitant with spinal cord trauma, contributing to the high rates of associated complications during the acute and long-term phases of care [1].

SCI impairs body's autonomic and biomechanical performance by interrupting communications between the brain, organ systems, muscles and bones. This carries important implications on patients' ability to perform basic daily-lifeactivities and reserve capacity to withstand illnesses and aging [2].

Dexmedetomidine, an imidazole compound, is a highly selective a2-adrenoreceptor agonist, even ten times more selective than Clonidine. It is a very versatile drug in anaesthesia practice, nowadays applied in increasing number of clinical scenarios. It is an analgesic with anaesthetic sparing effects, sympatholytic properties, applied for procedural sedation, displaying cardiovascular stabilizing properties. It reduces delirium and preserves respiratory function, adding benefits to its use [3].

The aim of this review is to present the evolving role of Dexmedetomidine in patients with Spinal Cord Injuries in anaesthesia and ICU sedation and discuss its limitations.

Key Words: Spinal Cord Injury, Dexmedetomidine, ICU, Surgery

Introduction

Dexmedetomidine is an a2-adrenoreceptor agonist with a broad range of pharmacological properties, reflecting the extensive distribution of a2-receptors throughout the body [4,5], registreted in FDA since 1999. Originally, it was approved for intravenous (iv) administration in the Intensive Care Unit (ICU) during sedation of mechanically ventilated adult patients, for up to 24 hours [2]. In 2008, an additional indication was granted in USA, allowing the use of DEX for the sedation of non-intubated patients prior to and/or during surgical and other procedures. Since 2011, Dexmedetomidine has been approved by the European Union for the sedation of adult ICU patients, requiring a sedation level at which patients remain awake in response to verbal stimulation [3]. It is commercially available as a water-soluble HCL salt under the brand name of Dexdor and Precedex and exerts its hypnotic action through activation of central presynaptic and postsynaptic a2-adrenoceptor in Locus Coeruleus, inducing a state of unconsciousness similar to natural sleep, with minimal respiratory depression [8-13].

The pharmacokinetic characteristics of dexmedetomidine have been reported and examined in many pre-clinical and clinical studies. In healthy adult volunteers, half-life elimination was described at 2.1 to 3.1 hours and the clearance from non-compartmental analysis varied from 0.51 to 0.89 L/min. Likewise, from pre-clinical studies, it was found that the drug distributes rapidly and widely throughout the body and

VOLUME 73 | ISSUE 1 | JANUARY - MARCH 2022

readily crosses the blood-brain and placental barriers [8,14]. Around 94% of Dexmedetomidine is bound to plasma albumin and a1-glycoprotein in healthy volunteers [8,15]. Elimination is performed mainly through glycoronidation in the liver, at its N3 and N1 position of the imidazole ring [16]. The direct N-glucoronidation products of Dexmedetomidine, namely N3- and N1- glucoronide (DG1) and (DG2) are the primary metabolites of Dexmedetomidine, accounting for about 41% of its metabolism in healthy volunteers [8,15], while other metabolites of Dexmedetomidine are N-methyl-O-glucoronidedexmedetomidine, 3-hydroxy dexmedetomidine, glucoronide of 3-hydroxy dexmedetomidine, 3 carboxylic acid dexmedetomidine, and N-methylated carboxylic acid dexmedetomidine [15]. Overall, less than 1% of Dexmedetomidine is excreted unchanged and 95% is eliminated via metabolism and subsequent excretion via urine [8,15]. The pharmacokinetic profile of Dexmedetomidine has been extensively evaluated in various populations and the reports revealed that covariates, including age, frailty, body size, hepatic impairment, plasma albumin, and cardiac output, may have a significant impact on the pharmacokinetics of Dexmedetomidine [9,11,14,16,17]

The aim of this article is to critically review and summarize published data on the clinical application of Dexmedetomidine in patients with Spinal Cord Injury as well as the usefulness of its administration. The MEDLINE database was searched through PubMed. All English articles and abstracts with a title containing the words Spinal Cord Injury, Dexmedetomidine, ICU, surgery were selected. Additional searches were performed including the keywords "interactions" and "analgesia". After screening titles for possible relevance, papers were added to the flowchart. All abstracts were screened and when considered relevant, the papers' full texts were obtained. Bibliographies of articles were reviewed and as such, additional potentially relevant papers were identified and added to the flowchart (Table 1).

Discussion

Injuries to the Spinal column and Spinal Cord frequently occur after high-energy mechanisms of injury, or with lower-energy mechanisms, in selected patient population, like the elderly. A focused, yet complete neurologic evaluation will guide subsequent diagnostic procedures and early supportive measures to help prevent further injury. For patients with osseous and/or ligamentous injury, the initial focus should be spinal immobilization and prevention of Spinal Cord lesions [18]. These injuries may often lead to significant disability in affected individuals and reduce life satisfaction [19]. Patients with Spinal Cord Injuries require multidisciplinary management to achieve optimal health outcomes [20].

Sedation

The sedative effects of Dexmedetomidine are well established. Dose-dependent sedation was seen in healthy volunteers receiving intravenous boluces of Dexmedetomidine 0,25-2μg/kg [21], while the sedative effect of Dexmedetomidine infusion were shown in both healthy volunteers [22-24] and ICU patients [25-28]. The drug induces sleep by decreasing the firing of noradrenic locus Coeruleus neurons in the brain stem and activating endogenous non-rapid eye movement sleep-promoting pathways [29]. It produces a state closely resembling to physiological state-2 sleep [30]. Thus, recipients can be easily roused to participate in testing [24] and cooperate during sedative procedures [30]. Dexmedetomidine has analgesic effects in healthy volunteers [22,24] and opioid-sparing effect in patients in ICU setting [26]. The analgesic effect appears to be exerted at the Spinal Cord level, supraspinal sites, as well as through nonspinal mechanisms [31]. Dexmedetomidine demonstrates sympatholytic activity [22,32-34]. Significant reductions from baseline in plasma noradrenaline (norepinephrine) and/or adrenaline (epinephrine) levels were observed in healthy volunteers [22,32,33] and surgically treated patients, postoperatively [34] .

Side effects are mainly restricted to hemodynamic alterations. These include hypertention, bradycardia, and hypotention, owing to pre- and postsynaptic a2- receptor activation as well as reflex bradycardia [35,36]. Moreover, it has been shown to attenuate stress responses, thereby creating a more stable hemodynamic profile during stressful events, such as surgery or anesthetic induction [37-39].

VOLUME 73 | ISSUE 1 | JANUARY - MARCH 2022

Clinical Applications of Dexmedetomidine

A. Intensive Care Unit (ICU)

Stable hemodynamic conditions are crucial for optimal clinical management of patients with acute Spinal Cord Injury, admitted to a neuricritical care unit [40].

Sedation in the ICU works both ways. Although it reduces anxiety and agitation, sedative drug therapy typically diminishes patients' level of arousal, often incites delirium during wakefulness, and may add greater dependence on assisted ventilation and need for hemodynamic support [41]. Dexmedetomidine combines analgesic, sedative and anxiolytic effects while maintaining patients' arousability without significant respiratory depression [42]. It is these characteristics that make this drug a potentially attractive sedative for Spinal Cord Injury (SCI) patients, since they often require awakening for thorough neurological assessment.

The Acute Neurological ICU Sedation Trial (ANIST), an Institutional Review Board-approved investigator initiated prospective, randomized, double-blinded, crossover study, demonstrated that Dexmedetomidine preserves the cognitive state and may improve intellectual function during active sedation, in patients with lower than normal baseline cognition. That was a great note to intensive care practitioners; incorporating strategies that render a calm and cooperative state while not impairing gross intellectual function can, in fact, yield objective improvement both in cognition as well as in functional neurological condition [43]. A recent well-designed randomized controlled-trial presented clinical evidence of adding Dexmedetomidine as an adjuvant agent or as the sole sedative in neurological patients, requiring postoperative mechanical ventilation in the ICU [44]. This study showed that Dexmedetomidine facilitated early extubation and was associated with more ventilator-free hours. It is exceptionally, important in the neurosurgical population, to control agitation and provide analgesia, so as to improve tolerance to mechanical ventilation and accelerate time to extubation, maintain homeostasis and enable early neurological assessment.

In a prospective randomized control study of 90 neurosurgical patients requiring short-term postoperative ventilation for about 12 hours, Dexmedetomidine, Midazolam or Propofol all provided effective sedation and stable hemodynamic stability. Compared to Propofol and Midazolam sedation, Dexmedetomidine was associated with a longer time to extubation [45]. A retrospective propensity-matched cohort data analysis of 342 patients from 2 medical centers showed that Dexmedetomidine and Propofol were associated with an equal prevalence of hypotention (defined as MAP<60 mmHg, 23% vs 26%) and bradycardia (defined as heart rate <50 beats/min, 8,6% vs 5,5%) [46]. However other studies frequently demonstrate that Dexmedetomidine is more commonly associated with bradycardia [45,47]. The prevailing thought is that Dexmedetomidine may be associated with less hemodynamic perturbation, minimal neurophysiological monitoring interference, greater ability to achieve cooperative sedation without respiratory compromise in awake procedures and acceptable pain control.

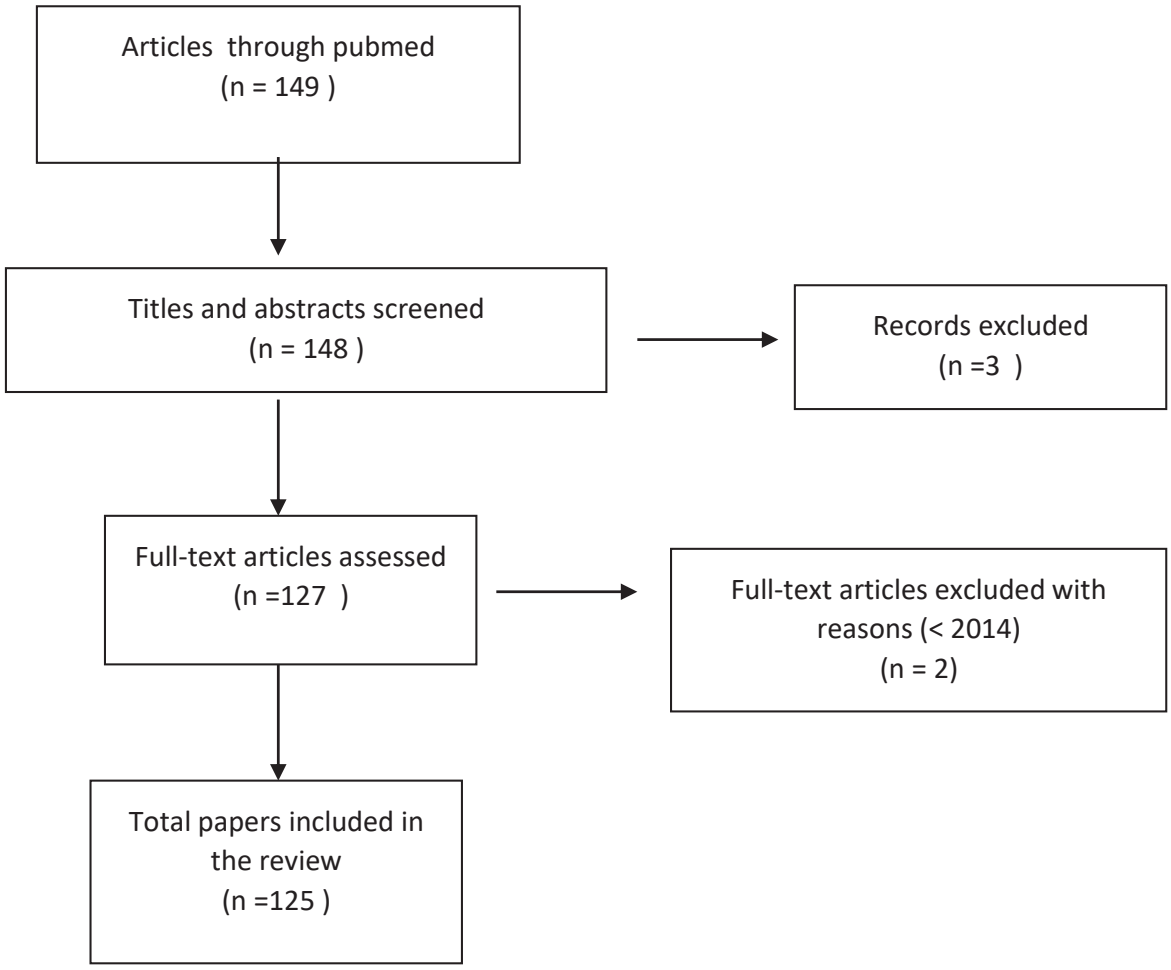
B. Surgery

Spinal surgery poses unique challenges concerning the provision of optimum perioperative management. Intraoperative hemodynamic changes, blood loss, requirement of augmented doses of anesthetics or potent opioids to suppress the hemodynamic responses evoked by noxious stimulation and rapid awakening for early neurological assessment, constitute the most prominent intraoperative concerns during spinal procedures [47-50]. Furthermore, spine surgeries are painful and often require significant perioperative analgesia [48,51].

As multiple pathways like nociceptive, inflammatory and neuropathic ones seem to be implicated in the occurrence of pain following major spine surgery, the ideal analgesic strategy for these procedures remains yet an intriguing issue. Aiming to avoid any possible adverse effects, an analgesic approach targeting multiple antinociceptive and antihyperalgesic pathways is considered as the best alternative choice [48,51].

Patients with high cervical lesions can suffer spinal cord injury during tracheal intubation and positioning. Although electrophysiological monitoring techniques can assist early detection, they may not be practical [52,53] and miss certain injuries [54]. With the patient awake, injury may be more easily prevented. Dexmedetomidine is increasingly used to provide sedation for awake fiberoptic intubation, as it maintains spon-

VOLUME 73 | ISSUE 1 | JANUARY - MARCH 2022



taneous respiration without airway obstruction [55-57]. Furthermore, its offset kinetics provides optimum conditions and fulfills the need of post-intubation neurological examination, required in such patients.

Cervical fixation along with spinal cord decompression is the most commonly performed surgical procedure for patients with cervical SCI. As there is high concern for further neurological damage during head extension and neck flexion for direct laryngoscopic intubation, awake flexible fiberoptic intubation (AFOI) is often the preferred method for airway management [58]. Adequate sedation with topical anesthesia of the airway may minimize undue discomfort, anxiety and sympathetic surge during AFOI, but respiratory depression and hypoxaemia may occur with excessive sedation [59]. Although various pharmacological agents have been used for conscious sedation during AFOI, most of them demonstratee respiratory depressant effect, in higher doses [59,60]. Consequently, there is a need for an ideal sedative agent for AFOI that will allow patients to maintain spontaneous respiration and protect their own airway with full cooperation, during application of the fibreoptic scope. The major advantage of Dexmedetomidine infusion during AFOI is a unique form of sedation where patients with cervical spinal cord injury remain sleepy but are easily aroused and cooperate with minimum respiratory impairment [55,61].

Neurological assessment can be performed immediately following intubation, as patients remain awake throughout the procedure [62]. Episodes of obstructive apnoea have been reported in one study when Dexmedetomidine was infused at 1 and 2 μg/kg rapidly over 2 min [63]. Additionally, episodes of loss of airway

VOLUME 73 | ISSUE 1 | JANUARY - MARCH 2022

patency with higher doses of Dexmedetomidine infusion (10 μg/kg) have also been reported [64]. In cases of lower maintenance dose of Dexmedetomidine (0,5 μg/kg), no adverse effects were observed.

Dose-depended biphasic alteration of BP with Dexmedetomidine has been reported [65]. It has been documented that hypertensive episodes are more frequent at higher doses (1-2 μg/kg) and hypotension at lower doses (0,25-0,5 μg/kg), when bolus infusions were administered over 2 min [66]. Initial increase in BP following loading dose may be due to vasoconstriction, caused by direct stimulation of a1- receptors on blood vessels and secondary decrease in BP in the subsequent period, due to inhibition of norepinephrine release from sympathetic terminals [67]. This biphasic BP response can be controlled by increasing the duration of the loading dose (1 μg/kg over 10 min) and lowering the maintenance dose (0,5 μg/kg/h). It has been documented that higher doses of Dexmedetomidine may be used safely with minimal changes in hemodynamics, when they are infused over 10 min [68]. It is also recommended that the use of Dexmedetomidine at 1 μg/kg bolus over 15 min, with maintenance rates of 0.2-0.7 μg/kg/h, is safe and beneficial for surgical patients [69].

C. *Neuroprotective effect*

Interest in the potential protective effects of Dexmedetomidine in relation to spinal cord injuries has grown in the past few years. Recent animal studies have shown that intravenous Dexmedetomidine attenuated spinal ventral neuronal degeneration and preserved neurological function and neuronal viability, following transient spinal cord ischemia [70] or ischemia-reperfusion [71]. These beneficial effects were associated with improved cell survival and antiapoptotic factors, as well as with the attenuation of microglial activation, proinflammatory cytokine production, decreased interleukin-6, tumor necrosis factor-alpha and reduced neurotrophil infiltration, indicating an anti-inflammatory effect [72,73]. In terms of injury biomarkers, a prospective study reported reduced levels of the stress hormone cortisol and the inflammatory response marker interleukin-10 following intraoperative Dexmedetomidine infusion in cervical spine surgery [74].

Conclusion

In the recent years, there has been increasing interest in the application of Dexmedetomidine to various neurological clinical scenarios, especially for SCI patients. Literature data on the use of Dexmedetomidine in the neurocritical patients, as sole sedation or as an adjuvant, supports that the drug is both efficient and safe. It may be associated with less hemodymamic perturbation, minimal neurophysiological monitoring interference, greater ability to achieve cooperative sedation without respiratory compromise in awake procedures and acceptable pain control.

Conflict of interest disclosure

"The authors declared no conflicts of interest".

VOLUME 73 | ISSUE 1 | JANUARY - MARCH 2022

REFERENCES

1. Herbert JS, Burnham RS. The effect of polytrauma in persons with traumatic spine injury. A prospective database of spine fractures. Spine 2000;(1):55-60.
2. Ong B, Wilson JR, Henzel MK. Management of the Patient with Chronic Spinal Cord Injury. 2019, doi:10.1016/j.mcna.2019.1006
3. Naaz S.C. Dexmedetomidine in Current Anaesthesia Practice. A Review Journal of Clinical and Diagnostic Research 2014, doi:10.7860/JCDR/2014/9624.4946
4. Panzer O, Moitra V, Sladen RN. Pharmacology of sedative analgesic agents:dexmedetomidine, remifentanyl, ketamine,volatile anesthetics, and the role of peripheral mu antagonists. Anesthesiol. Clin. 2011;29(4):587-605
5. European Medicines Agency. Dexmedetomidine: assessment report. 2011.http//www ema.europa.eu/ Assessed 4 May 2015
6. US Food and Drug Administration. Precedex label. Available from:http//www.accessdata.fda.gov/drugsafda_docs/label/1999/21038lbl. Accessed 14 Nov 2016
7. European Medicines Agency. European Public Assessment Report. 2016. Availablefrom:http//www.ema.europa.eu/docs/en_GB/document_library/EPAR__Product_Information/human/002268/WC500115631.pdf.Accessed 14 Nov. 2016
8. Weerink MS, Strugs RF, Hannivoort LN. Barends A.R. Absalom P. Colin, Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine, Clin. Pharmacokinetic 2017; 56:893-913
9. H. Yoo, T. Lirola, S. Vilo, T. Manner, R. Aantaa, M. Lahtinen, M. Scheinin, K.T. Olkkola, W.J. Jusco. Mechanism-based population pharmacokinetic and pharmacodynamics modeling of intravenous and intranasal dexmedetomidine in healthy subjects,Eur. J. Clin. Pharmacol. 2015;71:1197-1207
10. A.H.W. Tse, L. Ling, A. Lee, G.M. Joyut, Altered pharmacokinetics in prolonged infusions of sedatives and analgesics among adult critically ill patients: a systematic review, Clin.Ther. 2018;40:1598-1615,e2.
11. T. Lirola, H. Ihmsen, R. Laitio, E. Kentala, R. Aantaa, J.P. Kurvinen, M. Scheinin, H. Schwilden, J. Schttler, K.T. Olkkola, Population pharmacokinetics of dexmedetomidine during long-term sedation in intensive care patients, Br. J. Anaesth. 2012;108:460-468
12. P.A. Valitalo, T. Ahtola-Satila, A. Wighton, T. Sarapohja, P. Pohjanjousi, C. Garratt, Population pharmacokinetics of dexmedetomidine in critically ill patients, Clin. Drug Investig. 2013;33:579-587
13. T. Lirola, R. Aantaa, R. Laitio, E. Kentala, M. Lahtinen, A. Wighton, C. Garratt, T. Ahtola-Satila, K.T. Olkkola, Pharmacokinetics of prolonged infusion of high-dose dexmedetomidine in critically ill patients. Crit.Care 2011:15
14. P.Talke, B.J.Anderson, Pharmacokinetics and pharmacodynamics of dexmedetimidine-indused vasoconstriction in healthy volunteers, Br. J. Clin. Pharmacol. 2018;84:1364-1372
15. Abbott Laboratories, Precedex Approval documents, 2019
16. S. Kaivosaari, P.Toivonen, O. aitio, I. Sipila, M. Kskinen, J.S. Salonen, M. Finel, Regio- and stereospecific N-glucoronidation of medetimidine: the differences between UDP glucuronosyltransferase (UGT) 1A4 and UGT2BI0 account for the complex kinetics of human liver microsomes, Drug Metab. Dispos. 2008;36:1529-1537
17. A. Rlle, S. Paredes, L.I. Cortinez, B.J. Anderson, N. Quezada, S. Slari, F. Allende, J. Torres, D. Cabrera, V. Conteras, J. Cawona, C. Ramirez, A.M. Olivera, M. Ibacache, Dexmedetomidine metabolic clearance is not affected by fatmass in obese patients, Br. J. anaesth. 12092018)969-977
18. Trauma: Spinal Cord Injury. Matthew J,Eckert et al. Surg Clin North Am. 2017 Oct;97(5):1031-1045 doi:10.1016/j.suc.2017.06.008
19. Gulsah Karatas, Neslihan Metli, Mufit Akyuz,et al. Sz 2020 Jan 30;73(1-2):27-34 doi:10.18071/isz.73.0027
20. Ong B, Wilson I.R, Henzel M.K (2019). Management of the patient with Chronic Spinal Cord

VOLUME 73 | ISSUE 1 | JANUARY - MARCH 2022

Injury. Medical Clinics of North America. doi: 10.1016/j.mcna.2019.10.006
21. Belleville JP, Ward DS, Bloor BC, et al. Effects of intravenous dexmedetomidine in humans.I.Sedation, ventilatin, and metabolic rate. Anaesthesiology. 1992;77(0)1125-33
22. Ebert TJ, Hall JE, Barney JA, et al. The effects of increasing plasma concentration of dexmedetomidine in humans. Anesthesiology. 2020;939(2):382-94
23. Hsu Y-W, Cortinez LI, Robertson KM, et al. Dexmedetomidine pharmacodynamics; part I. Crossover comparison of the respiratory effects of dexmedetomidine and remifentanyl in healthy volunteers. Anesthesiology 2004;(5):1066-76
24. Hall JC, Uhrich TD, Barney JA, et al. Sedative, amnestic and analgesic properties of small-dose dexmedetomidine infusions. Anesth. Analg. 2000;90(3):699:705
25. Shehabi Y, Ruettimann U, Adamson H, et al. Dexmedetomidine infusion for more than 24 hours in critically ill patients: sedative and cardiovascular effects. Intensive Care Med. 2004;30(12);2188-96
26. 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):684-90
27. Triltsch AE, Welte M. von Homeger P, et al. Bispectral index-guided sedation with dexmedetomidine in intensive care: a prospective, randomized, double-blinded, placebo-controlled phase II study. Crit. Care Med. 2002;30(5):1007-14
28. Venn RM, Newman PJ, Grounds RM. A phase II study to evaluate the efficacy of dexmedetomidine for sedation in the medical intensive care unit. Intensive Care Med. 2003;29(2):201-7
29. Nelson LE, Lu J, Guo T, et al. The a2-adrenoreceptor agonist dexmedetomidine conveges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiology 2003;98(2):428-36
30. Huupponen E, Maksimow A, Lapinlampi P, et al. Electroencephalogram Spindle activity during dexmedetomidine sedation and physiological sleep. Acta Anaesthesiol. Scand.2008;52(2):289-94
31. Panzer O, Moitra V, Sladen RN. Pharmacology of sedative-analgesic agents: dexmedetomidine, remifentanyl, ketamine, volatile anesthetics, and the role of peripheral mu antagonists. Anesthesiol. Clin. 2011;29(4):587-605
32. Bloor BC, Ward DS, Belleville JP, et al. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesilogy. 1992;77(6):1134-42
33. Kallio A, Scheinin M, Koulu M, et al. Effects of dexmedetomidne, a selective a2-adrenoceptor agonist, on hemodynamic control mechanisms. Clin Pharmacol Ther.1989;46(10:33-42
34. Talke P, Richardson CA, Scheinin M, et al. Postoperative pharmacokinetics and sympatholytic effects of dexmedetomidine. Anesth. Analg. 1997;85(5):1136-42
35. MacMillan LB, Hein L, Smith M, et al. Central hypotensive effects of the alpha2 adrenergic receptor subtype. Science. 1996;273:801-3
36. Ebert T, Hall JE, Barney JA, et al. The effects of increasing plasma concentrations of dexmedetomdine in humans. Anesthesiology. 2000;93:382-94
37. Sulaiman S, Karthekeyan RB, Vakamudi M, et al. The effects of dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off-pump coronary artery bypass grafting. Ann Card Anaesth. 2012;15:39-43
38. Kunisawa T, Ueno M, Kurosawa A, et al. Dexmedetomidine can stabilize hemodynamics and spare anesthetics before cardiopulmonary bypass. J Anesth. 2001;25:818-22
39. Yildiz M, Tavlan A, Tuncer S, et al. Effect of dexmedetomidine on hemodynamic responses to laryngoscopy and intubation: perioperative haemodynamics and anaesthetic requirements. Drugs R D. 2006;7:43-52
40. Tsaousi G, Lamperti M, Bilota F. Role of Dexmedetomidine for Sedation in Neurocritical Care Patients: A Qualitative Systematic Review and Meta-analysis of Current Evidence. Clin Neuropharm 2016;39:144-151
41. Thomason JW, Shintani A, Peterson JF, Pun BT,

VOLUME 73 | ISSUE 1 | JANUARY - MARCH 2022

Jackson JC, Ely EW (2005) Intensive care unit delirium is an independent predictor of longer hospital stay: a prospective analysis of 261 non-ventilated patients. Crit Care 9:R375-R381

42. 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;30:2188-96.doi:10.1007/s00134-004-2417-z
43. Marek A. Mirski et al. Cognitive improvement during continuous sedation in critically ill, awake and responsive patients: The Acute Neurological ICU Sedation Trial (ANIST) (doi:10.1007/s00134-010-1874-9).
44. Reade MC, Eastwood GM, Bellomo R et al. Effect of dexmedetomidine added to standard care on ventilator-free time in patients with agitated delirium: a randomized clinical trial. JAMA. 2016;315:1460-1468
45. Srivastrava VK, Agrawal S, Kumar S, et al. Comparison of dexmedetomidine, propofol and midazolam for short-term sedation in postoperatively mechanically ventilated neurosurgical patients. J. Clin Diagn Res. 2014;8:GC04-GC07
46. Erdman MJ, Doepker BA, Gerlach AT. et al. A comparison of severe hemodynamic disturbances between dexmedetomidine and propofol for sedation in neurocritical care patients. Crit Care Med. 2014;42:1696-1702
47. Zhao LH, Shi ZH, Chen GQ, et al. Use of dexmedetomidine for prophylactic analgesia and sedation in patients with delayed extubation after craniotomy; a randomized controlled trial. J. Neurosurg Anesthesiol. 2017;29:132-139
48. Edgcombe H, Carter K, Yarrow S 92008). Anesthesia in the prone position. Br J anaesth 100:165-183
49. Willner D, Spennativ V, Stohl S, Tosti G, Aloisio S, Bilotta F (2016) Spine surgery and blood loss: systematic review of clinical evidence. Anesth Analg 123:1307-1315
50. Sharma S, Balireddy RK, Vorenkamp KE, Durieux ME. Beyond opioid patient-controlled analgesia: a systematic review of of analgesia after major spine surgery. Reg Anesth Pain Med 2012;37:79-98
51. Sekimoto K, Nishikawa K, Ishizeki J, Kubo K, Sato S, Goto F. The effects of volatile anesthetics on intraoperative monitoring of myogenic motor-evoked potentials to transcranial electrical stimulation and on partial neuromuscular blockade during propofol/fentanyl/nitrous oxide anesthesia in humans. J Neurosurg Anesthesiol 2006;18:106-111
52. Mathiesen O, Dahl B, Thomsen BA, Kitter B, Sonne N, Dahl JB, Kehlet H. A comprehensive multimodal pain treatment reduses opioid consumption after multilevel spine surgery. Eur Spine J 2013;22;2089-2096
53. Deinsberger W, Christophis P, Jodicke A, Iteesen M, Boker DK, Somatosensory evoked potential monitoring during positioning of the patient for posterior fossa surgery in the semisitting position. Neurosurgery 1998;43:36-40
54. Ofiram E, Lonstein JE, Skinner S, Perra JH. The disappearing evoked potentials; a special problem of positioning patients with skeletal dysplasia. Spine 2006;31;E464-70
55. Lorenzini NA, Poterack KA. Somatosensory evoked potentials are not a sensitive indicator of potential positioning injury in the prone patient. Journal of Clinical Monitoring and Computing 1996;12:171-6
56. Avitsian R, Lin J, Lotto M, Ebrahim Z. Dexmedetomidine and awake fibreoptic intubation for possible cervical spine myelopathy. A clinical series. Journal of Neurosurgical Anesthesiology 2005;17:97-9
57. Bergese SD, Khabiri B, Roberts WD, Howie DJ. Dexmedetomidine for conscious sedation in difficult awake fibreoptic intubation cases. Journal of Clinical Anesthesia 2007;19:141-4
58. Abdelmalak B, Makaryl L, Hoban J, Doyle Dj. Dexmedetomidine as a sole sedative for awake intubation in management of the critical airway. Journal of Clinical Anesthesia 2007;19:370-3
59. Rosenblatt WH. Airway management In: Barash PG, Cullen BF, Stoelting RK, editors . Clinical Anesthesia. 4th ed. Philadelphia; Lippincott Williams & Wilkins; 2001:595-638
60. Bailey PL, Pace Nl, Ashburn MA, Moll Jw, East

VOLUME 73 | ISSUE 1 | JANUARY - MARCH 2022

KA, Stanley TH. Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. Anesthesiology. 1990;73:826-30 [PubMed] [Google Scholar]
61. Callo A, Billard V, Bourgan JC. A comparison of propofol and remifentanyl target-controlled infusions to facilitate fibreoptic nasotracheal intubation. Anesth. Analg. 2009;108:852-7
62. Neumann MM, David MB, Macknet MR, Applegate RL. 2nd Dexmedetomidine for awake fiberoptic intubation in a patient with spinal muscular atrophy type III for cesarean delivery. Int J Obstet Anesth. 2009;18:403-7
63. Stanenkovic DM, Hassid M. Dexmedetomidine for fiberoptic intubation of a patient with severe mental retardation and atlantoaxial instability. Acta Anaesthesiol Scand. 2006;50:1314-5
64. Belleville JP, Ward DS, Bloor BC, Maze M. Effects of intravenous dexmedetomidne in humans I. Sedation, ventilation, and metabolic rate. Anesthesiology 1992;77:11-25-33
65. Ramsay MA, Luterman DL. Dexmedetomidine as atotal intravenous anesthetic agent. Anesthesiology. 2004;101:787-90
66. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs 2000;59:263-8
67. Bloor BC, Ward DS, Belleville JP, Maze m. Effects of intravenous dexmedetomidine in humans II. Hemodynamic changes. Anesthesiology 1992;77:1134-42
68. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg. 2000;90:699-705
69. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the Intensive Care Unit: Patient and clinician perceptions. Br J Anaesth. 2001;87:684-90
70. Jorden VS, Ponsman RM, Sanford MM, Thorborg PA, Hutchens MP. Dexmedetomidine overdose in the perioperative setting. Ann Phar 2004;38:803-7
71. Goyagi T, Tobe Y. Dexmedetomidine improves the histological and neurological outcomes 48 h after transient spinal ischemia in rats. Brain Res. 2014;1566:24-30
72. Bell MT, Puskas f, Bennett DT, et al. Dexmedetomidine , an aipha-2a adrenergic agonist, promotes ischemic tolerance in a murine model of spinal cord ischemia-reperfusion. J Thorac Cardiovasc Syrg. 2014;147;500-506
73. Bell MT, Agoston VA, Freeman KA, et al. Interruption of spinal cord microglial signaling by alpha-2 agonist dexmedetomidine in murine model of delayed paraplegia. J Vasc Surg 2014;59:1090-1097
74. Can M, Gul S, Bektas S, et al. Effects of dexmedetomidne or methylprednisolone on inflammatory responses in spinal cord injury. Acta Anaesthesiol Scand 2009;53:1068-1072

READY - MADE CITATION

Afrati S, Vlamis J, Pneumaticos S. The use of Dexmedetomidine in patients with Spinal Cord Injury. *Acta Orthop Trauma Hell* 2022; 73(1): 82-90.