Title: HISTOPATHOLOGIC CONSEQUENCES OF EPIDURAL BLOOD PATCH AND EPIDURALLY ADMINISTERED DEXTRAN 40

Authors: C. J. Lander, M.D., G. A. Korbon, M.D.

Affiliation: Department of Anesthesiology, University of Virginia Medical Center, Charlottesville, VA 22908

Introduction. Epidural blood patch (EBP) is the most commonly utilized therapy for the treatment of postdural puncture cephalgia (PDPC). Complications including paresthesias upon injection, radiculitis, cranial nerve dysfunction, neckache, and back pain occurring in 35% of patients have prompted study of alternative treatments.[1,2] Recently, the epidural administration of dextran 40 has been reported to be efficacious in relieving PDPC.[3] Although transient dysthesia was noted in 7% of patients upon injection, no other complications were observed in long-term follow-up. Little is known of the neurotoxic potential of epidurally injected blood or dextran 40. The purpose of this study is to determine the pathologic consequences of epidurally administered dextran 40 and EBP in an animal model.

Methods. Twelve Western female sheep (weighing 50-60 kg) were randomly assigned to one of three groups: Group A (EBP), Group B (epidural dextran 40), and Group C (control). After induction of general anesthesia (GA) with 0.22 mg/kg xylazine IM and 10 mg/kg ketamine HCl IV, the animals' backs were shaved and sterilely prepared. Dural puncture was performed in all animals with a 22g spinal needle at the L4-5 interspace. The animals were recovered and 48 hours later, after induction of GA, epidural puncture was performed with a 17g Tuohy needle utilizing the loss of resistance technique using 0.9% NaCl. A 19g nylon epidural catheter (Encapsulon #1200, TMX Med.) was placed 2 cm into the epidural space, and the needle removed. After recovery from GA, a test dose of 5 ml of 1.5% lidocaine was injected to ensure proper placement of the epidural catheters. After recovery of motor and sensory function, Group A received 10 ml of autologous blood; Group B received 30 ml of dextran 40 while Group C received no further injections. All catheters were then removed. Animals were examined for evidence of neurologic deficit. Animals in each group were sacrificed at 24 and 48 hours, and at 7 and 30 days following epidural injection. The vertebral column was dissected and placed in NaPO4 buffered 10% formulin fixative for 14 days. L2-3 and L5-6 sections were frozen at -100°C for 24 hours, decalcified using a formic acid-sodium citrate solution, embedded in paraffin, sectioned, and stained with hematoxylin and eosin, hematoxylin Van Gieson (for connective tissue), and Luxol fast blue (for myelin). Spinal histologic evaluation was performed by a neuropathologist blinded to the treatment groups.

Results. All animals displayed evidence of motor and sensory block after injection of lidocaine into the epidural catheter indicating correct placement. There were no traumatic epidural or subarachnoid punctures. Group A (EBP) animals displayed blood within the epidural space. Progressive, widespread fibroblastic activity and collagen formation were noted and were most prevalent at 7 days. Focal areas of fat necrosis were observed at 7 days; no significant inflammation was noted. Both spinal cord and nerve root neuronal structures were intact, and there was no evidence of axonal edema, necrosis or demyelinization. Group B (dextran) showed no significant pathology of the epidural, subdural or subarachnoid spaces or of the spinal cord and nerve roots. Group C (control) also failed to display any significant pathology. There was no evidence of neurologic deficit in any of the animals.

Discussion. Our findings demonstrate that significant pathology occurs when blood is introduced into the epidural space, but not with epidural dextran 40 or lidocaine. The presence of blood and activated factor XII initiates an enzymatic cascade resulting in the formation of bradykinin, a potent vasodilator and primary mediator of pain. Plasmin generates kinins and activates the complement system, resulting in the formation of further nociceptive mediators and inflammation. These factors may be responsible for the side effects observed with EBP. The epidural administration of dextran 40 appears to be devoid of neurotoxic effects and induces no pathology within the epidural space. This may explain the lack of significant side effects noted in a preliminary study in humans.[3] It appears that the efficacy of EBP and epidural dextran 40 is a direct result of the tamponading effect of increased volume within the epidural space, and that the secondary fibrosis and inflammatory nature of blood may be unnecessary for the therapeutic effect. The epidural administration of dextran 40 for the treatment of PDPC may prove to be as efficacious as EBP, while lacking in significant side effects. Further investigation is warranted.

References.

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