

15. SPINAL ADENOSINE REDUCES HYPERSENSITIVITY FROM CAPSAICIN IN HUMANS BY A PURINERGIC MECHANISM

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Introduction: Spinal adenosine reduces allodynia and hyperalgesia in animal models of neuropathic pain, reduces areas of hyperalgesia and allodynia in volunteers following intradermal capsaicin, and reduces pain in patients with peripheral nerve injury and chronic pain. The purpose of the current study was to determine the dose-response for intrathecal adenosine to reduce areas of allodynia and hyperalgesia from topical capsaicin in volunteers and to determine whether the effect of adenosine can be reversed by a purinergic antagonist.

Methods: Following IRB approval and written informed consent, 13 healthy volunteers were studied in the General Clinical Research Center. A 5 cm² area of skin on the lateral calf was heated and sensitized by 30 min application of capsaicin cream. This resulted in areas of hyperalgesia to von Frey filament application, and allodynia to cotton wisp application. The area of skin was heated for 5 min every 40 min in order to maintain a constant area of hypersensitivity (1). Following induction of hypersensitivity, volunteers were randomized to receive an intrathecal injection of adenosine, 0.5 or 2.0 mg. Two hr later, they were randomized to receive IV saline, or theophylline, 5 mg/kg, over 20 min. Areas of hyperalgesia and allodynia were compared by drug dose and by IV treatment.

Results: A total of 30 volunteers will be completed by May. Interim analysis of the first 13 volunteers demonstrates that capsaicin and heat induced areas of hyperalgesia and allodynia of 83 +/- 9 and 56 +/- 8 cm. Spinal adenosine reduced the area of hyperalgesia by 23 +/- 9% and allodynia by 45 +/- 12% 2 hr after injection, with no difference between doses. This reduction in hypersensitivity from adenosine was stable after IV saline infusion, but was completely abolished after IV theophylline infusion.

Discussion: These data suggest that there is a plateau of intrathecal adenosine's effect in this experimental model of hypersensitivity that occurs at < 0.5 mg. Reversal of the effect of intrathecal adenosine by IV theophylline suggests that central effects of adenosine by this route of injection can be reversed by IV administration of this antagonist, and that adenosine is acting on adenosine receptors, to reduce hypersensitivity.

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1. K. L. Petersen and M. C. Rowbotham. A new human experimental pain model: the heat/capsaicin sensitization model. *Neuroreport* 10 (7):1511-1516, 1999.