Editorial

Is dexmedetomidine a favorable agent for cerebral hemodynamics?

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Hemodynamic stability, with special attention to arterial pressure in order to warrant an adequate cerebral perfusion, is a cornerstone of neuroanesthesia (NA) and neurocritical care (NCC) management. An abrupt elevation of arterial blood pressure can aggravate cerebral edema or induce cerebral hematoma, resulting in a prolonged NCC unit stay. On the other hand, hypotension is associated with an increased risk for cerebral ischemia that is more pronounced when autoregulation of cerebral blood flow (CBF) is impaired, and there is a compromised cerebral compliance.[1,2] However, NCC encompasses subgroups of patients such as traumatic brain injury (TBI), subarachnoid hemorrhage (SAH), and intracerebral hemorrhage ones in whom there is the unique need to maintain supranormal blood pressure values with a view to ensure adequate cerebral perfusion and to optimize outcome.[1-3] Moreover, any derangement of cerebrovascular hemodynamics may contribute to intracranial pressure (ICP) elevation with concomitant cerebral perfusion pressure (CPP) deterioration, which can further exacerbate ischemic damage.[3]

Thus, the ideal sedative agent in NA and NCC setting should have minimal impact on hemodynamics. Dexmedetomidine (Dex), a highly selective a2-adrenoreceptor agonist, is emerging as a potentially attractive adjunct in the neurosurgical practice due to its pharmacology promise benefits.[4] Nonetheless, the appealing performance of Dex is tempered by the reported unfavorable hemodynamic sequelae, consisting of bradycardia, hypotension, and hypertension, an effect being more apparent with rapid infusion.[2,3]

Of utmost interest in populations with intracranial pathology is also the impact of Dex on CBF and metabolism (cerebral metabolic rate of oxygen [$CMRO_2$]) coupling. Existing evidence supports a dose-dependent decline in both global and regional CBF after Dex administration, which cannot be solely addressed to its impact on systemic hemodynamic performance.[2-4] This is thought to be via direct vasoconstriction of the cerebral vasculature and indirectly via effects on the intrinsic neural pathways modulating vascular effects, being almost 30% at clinically relevant Dex concentrations.[4-6] Serial transcranial Doppler (TCD) exams in healthy volunteers confirm previous findings in animal models showing a strong linear relationship between middle cerebral artery (MCA) flow velocity (FV) and Dex infusion.[7] The concomitant elevation of pulsatility index (PI) indicates vasoconstriction of the cerebral vasculature as the most profound underlying mechanism.[7]

The authors of the present study used TCD imaging to test the effects of the loading dose of Dex 1 mcg/kg over 10 min on cerebral hemodynamic in patients without

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any co-morbidity scheduled to undergo lumbar discectomy.[8] A notable decline of mean FV in MCA and an augmentation of PI and cerebral vascular resistance index were recorded.[8]

It seems that the clinical impact of CBF deterioration is directed by the clinical circumstances. The use of Dex might be useful adjunct in clinical situations when an increase in CBF could be detrimental such as vasogenic cerebral edema (i.e., TBI, large brain tumors). Nevertheless, Dex infusion is questionable in patients with SAH and acute stroke, since the associate drop in arterial pressure could worsen the coexisting increase in circulating catecholamines and massive sympathetic outflow. Furthermore, the magnitude of cerebral hemodynamic alterations induced by Dex sedation can possibly be modified by confounding factors such as vasomotor reactivity to carbon dioxide (CO_2)-challenge, adequacy of cerebral autoregulation, and background anesthetic regimens administration.[5] In the current study, any possible influence of intraoperative confounding factors was eliminated by maintaining stable systemic hemodynamics, end-tidal CO_2 tension, and oxygenation status.[8]

A possible triggering mechanism for CBF deterioration could be a $CMRO_2$ reduction. Nonetheless, evidence from experimental studies shows that $CMRO_2$ remains unaffected by the use of Dex; no relevant data from human studies exist.[4] Despite the reported neuroprotective effects of Dex in models of ischemic brain injury, the aforementioned clinical features raise concerns that reduction of CBF in the face of an unaltered reduction of $CMRO_2$, potentially limits adequate cerebral oxygenation of brain tissue at risk for ischemic injury.

The last key element of cerebral hemodynamics is ICP, as the elevated ICP promotes CBF deterioration, thus leading to a potential global or regional cerebral ischemia. In the present study, the estimated CPP presented a significant deterioration, mainly attributed to the concomitant elevation of zero flow pressure. The authors explained this finding under the light of cerebral vascular resistance elevation. The extremely limited clinical data, however, have failed to confirm a notable alteration of ICP during Dex administration, so the clinical relevance of these effects is uncertain at the present time.[5,6] It should be underlined that a2-agonists are more potent vasoconstrictors on the venous than on the arteriolar side of the cerebral vasculature.[5] Because the venous compartment comprises most of the cerebral blood volume, a2-agonists could presumably decrease ICP without greatly increasing arteriolar cerebrovascular resistance.

Much of the knowledge accumulated on the impact of Dex upon cerebral hemodynamics is derived by limited quality evidence, mainly supported by experimental data and observational clinical trials with variable methodological quality, nonconsistent design, and selected target population with no significant comorbidities and intracranial pathology; this was also the case in this study.[7-9] Thus, an in-depth assessment of the impact of Dex on cerebral vasomotor reserve and adequacy of substrates supply in different clinical scenarios based on markers obtained from reliable and objective tools, is warranted.[7] Albeit, the accuracy of TCD is limited by the intrinsic technical limitations, operator dependency, and assumptions made regarding vessel diameter, it seems that it can serve as a valid tool to monitor at the bedside the evolution of CBF alterations and possibly cerebral autoregulation performance and ICP estimation in patients presenting with cerebral pathology.[7,9]

In conclusion, available clinical evidence on the use of Dex in neurosurgical and NCC is limited, and no definite conclusion can be drawn until more rigorously designated trials to elucidate the effect of Dex administration in different dose regimens as a sole sedative agent or as adjunct to other sedatives on systemic and cerebral hemodynamics, brain metabolism and its impact on short- and long-term outcomes in various neurosurgical populations. According to the available evidence, there are possible warnings about the safety of Dex in intracranial pathology due to associated hemodynamic effects that might ultimately lead to suboptimal cerebral perfusion.

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