

PD-33. QUANTITATIVE EVALUATION OF LIDOCAINE NEUROTOXICITY BY CURRENT PERCEPTION THRESHOLD TESTING IN RATS

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Background: Since Riglar et al. (1) have reported the four cases of cauda equina syndrome after continuous spinal anesthesia, the neurological sequelae following spinal anesthesia have still great concern. There are many animal studies to clarify the mechanism of local anesthetic neurotoxicity. Especially, quantitative evaluation of neurotoxicity is most important on the animal study. Nociceptive tests or behavioral examination are usually employed to assess the neurological damage. However, the assessments of neurological damage by using these conventional examinations often fluctuate. Recently, current perception threshold (CPT) is widely used for the evaluation of sensory impairment in human, for example the degree of diabetic neuropathy (2) or recovery from spinal anesthesia (3). Although CPT testing is established for the evaluation of neurological function in human, the reports of application of CPT for animal study are few (4). In this study, we investigated whether CPT could be utilized for the quantitative evaluation of neurological damage caused by intrathecal lidocaine in rat.

Methods: After institutional approval, rat was implanted with intrathecal polyethylene catheter (PE10) under ketamine anesthesia. Seven days after the surgery, rats with normal motor function and behavior were used in our study. CPT at 2000 Hz, 250 Hz and 5 Hz which stimulate A β , A δ and C fibers, respectively, were determined by using Neurometer CPT/C(r) (Neurotron Inc, Baltimore, MD). The electrode for stimulation was placed on the hindpaw of rat. CPT was defined as the minimum current value (mA) when rat squeaked or withdrew a hindpaw. CPT measurement was performed before lidocaine or saline infusion and four days after drug administration. The lidocaine (2%, 5%, 10%, 20%) and saline were administered intrathecally by mechanical micro-infusion pump at rate of 1 μ l/min for 80 min. For comparison with the Neurometer findings, we carried out the nociceptive test and behavioral examination also. Mann-Whitney's U test was used for statistical analysis, and P values less than 0.05 were considered significant.

Results: Four days after intrathecal infusion of drug and saline, sensory and/or motor impairment of rats was observed in 5 %, 10 % and 20% lidocaine groups. CPT values in these groups increased with clearly concentration-dependent manner. Especially, the increases of CPT value at 5 Hz and 250 Hz were remarkable comparing to that at 2000 Hz. In the other hand, no changes on both behavioral examination and CPT value between before and four days after intrathecal infusion were found in saline and 2% lidocaine groups.

Discussion: As many investigators have reported, our data also showed that 5% or higher concentrated lidocaine solution caused irreversible neurological sequelae in rats. Higher concentrated lidocaine caused more serious neurological damage. CPT values were correlated with the seriousness of neurological sequelae. In addition, Neurometer enable us to evaluate the function of different nerves, i.e. A β , A δ and C fiber.

Conclusion: A CPT testing seemed to be more sensitive and quantitative than conventionally nociceptive or behavioral examination for the assessment of neurological damage in rat. The Neurometer is useful device for the quantitative evaluation of lidocaine neurotoxicity in the animal study.

1. *Anesth Analg* 72: 275-81, 1991.

2. *Diabetic Medicine* 8: S63-6, 1991.

3. *Anesthesiology* 82: 60-3, 1995.

4. *J Pharmacol Exp Ther* 297: 352-6, 2001.