

# Dexmedetomidine and the Upper Airway

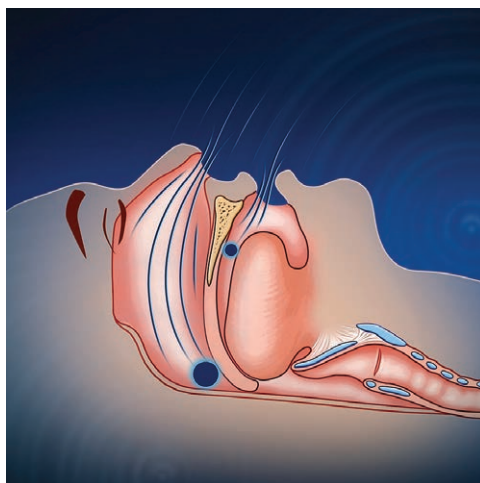
## Not as Simple as We Hoped

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*“Breathing is truly a strange phenomenon of life, caught between the conscious and the unconscious, and peculiarly sensitive to both”<sup>1</sup>*

With the epidemic of obstructive sleep apnea syndrome, concern about airway obstruction during sedation has increased. Dexmedetomidine, used for sedation in the intensive care unit and during procedures, has been thought to have fewer respiratory depressive effects than other sedatives, although airway obstructions and apneas with dexmedetomidine have been noted in several studies.<sup>2,3</sup> This issue of *ANESTHESIOLOGY* features work by Lodenius *et al.*,<sup>4</sup> who found that dexmedetomidine is not superior to propofol in the propensity for causing airway obstruction at comparable sedation levels.

Sedative agents depress ventilation through a variety of actions including direct actions on upper airway muscle tone,<sup>5</sup> on chemosensory pathways, and by removal of the “wakefulness” drive.<sup>6</sup> Loss of the wakefulness input can unmask a profound depression of the chemosensory drive from sedatives and analgesics<sup>7</sup> and reduce the drive to the pharyngeal dilator muscles. Respiratory physiologists routinely discriminate new sedative and opioid agents by their effects on the depression of the hypoxic and hypercapnic chemosensitivity.<sup>8</sup> Moderate depression of the chemoreflexes is well tolerated, particularly when supplemental oxygen is supplied. However, even with supplemental oxygen, upper airway obstruction may result in serious hypoxemia in a matter of minutes. In sleep apnea research, the collapsibility of the upper airway during sleep has been quantified by the estimation of the pharyngeal pressure that is required to close the airway or keep it open.<sup>9,10</sup> This methodology is being used to assess the propensity of medications to increase airway collapsibility.



**“[D]exmedetomidine seems to cause no less propensity for airway obstruction than does propofol at a similar level of sedation.”**

a similar level of sedation. Interestingly, the three measures of sedation depth did not all show the same dose–response relationship even though the chemoreflex depression as measured by the increase in transcutaneous carbon dioxide (a measure of tissue partial pressure of carbon dioxide that is slightly higher than  $P_{aCO_2}$ ) showed similar increases for both drugs.

Second, and equally interesting, is the wide variation in the primary outcome of pharyngeal critical pressure. There were several subjects whose airways were resistant to collapse, requiring a subatmospheric pressure to collapse the airway, for both drugs. There are not enough subjects in this study to determine whether there were correlations with any of the subject characteristics. This underscores the need for more studies focused on patient characteristics that may predict airway collapsibility during sedation.

The precise relationship between airway collapsibility measured in a supine subject whose mouth is taped closed and the routine clinical situation during painful stimulation

The subjects in this study had a wider range of age (23 to 66 yr), body mass index (20.3 to 32.4 kg/m<sup>2</sup>), Mallampati score (1 to 4), neck circumference (31 to 45 cm), and risk for sleep disordered breathing (as indicated by the STOP–BANG questionnaire and apnea hypopnea values) than is usually found in a tightly controlled laboratory study. The subjects were also extensively instrumented, which included an esophageal pressure catheter, Bispectral Index, and three-lead electroencephalogram in addition to the usual laboratory respiratory physiology monitors. The sedation level was assessed by three well established methods. There are two important outcomes from this well designed and executed complex study. The first is that dexmedetomidine seems to cause no less propensity for airway obstruction than does propofol at

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is not clear. This study was done in human subjects who were not exposed to painful stimulation, although dexmedetomidine provides analgesia and propofol does not. In clinical situations that require analgesia as well as sedation, the analgesic effect of dexmedetomidine may allow for lighter sedation than with propofol and thus less adverse ventilatory effects.

Nonetheless, to the extent that this laboratory study can be extrapolated to routine clinical situations, it does not appear that light to moderate sedation with dexmedetomidine offers any protection from central ventilatory apneas and airway obstructions over the commonly used sedative, propofol.

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### References

1. Richards DW Jr: The Lewis A. Conner memorial lecture, the nature of cardiac and of pulmonary dyspnea. *Circulation* 1953; 7:15–29
2. Belleville JP, Ward DS, Bloor BC, Maze M: Effects of intravenous dexmedetomidine in humans: I. Sedation, ventilation, and metabolic rate. *ANESTHESIOLOGY* 1992; 77:1125–33
3. Lodenius Å, Ebberyd A, Hårdemark Cedborg A, Hagel E, Mkrtchian S, Christensson E, Ullman J, Scheinin M, Eriksson LI, Jonsson Fagerlund M: Sedation with dexmedetomidine or propofol impairs hypoxic control of breathing in healthy male volunteers: A nonblinded, randomized crossover study. *ANESTHESIOLOGY* 2016; 125:700–15
4. Lodenius Å, Maddison KJ, Lawther BK, Scheinin M, Eriksson LI, Eastwood PR, Hillman DR, Fagerlund MJ, Walsh JH: Upper airway collapsibility during dexmedetomidine and propofol sedation in healthy volunteers: A nonblinded randomized crossover study. *ANESTHESIOLOGY* 2019; 131:962–73
5. Hillman DR, Platt PR, Eastwood PR: The upper airway during anaesthesia. *Br J Anaesth* 2019; 131:962–73
6. Fink BR: Influence of cerebral activity in wakefulness on regulation of breathing. *J Appl Physiol* 1961; 16:15–20
7. Forrest WH Jr, Belleville JW: The effect of sleep plus morphine on the respiratory response to carbon dioxide. *ANESTHESIOLOGY* 1964; 25:137–41
8. Ward DS: Measurement of drug effects on ventilatory control, Pharmacology and Pathophysiology of the Control of Breathing. Edited by Ward DS, Dahan A, Teppema LC. Boca Raton, Taylor & Francis, 2005, pp 103–53
9. Smith PL, Wise RA, Gold AR, Schwartz AR, Permutt S: Upper airway pressure–flow relationships in obstructive sleep apnea. *J Appl Physiol* (1985) 1988; 64:789–95
10. Litman RS, Hayes JL, Basco MG, Schwartz AR, Bailey PL, Ward DS: Use of dynamic negative airway pressure (DNAP) to assess sedative-induced upper airway obstruction. *ANESTHESIOLOGY* 2002; 96:342–55