142. Neurotoxicity of bupivacaine, but not ropivacaine, is attenuated by inhibition of mitogen-activated protein kinases

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Background: Activation of stress-activated protein kinases (SAPK) is a pivotal step in lidocaine neurotoxicity, but this has not been investigated in the case of the two very widely used local anesthetics bupivacaine and ropivacaine. The present study aimed to investigate the hypotheses that bupivacaine and ropivacaine neurotoxicity is similar to the neurotoxicity of the prototype local anesthetic, lidocaine, selective for subcategories of dorsal root ganglion neurons, and mediated by specific activation of stress-activated protein kinases.

Material and Methods: We incubated primary sensory neuron cultures with lidocaine, bupivacaine, and ropivacaine at doses determined as equipotent using patch-clamp recordings. We sought to determine potential selectivity of bupivacaine and ropivacaine toxicity on specific neuron categories. Moreover, we tested whether stress-activated protein kinases are relevant to local anesthetic neurotoxicity using pharmacologic inhibition of SAPK and enzyme-linked immunosorbent assays. In a second line of experiments, we confirmed our results in pheochromocytoma (PC-12) neuronal cell line cultures using fluorescence-activated cell sorting and protein analysis.

Results: The neurotoxic potency of lidocaine, bupivacaine and ropivacaine is similar in vitro. We found a dose-dependent neurotoxic effect in neuron cultures incubated with bupivacaine and ropivacaine, which was not selective for any of the investigated subgroups of neurons. Neurotoxicity of bupivacaine, but not ropivacaine, was mediated, at least in part, by stress-activated protein kinases.

Conclusion: Co-injection of SAPK inhibitors may be a potential therapeutic option to decrease the incidence, or minimize the extent, of bupivacaine-, but not ropivacaine-induced neurotoxicity.

145. Preventing pain during injection of propofol: effects of a new emulsion with lidocaine addition

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Background and Aims: Previous studies found that lidocaine addition to propofol LCT (long chain triglyceride) was associated with a lower incidence of injection pain than MCT (medium chain triglyceride) / LCT formulation, but the incidence was still high (31 – 40%). Our study investigated whether the incidence of injection pain could be further reduced by the addition of lidocaine (10 mg, 20:1) to propofol MCT/LCT.

Methods: In a randomized double-blind controlled trial, 464 patients scheduled to undergo regional anesthesia were assigned to receive one of the following options: propofol MCT/LCT + lidocaine, propofol LCT + lidocaine, propofol MCT/LCT or propofol LCT. Propofol was injected to reach grade 3 of the Observer's Assessment of Alertness/Sedation scale.

Results: Incidence of injection pain was 18% in the propofol MCT/LCT + Lido group, 31% in the propofol LCT + Lido group, 47% in the propofol MCT/LCT group, and 60% in the LCT group. Propofol MCT/LCT + Lido was associated with a statistically significant reduced incidence of injection pain compared with propofol LCT + Lido ($p=0.0249$, number needed to treat = 7.7).

Conclusions: Premixing propofol MCT/LCT with lidocaine is one of the most effective measures currently available to reduce the incidence of injection pain in sedated patients during regional anesthesia.