Dexmedetomidine

Anthony Absalom,
University Medical Center Groningen, University of Groningen, The Netherlands

Dexmedetomidine, the R-isomer of medetomidine, is a highly selective α_2 agonist that has been available for use in several countries outside of Europe (including the USA) for >10 years. Although initially only licensed for use as an ICU sedative, later the indications were expanded to include sedation outside of the intensive care, and considerable experience has accumulated in its use for other indications. In Europe it was registered in September 2011 for use by intravenous administration for sedation in intensive care patients since September 2011, and in 2017 the EMA approved its use for procedural sedation..

Dexmedetomidine has reasonably rapid pharmacokinetics, making it suitable for use by infusion. It possesses a unique constellation of pharmacodynamic effects, which offer clear advantages in some specific clinical situations. It is a sedative and anxiolytic that appears to have an effect on neuronal pathways controlling natural sleep, and indeed at usual clinical doses, it causes a reversible sedation not dissimilar from natural sleep. The rousability improves safety, and is a useful feature for intensive care sedation, as patients can co-operate with care interventions. During moderate sedation, the EEG appearance is very similar to that of slow-wave sleep. In contrast with other sedatives t has no anti-epileptic effects, and is thus an ideal choice of agent for sedation of restless children undergoing EEG recording.

In addition to sedation and anxiolysis, the agent possesses mild analgesic effects, another useful feature for intensive care and procedural sedation. Unlike other sedatives, it is not a potent amnesic, which can be a disadvantage when it is used as the sole agent during uncomfortable procedures. Another major advantage of dexmedetomidine is that, in contrast with all the other sedatives, it does not cause respiratory depression, even at high doses. In fact, when used in high doses for general anaesthesia for surgery for tumours obstructing the airway, spontaneous ventilation was maintained (jaw lift was sometimes needed).

Another contrast with other intravenous sedatives is the effect on the cardiovascular system. At low doses dexmedetomidine causes a modest decrease in heart rate and blood pressure, which is often advantageous in anxious patients, and for which treatment is seldom needed. In moderate and high doses vasoconstriction can cause bradycardia and hypertension, with a significant decrease in cardiac output.

There is a growing body of evidence, albeit not yet conclusive, that use of dexmedetomidine might have other beneficial effects. These benefits include a reduction of the incidence of delirium in intensive care patients, and attenuation of immune responses and ischemia-reperfusion injuries.

Although most commonly administered by intravenous infusion, ~~dexmedetomidine~~Dexmedetomidine is also sometimes administered as an intranasal spray (using the usual intravenous formulation). This is particularly useful for dental sedation in anxious children, and in dental and needle phobics. Other indications include sedation for deep brain electrode implantation, sedation for awake craniotomy, sedation for awake fibre-optic intubation and for gastro-intestinal endoscopy procedures.

References:

1. Nelson LE, Guo TZ, Lu J, Saper CB, Franks NP, Maze M. The sedative component of anesthesia is mediated by GABA(A) receptors in an endogenous sleep pathway. Nat Neurosci 2002;5:979-984.

2. Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiol 2003;98:428-436.
3. Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, et al. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. JAMA 2009;301:489-499.
4. Jakob SM, Ruokonen E, Grounds RM, Sarapohja T, Garratt C, Pocock SJ, et al. Dexmedetomidine vs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials. JAMA 2012; 307:1151-1160.
5. Mason KP, Lubisch NB, Robinson F, Roskos R. Intramuscular dexmedetomidine sedation for pediatric MRI and CT. AJR Am J Roentgenol 2011;197:720-725.
6. Mason KP, Lubisch N, Robinson F, Roskos R, Epstein MA. Intramuscular dexmedetomidine: an effective route of sedation preserves background activity for pediatric electroencephalograms. J Pediatr 2012;161:927-932.
7. Yuen VM, Hui TW, Irwin MG, Yuen MK. A comparison of intranasal dexmedetomidine and oral midazolam for premedication in pediatric anesthesia: a double-blinded randomized controlled trial. Anesth Analg 2008;106:1715-1721.
8. Yuen VM, Hui TW, Irwin MG, Yao TJ, Wong GL, Yuen MK. Optimal timing for the administration of intranasal dexmedetomidine for premedication in children. Anaesthesia 2010;65:922-929.
9. Yuen VM, Hui TW, Irwin MG, Yao TJ, Chan L, Wong GL, et al. A randomised comparison of two intranasal dexmedetomidine doses for premedication in children. Anaesthesia 2012;67:1210-1216.
10. 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;107:430-437.
11. Iirola T, Vilo S, Manner T, Aantaa R, Lahtinen M, Scheinin M, et al. Bioavailability of dexmedetomidine after intranasal administration. Eur J Clin Pharmacol 2011;67:825-831.
12. Cheung CW, Ying CL, Chiu WK, Wong GT, Ng KF, Irwin MG. A comparison of dexmedetomidine and midazolam for sedation in third molar surgery. Anaesthesia 2007;62:1132-1138.
13. Rozet I, Muangman S, Vavilala MS, Lee LA, Souter MJ, Domino KJ, et al. Clinical experience with dexmedetomidine for implantation of deep brain stimulators in Parkinson's disease. Anesth Analg 2006;103(5):1224-1228.
14. Souter MJ, Rozet I, Ojemann JG, Souter KJ, Holmes MD, Lee L, et al. Dexmedetomidine sedation during awake craniotomy for seizure resection: effects on electrocorticography. J Neurosurg Anesthesiol 2007;19(1):38-44.
15. Rozet I. Anesthesia for functional neurosurgery: the role of dexmedetomidine 1. Curr.Opin.Anaesthesiol. 2008;21:537-543.
16. Hwang L, Choi IY, Kim SE, Ko IG, Shin MS, Kim CJ, et al. Dexmedetomidine ameliorates intracerebral hemorrhage-induced memory impairment by inhibiting apoptosis and enhancing brain-derived neurotrophic factor expression in the rat hippocampus. Int J Mol Med 2013;31:1047-1056.
17. Aydogan MS, Korkmaz MF, Ozgul U, Erdogan MA, Yucel A, Karaman A, et al. Pain, fentanyl consumption, and delirium in adolescents after scoliosis surgery: dexmedetomidine vs midazolam. Paediatr Anaesth 2013;23:446-452.
18. Farag E, Argalious M, Abd-Elsayed A, Ebrahim Z, Doyle DJ. The Use of Dexmedetomidine in Anesthesia and Intensive Care: A Review. Curr Pharm Des 2012 Jul 2.
19. Mo Y, Zimmermann AE. Role of dexmedetomidine for the prevention and treatment of delirium in intensive care unit patients. Ann Pharmacother 2013;47:869-876.