

Title: SUBARACHNOID SODIUM BISULFITE (THE ANTIOXIDANT IN NESACAINE) CAUSES CHRONIC NEUROLOGICAL DEFICIT

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Introduction. When spinal anesthesia was repeatedly produced in rabbits using 0.1 ml of 2% 2-chloroprocaine-CE (Nesacaine), chronic hindlimb paralysis occurred with cumulative subarachnoid doses reaching 16-20 mg. (1) This dosage of Nesacaine contains 1.6-2.0 mg of sodium bisulfite. If pure 2-chloroprocaine (2-CP) without antioxidant was substituted for Nesacaine, animals recovered normally from each repetitive block, even when the cumulative dose of 2-CP reached 36-40 mg. This study demonstrates that subarachnoid sodium bisulfite alone produces long lasting limb paralysis when administered in quantities equivalent to those contained in chronic paralyzing doses of Nesacaine.

Method of Study. After anesthetizing 13 New Zealand albino rabbits with nitrous oxide and halothane in oxygen, a lumbar laminectomy was done aseptically and a PE 10 catheter was inserted into the lumbar subarachnoid space. Following recovery from anesthesia animals were examined for evidence of neurological impairment. Only those with no deficits 24 hours later were studied. Proper subarachnoid catheter placement was first demonstrated by observing nearly immediate hindlimb paralysis after 0.2 ml of 1% procaine or 0.1 ml of 2% pure 2-CP. Recovery was always complete within 30-40 minutes. After recovery, a single subarachnoid injection with 1.2 mg of sodium bisulfite (i.e. 0.6 ml of 0.2% NaHSO_3 — same concentration as in Nesacaine) was made through a 0.22 micron filter. One animal was given a second 1.2 mg dose of NaHSO_3 sixty minutes after the first dose. Similar volumes of normal saline, Ringers Lactate, and sodium sulfate, the oxidation product of sulfite, were injected in four control animals.

Results. Within 40 minutes of sodium bisulfite injection, 12 rabbits developed profound paralysis of both hindlimbs. One animal was only partially paralyzed after 60 minutes. This animal was given an additional 1.2 mg sodium bisulfite and remained paralyzed until death 3 days later. Another animal recovered motor function after 11 days and a third recovered after 20 days. The remainder had functionless hindlimbs until sacrificed under anesthesia between three days to seven weeks for subsequent pathological examination or until death occurred as long as seven weeks later. Control animals showed no evidence of subarachnoid block or any neurological changes.

Discussion. Chronic hindlimb paralysis was produced by subarachnoid sodium bisulfite given in amounts equivalent to the quantity administered during repetitive Nesacaine blockade. Since chronic paralysis did not occur with bisulfite-free 2 CP, even at any of the very large doses used, it appears that the sodium bisulfite itself is likely to be the causative agent of chronic hindlimb paralysis. The total dosage of sodium bisulfite administered was essentially identical to the quantity contained in chronic paralyzing doses of Nesacaine. The neurotoxic mechanism is not known but may be related to the reactivity of bisulfite (HSO_3^-), or its interconversion products: sulfite (SO_3^{--}) sulfurous acid (H_2SO_3) or sulfur dioxide (SO_2). These products interact with organic groups of proteins and lipids (2) and may exert deleterious effects. This investigation indicates that sodium bisulfite in the subarachnoid space causes chronic neurological deficits. Clinically, this complication may occur when large doses of Nesacaine-CE are inadvertently injected into the subarachnoid space while performing epidural anesthesia.

References.

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