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SOCIETY FOR NEUROSCIENCE IN ANESTHESIOLOGY AND CRITICAL CARE

ARTICLE OF THE MONTH

Mild Sedation Exacerbates or Unmasks Focal Neurologic Dysfunction in Neurosurgical Patients with Supratentorial Brain Mass Lesions in a Drug-specific Manner

Lin N, Han R, Zhou J, Gelb AW.
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Welcome to the June 2016 installment of the SNACC Article of the Month featuring the winner of the SNACC Michenfelder award 2015. In this article Dr. Lin *et al.* look at the effects of four of the most commonly used sedatives in neuroanesthesia practice on differential awakening in patients with frontal-temporal- parietal brain tumors. The study makes an important step forward in understanding this commonly observed phenomenon in patients with neurological pathology undergoing sedation for different procedures. This month we are fortunate to have Dr. Laurel Moore give us her thoughts on this article. Dr. Moore is Clinical Associate Professor and Director of the Division of Neuroanesthesia at University of Michigan and an active and respected member of SNACC. We encourage all of our readers to tell us what they think by joining us on ***SNACC LinkedIn feed*** the ***Twitter feed***, or the ***Facebook page***.

~ Oana Maties, MD and John F. Bebawy, MD

Commentary

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In 1992 Dr. Roy Cucchiara described a fascinating clinical finding that neuroanesthesiologists encounter with some frequency: what he termed “Differential Awakening” or the unmasking of neurologic deficits not present on preoperative exam during emergence from general anesthesia (*Anesth Analg* 1992:75:467). In our Article of the Month, “Mild Sedation Exacerbates or Unmasks Focal Neurologic Dysfunction in Neurosurgical Patients with Supratentorial Brain Mass Lesions in a Drug-specific Manner,” Lin *et al*. investigate this phenomenon in an elegant manner. Widely perceived by neuroanesthesiologists (and hypothesized by the authors of this manuscript) to be a nonspecific phenomenon associated with general sedation, the authors chose four anesthetic agents frequently employed for neurosurgery targeting different mechanisms of action (midazolam, propofol, fentanyl and dexmedetomidine). Agents were titrated to an equivalent level of sedation. Against expectations, the authors found that “differential awakening” varied depending on the anesthetic agent administered.

This single center (Beijing Tiantan Hospital) prospective randomized study was done on 135 patients undergoing supratentorial craniotomy for mass. Patients were randomly assigned to one of the four anesthetic techniques, but given variable onset times for the different anesthetic agents, anesthesia teams were not blinded to the anesthetic assignment. The study protocol was completed prior to formal induction of anesthesia. All anesthetics were titrated in a step-wise manner to a goal of “lethargy” – a level of sedation between “alert” and “aroused by voice” on the Observer’s Assessment of Alertness/Sedation Scale (OAA/S). The National Institutes of Health Stroke Score (NIHSS) was used to evaluate and document neurologic function. The primary outcome was the proportion of patients for each anesthetic subgroup who demonstrated NIHSS-positive changes (i.e. deterioration) in their neurologic exam with equivalent sedation to an OAA/S score of four. By definition, all sedated patients had an NIHSS of one, so a “positive” result required an NIHSS score of two or greater.

The authors found that there are anesthetic-specific differences in development of differential awakening. Patients receiving midazolam or propofol were more likely to develop NIHSS-positive changes than patients receiving fentanyl or dexmedetomidine. Among patients randomized to receive midazolam 72% demonstrated an increase of one or more in their NIHSS (18/27 with no pre-existing motor deficit, 5/5 with pre-existing motor deficit), a remarkably high incidence. In comparison, only 31% of patients randomized to dexmedetomidine had NIHSS-positive changes (3/25 with no pre-existing deficit, 4/6 with pre-existing deficit). The “unmasked” or exacerbated neurologic deficits primarily involved limb motor function or ataxia. Patients with high grade gliomas were more susceptible to deterioration regardless of anesthetic technique. MRI results were not predictive of sensitivity to anesthetics.

The phenomenon of differential awakening has long interested neuroanesthesiologists and concerned neurosurgeons. While the authors clearly demonstrated that different anesthetics working by different mechanisms variably affect the incidence of differential awakening, the study was not designed to further investigate the mechanism of this clinical finding. The authors posit that brain tumors may “remodel” regional synaptic connectivity or alter receptor density and this may explain some of the anesthetic-specific differences in patient responses. Many of the study patients had no deficit at baseline yet deteriorated neurologically with mild sedation, suggesting that compensatory measures are particularly sensitive to anesthetic inhibition. For those of us who see differential awakening in our day-to-day practice, the authors have made a huge step forward in our understanding of this phenomenon, but further work is required to clarify the mechanism(s). These results may be particularly pertinent in determining anesthetic technique for patients undergoing awake craniotomy or other neurosurgical procedures requiring low dose sedation.