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ARTICLE OF THE MONTH

Effect of Perioperative Intravenous Lidocaine Administration on Pain, Opioid Consumption and the Quality of Life After Complex Spine Surgery

Farag E, Ghobrial M, Sessler DI, Dalton JE, Liu J, Lee JH, Zaky S, Benzel E, Bingaman W, Kurz A.
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In this June edition of SNACC's Article of the Month, we examine a paper with potentially significant ramifications for those of us who care for complex spine surgery patients. Farag *et al*. explored the effects of intravenous lidocaine both intraoperatively and postoperatively on pain and other quality indicators for patients undergoing major spine surgery. Many investigators have sought "non-traditional" adjuncts to our anesthetic regimens to help improve the operative course as well as the postoperative experience. Lidocaine is one of those adjuncts that has received a significant amount of attention, but only recently in this patient population. The commentary you will find below, written by Dr. James Blair and Dr. Lorri Lee from Vanderbilt University,does an excellent job of shedding light on some of the historical aspects of lidocaine use as an adjunct in other arenas, such as bowel surgery, and on the significance of the current study in terms of its outcomes and limitations. We hope you will enjoy this commentary, that it will make you think about your own practice, and we encourage you to share your thoughts with us on the ***SNACC LinkedIn Feed***.

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Commentary

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To date, there are few studies evaluating the potential for improved outcomes (reduced pain, shortened LOS) with lidocaine infusion peri-operatively for spinal surgery. Farag, *et al.*, recently performed a study of lidocaine infusion (2mg.kg-1.min-1) during "complex" spine surgery (*Anesthesiology* May 2013). The study hypothesis was that IV lidocaine infused continuously during and after spine surgery for < 8 hours after spine surgery could reduce pain and/or opioid requirements in the first 48 hours. Secondary outcomes included reduction in major complications, PONV, hospital LOS and quality of life. In 116 adults undergoing complex spine surgery, lidocaine yielded a mean

verbal response pain score of 4.4 [4.2-4.7] for lidocaine vs 5.3 [5.0-5.5] for placebo ($p < 0.001$), but opioid consumption did not differ significantly between groups. Quality of life (QOL) measured by SF-12 at 1 and 3 months was better with lidocaine ($p=0.04$), but other secondary outcome measures such as PONV and length of stay (LOS) were not significantly different between groups.

Since its introduction into clinical practice in the late 1940's, the amino amide local anesthetic lidocaine has been studied extensively for its multiple effects including voltage-gated sodium channel blockade, NMDA antagonism and G-protein-coupled receptor activity. Lidocaine blocks GPCR cytokine receptors on white cells, mast cells and tissue macrophages yielding anti-inflammatory effects and may be a major contributor to shorter length of stay with its use – especially in abdominal procedures. The liver avidly metabolizes lidocaine, promoting a relatively short half-life (20 minutes) in patients with normal liver function, protein status and cardiac output, making it ideal for continuous infusion in a variety of patients and clinical settings.

Since the 1950's, there have been a huge variety of studies evaluating the local anesthetic (VGSA), antiarrhythmic (Class 1B), neuroprotective, central analgesic and antiinflammatory properties of lidocaine. More recently, the potential for lidocaine to improve clinical outcomes as a continuous infusion is becoming more widely evaluated. Both McCarthy (2010) and Vigneault (2011) performed meta-analyses of randomized, controlled trials evaluating post-op pain control and improved outcomes using peri-operative lidocaine infusion. Both studies noted opioid sparing effects, reduced sympathetic tone, a direct effect on intestinal smooth muscles, with reduced post-op pain at rest, with cough and during movement. They also showed a reduction in hospital length of stay, but these benefits were associated primarily with abdominal procedures.

There is evidence that the inflammatory response from the surgical abdomen is quite robust and that the major benefit of lidocaine in that space is a reduction of cytokine signaling at GPCRs on inflammatory cells, as well as a reduction of ileus (likely from less narcotic use). For example, using perioperative lidocaine infusions, Herroeder, Kaba and others demonstrated reduced inflammatory markers, less pain and reduced length-of-stay related to substantial suppression of such signaling during low colorectal procedures and laparoscopic colectomy. As suggested by Cui, et al., alteration of pain scores may relate to the capacity of lidocaine to attenuate the hyperalgesic effects of concomitantly administered narcotics.

Farag and colleagues made the first bold attempt at answering the question of whether the anti-inflammatory and analgesic effects of lidocaine infusion are generalizable away from the peritoneum and into the complex pain dynamics of spine surgery patients. Since their publication in August 2013, one additional group from South Korea has published similar results with approximately half the sample size in each group. Randomized controlled trials for pain outcome measures are difficult to perform in general, but particularly challenging in spine surgery because of the numerous confounders present in this patient population including a high rate of preoperative chronic opioid use, a high rate of psychiatric disease and somatization, and the large variability in the surgical invasiveness of procedures between patients.

The paper was reviewed by Chi in Neurosurgery (August 2013). While mean pain scores were better with lidocaine ($p < .001$), Chi noted marginal differences in narcotic use between lidocaine and placebo post-op. In a letter to Anesthesiology, Fry, *et al.*, also cited several issues with Farag's study design, noting chronic use of opioids in 32.8% of the control group compared with 15.8% in the treatment group. They further noted that there was apparently no control for intraoperative opioid use or whether pre-op opioids were subtracted from post-op.

In summary, Farag and colleagues should be congratulated for their pioneering attempt to determine if lidocaine infusion can have similar beneficial effects in spine surgery patients as it does in abdominal surgery patients. Their paper highlights the need for a very complex study design when examining pain outcomes in this patient population with numerous confounders.