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TITLE: EPIDURAL CLONIDINE FOR REFRACTORY REFLEX SYMPATHETIC DYSTROPHY

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Introduction: Intractable reflex sympathetic dystrophy (RSD) is a difficult pain syndrome often insensitive to opiates. Clonidine (C), an α-2 agonist, produces analgesia in the spinal cord by mimicking a noradrenergic pathway and can produce analgesia in deafferentation pain syndromes.[1,2]
Methods: With IRB approval, 10 pts with upper (6) or lower (4) extremity refractory RSD had cervical or lumbar epidural catheters inserted. Each patient received in random order (double-blind) normal saline, 300 and 700 μg C on 3 consecutive days. Visual analog pain scores (VAS), blood pressure (BP), heart rate (HR), and degree of sedation (SE) were recorded during the 6-hr period after each injection. After the 3-day trial, the code was broken and those pts (n=7) who responded to C, but not placebo, began a C infusion of 20 μg/hr, which was titrated to a VAS≤3, intolerable side effects, or a maximum of 50 μg/hr.
Results: C, but not saline bolus, produced analgesia (Fig 1). C bolus produced dose-dependent SE and decreased BP and HR. All pts received additional IV fluids for decreased BP, with two also requiring ephedrine. C infusion produced analgesia (Fig 2) without SE or hypotension. Average infusion duration was 30 days (range 14-67).
Discussion: How RSD pain is perpetuated is unknown, but it clearly exists outside the sympathetic system in refractory cases. Our study demonstrates the effectiveness of an α-2 agent in producing significant symptomatic relief in a very difficult subset of chronic pain pts; whether this will affect outcome or long-term relief requires further investigation.
References:

1. Eisenach J et al. Anesthesiology 1989;71:647-652.
2. Glynn C et al. Lancet 1986;2:1249-1250

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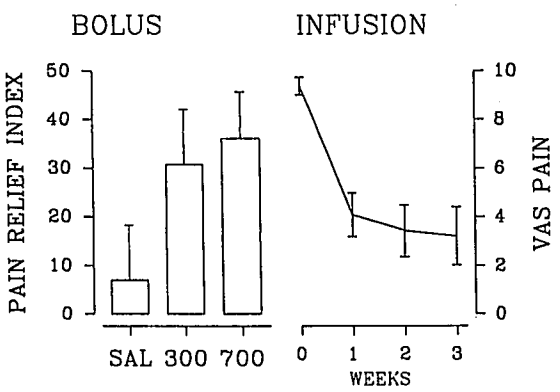
EPIDURAL CLONIDINE ANALGESIA



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TITLE: DOES INTRATHECAL CLONIDINE RELEASE ACETYLCHOLINE (ACH)?

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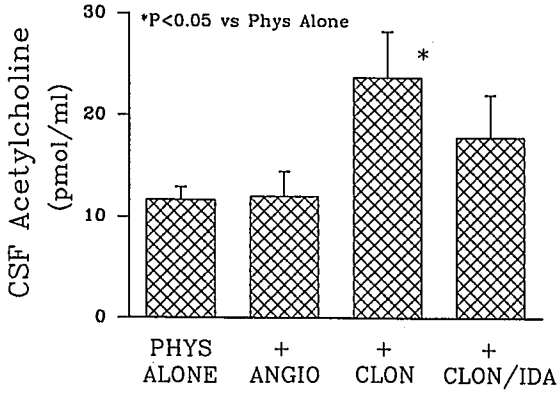
Introduction: Spinal injection of either cholinergic or α_2-adrenergic agonists produces analgesia. Preliminary studies suggest that α_2-adrenergic agonists produce analgesia via a cholinergic mechanism. We examined the effect of intrathecally applied clonidine on the release of ACh into cerebrospinal fluid (CSF). Since CSF contains cholinesterase activity, physostigmine was included in all injections.
Methods: Following approval by the Animal Care and Use Committee, intrathecal catheters were inserted in 9 ewes via a mid-lumbar laminectomy, with catheter tip advanced to mid-thoracic levels. At least 3 days after surgery, ewes received intrathecal injections, in random order, of physostigmine, 2 mg alone, or with clonidine, 300 μg. To test whether clonidine's effect was on α-adrenoceptors, ewes received physostigmine + clonidine + idazoxan (1 mg). To test whether vasoconstriction alone would alter CSF ACh, ewes received physostigmine + angiotensin II (1 mg). CSF samples were collected before the injection, then every 20 min x 5 for the measurement of ACh by HPLC.
Results: ACh was not detectable in any sample before physostigmine injection. Clonidine, but not angiotensin II, increased CSF ACh, as measured by peak concentrations, and this effect was reversed by idazoxan (Fig. 1). Area under curve analysis produced the same result (physostigmine alone = 693±123; plus angiotensin II = 619±55; plus clonidine = 1511±265; plus clonidine + idazoxan = 1135±269 $pmol \cdot ml^{-1} \cdot min^{-1}$).
Discussion: These data support functional studies in rats demonstrating a spinal α_2-adrenergic-cholinergic link in analgesia. Since spinal cholinergic systems increase BP, these data support the concept of addition of cholinesterase inhibitors to α_2-adrenergic agonists to enhance spinal analgesia while minimizing cardiovascular depression.



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