Dexmedetomidine-Induced Thermodynamics in the Intensive Care Unit

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Rationale: The α₂-adrenoreceptor agonist, dexmedetomidine, is emerging as a popular sedative in the intensive care unit (ICU) based on its favorable side effect profile and lower association with delirium compared to alternative agents. Despite the insignificant rate of dexmedetomidine-induced fever reported in the package insert, several case series and small-scale cohort studies have called attention to its apparent hyperthermic effects. Given the potential harm associated with delayed recognition of this phenomenon, as well as the rapidly increasing use of dexmedetomidine in the ICU, we sought to more fully elucidate its thermodynamics effects.

Methods: We conducted a retrospective clinical analysis of 2760 patients exposed to dexmedetomidine during admission to Yale-New Haven Hospital from 2013-2019. After excluding patients with insufficient data and/or treatment with extracorporeal circuits such as dialysis and ECMO, 2169 patients remained; they were categorized as hyperthermic, hypothermic, or having no significant temperature change during administration of the drug.

Results: We found that patients on dexmedetomidine were five times more likely to develop hyperthermia compared to control patients on propofol (p=0.00005), with rates of 7.2% and 1.5%, respectively. We also noted a highly distinctive feature of dexmedetomidine-induced hyperthermia (DIH): sustained temperature elevation, with decreased variability while on the drug, as quantified by a decrease in sample entropy (p=0.04). There was a substantial lag time between drug initiation and onset of DIH (median 5.4 hours), and between drug cessation and temperature normalization (median 7.0 hours). Additionally, we found that 1.9% of the cohort had hypothermic episodes linked to dexmedetomidine, consistent with pre-clinical data demonstrating inhibition of thermogenesis in mice and healthy human volunteers. Similar to DIH, lengthy lag times were seen between drug initiation and hypothermia onset (median 5.5 hours) and drug cessation and temperature normalization (median 8.4 hours). Lastly, we observed that cardiothoracic ICU (CTICU) patients were 1.5 times as likely to have DIH (p=0.003), while cirrhotic patients and patients with diabetes with complications were 2.2 and 2.4 times as likely to develop hypothermia, respectively (p=0.01; p=0.001). Conclusion: We observed a surprisingly high rate of thermodynamics events in patients on dexmedetomidine in the ICU (9%), the majority being hyperthermic, but also a considerable number being hypothermic. Given the well-described role of α₂ agonists in hypothalamic control of temperature, we suspect these events are centrally mediated. Better identification of dexmedetomidine-induced temperature changes should lead to more prompt drug cessation and prevent unnecessary workup and empiric therapy for suspected infection.