Title: EVALUATION OF NEUROTOXICITY OF LOCAL ANESTHETICS FOLLOWING SUBARACHNOID INJECTION

Authors: M. A. Rosen, M.D., C. L. Baysinger, M.D., S. M. Shnider, M.D., P. A. Dailey, M.D., M. Norton, M.D., G. Levinson, M.D., J. D. Curtis, M.D., W. Collins, M.D., R. L. Davis, M.D.

Affiliation: Departments of Anesthesia and Pathology, University of California, San Francisco California 94143

Introduction. Several case reports have described prolonged sensory and motor deficits following accidental spinal anesthesia with large volumes of chloroprocaine.[1,2] Although it is well established that small amounts of local anesthetics injected into the subarachnoid space do not produce neurotoxicity, the effect of large amounts is controversial. We evaluated the possible neurologic sequellae from subarachnoid administration of large volumes of local anesthetics in sheep and monkeys.

Methods. Under general anesthesia, arterial and venous catheters were placed in 50 sheep and 8 monkeys. A lumbar puncture was performed with a 22-gauge needle. At the L_{4-6} level, sheep randomly received subarachnoid administration of 10 ml (0.22-0.33 ml/kg) of 3% chloroprocaine, 2% lidocaine, 0.75% bupivacaine, the carrier agent of 3% chloroprocaine (pH 2.32-3.3), or Elliot's B solution (mock CSF). Another group received only lumbar puncture. Cerebrospinal fluid was collected for analysis of protein, glucose, lactic acid, and creatinine phosphokinase and cell counts both at lumbar puncture and on day 7. Also, at level L_{4-6}, monkeys randomly received 2.1 to 4.5 ml (0.5 ml/kg) of 3% chloroprocaine or 0.75% bupivacaine. Although CSF was not collected, CSF pressures were recorded before and after injection of local anesthetics. After removal of the spinal needle, general anesthesia was discontinued and animals were ventilated with 100% O_2 to maintain normal $PaCO_2$. Each animal receiving a local anesthetic rapidly achieved high spinal anesthesia and hypotension. Hypotension was rapidly corrected with IV infusion of a balanced salt solution and ephedrine. Once the animal was awake and able to sustain normal spontaneous ventilation and blood pressure, the trachea was extubated and the animal was returned to a holding cage. Each animal was observed daily for signs of neurologic deficit. On day 7, motor and sensory functions were tested, lumbar punctures were repeated in the sheep to collect CSF, and animals were sacrificed. An autopsy was performed for gross and microscopic examination of the lumbar and lower thoracic spinal cord, meninges, and brain.

Results. The monkeys had no sensory or motor deficits. Twelve sheep were unable to stand after lumbar puncture despite normal sensory, bowel, and bladder function. Five sheep with neurologic deficit had lumbar subpial demyelination with macrophage infiltration: two had received lidocaine; two, chloroprocaine; and one, lumbar puncture only. (This animal also had a cord laceration.) Of the other sheep unable to stand, two had cord lacerations; two, dislocated hips; one, a systemic viral syndrome; and two, deficits of unknown cause. Two sheep had subpial demyelination but no neurologic deficit. Two monkeys (one had received bupivacaine and one chloroprocaine) also had lumbar subpial demyelination with macrophage infiltration, but no neurologic deficit. No sheep or monkey developed clinical or pathologic evidence of meningitis, transverse myelitis, or arachnoiditis. No one solution produced consistent abnormalities on biochemical analysis of sheep CSF. In the monkeys, CSF pressure more than doubled after injection of the local anesthetic.

Discussion. No local anesthetic tested was more neurotoxic than any of the others when injected in large amounts into the lumbar subarachnoid space of sheep or monkeys. Subpial demyelination with peripheral macrophage infiltration occurred infrequently in sheep receiving chloroprocaine, lidocaine, or lumbar puncture alone; and in monkeys receiving bupivacaine or chloroprocaine. Similar lesions have been reported following spinal fluid barbotage in cats.[3] Such lesions could in part be the result of mechanical trauma secondary to tremendous increases in CSF pressure of unknown duration as occurred in our monkeys.

References.

1. Reisner LS, Hochman BN, Plumer MH: Persistent neurologic deficit and adhesive arachnoiditis following intrathecal 2-chloroprocaine injection. Anesth Analg 59:452, 1980

2. Ravindran RS, Bond VK, Tasch MD, et al: Prolonged neural blockage following regional analgesia with 2-chloroprocaine. Anesth Analg 59:447, 1980

3. Bunge RP, Settlage MH: Neurological lesions in cats following cerebrospinal fluid manipulation. J Neuropathol Exp Neurol 16:471, 1957