SNACC

SOCIETY FOR NEUROSCIENCE IN ANESTHESIOLOGY AND CRITICAL CARE

ARTICLE OF THE MONTH

Neurodevelopmental outcome at 2 years of age after general anaesthesia and awake-regional anaesthesia in infancy (GAS): an international multicentre, randomised controlled trial.

Davidson AJ, Disma N, de Graaff JC, Withington DE, Dorris L, Bell G, Stargatt R, Bellinger DC, Schuster T, Arnup SJ, Hardy P, Hunt RW, Takagi MJ, Giribaldi G, Hartmann PL, Salvo I, Morton NS, von Ungern Sternberg BS, Locatelli BG, Wilton N, Lynn A, Thomas JJ, Polaner D, Bagshaw O, Szmuk P, Absalom AR, Frawley G, Berde C, Ormond GD, Marmor J, McCann ME; GAS consortium.

Lancet. 2016 Jan 16;387(10015):239-50. doi: 10.1016/S0140-6736(15)00608-X. Epub 2015 Nov 4.

PMID: 25920958

Welcome to the May 2016 installment of the SNACC Article of the Month. This month, we deal with a topic that is of great interest, namely neurodevelopmental outcomes in infants exposed to general (sevoflurane) anesthesia, and an important paper on this topic. Davidson et al. have shown, in their analysis, that such outcomes are equivocal between a general anesthesia and a regional (awake) anesthesia cohort. Their paper is, however, not without certain limitations. To shed an expert light on this article, we have enlisted the help of Dr. Jeffrey Sall. Dr. Sall is an M.D., Ph.D. Associate Professor at UCSF whose research focuses on the effects of anesthetics on brain development. Dr. Sall coordinates the UCSF human trial that is evaluating cognitive function in school aged children that were anesthetized early in life. We are so pleased to have his expert opinion on this article. We encourage all of our readers to tell us what they think by joining us on LinkedIn, Facebook, and the SNACC Twitter feed.

-John F. Bebawy, M.D. and Oana Maties, M.D.

Commentary

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So I should tell the parents of my pediatric patient that there are no lasting effects of general anesthesia?

Andrew Davidson and the GAS consortium recently published results from an ongoing randomized equivalence trial comparing outcomes after general vs. regional anesthesia for herniorrhaphy in young children. They found no difference

in cognitive scores between the groups. So this line of research is closed and the question is answered right? I believe it is not and there is still work to be done, let's take a closer look. Most members of SNACC and readers of its journal are by now aware that neonatal anesthesia exposure leads to immediate brain cell death and long-term cognitive dysfunction in rodents. A number of retrospective studies have shown mixed results as to whether the same occurs in humans. The GAS consortium's well-designed prospective clinical trial was planned with the primary outcome of the Wechsler full-scale intelligence quotient at five years of age, however, most children in the study haven't reached that end point yet so this data was not reported. Planned secondary outcomes were hypotension and apnea at the time of surgery, and the Bayley Scales of Infant and Toddler Development III at two years of age - the latter being recently reported in the Lancet. Why isn't this a definitive result?

Animal studies would suggest that both age at the time of exposure and duration of exposure are important factors leading to a cognitive deficit. The average anesthetic duration in the general anesthesia group in this study was 54 minutes. This is shorter than the durations reported in previous studies that have identified deficits in anesthetized children. Pre-clinical rodent studies have also suggested that cognitive deficits become easier to identify as the animals get older. This is a concept supported in neonatal stroke literature and by pediatric neurologists who find that children "grow into" a final cognitive deficit over time, even if one is not immediately apparent after an event. Two years of age is an early time-point to assess a child's cognitive development and precludes the use of sophisticated neuropsychological analyses (the Bayley was not designed to diagnose subtle cognitive abnormalities). Over time, as the brain becomes increasingly developed, more complicated cognitive processes are possible. It is likely that if a deficit exists, it will be found in these complex processes that are fundamental to complete cognitive development in humans. A large change in acquisition of gross motor skills or cognitive developmental milestones would likely have been noticed after a hundred years of delivering anesthesia.

The results of the GAS trial can provide some reassurance that a brief general anesthetic, even at an early age, does not affect achievement of two year developmental milestones. This is an important step in understanding whether early exposure is safe for all children. However, further studies will be needed to understand whether children with an early anesthetic exposure achieve normal cognitive development required for more complex tasks and whether the same normal development can occur after longer anesthetic exposures.