The effects of dexmedetomidine alone and in combination with tramadol or amitriptyline in a neuropathic pain model.

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Abstract:

Abstract BACKGROUND: Interactions between the sympathetic and somatic nervous system play an essential role in the pathophysiologic mechanisms of neuropathic pain. The α2-adrenoceptor agonists produce effective antinociception, but sedation is an important adverse effect. Multidrug therapy is potentially valuable to decrease side effects. OBJECTIVE: The aim of the present study was to investigate the possible antinociceptive effect of dexmedetomidine, an α2-adrenoceptor agonist, and its combination with front-line treatment of neuropathic pain, i.e., amitriptyline or tramadol, in a chronic constriction injury (CCI) model of the sciatic nerve in rats. STUDY DESIGN: Controlled animal study. METHODS: Following unilateral ligation of the left sciatic nerve, the effect of intraperitoneal (i.p.) dexmedetomidine (5 ug/kg), tramadol (5 mg/kg), and amitriptyline (30 mg/kg) on mechanical allodynia (measured by electrical von Frey apparatus) and hyperalgesia (measured by Randall and Selitto test) was studied. RESULTS: The sham-operated rats and un-operated hind paw (right paw) press normally on the floor reproduced by a weighted pain score of 0. Behavioral and mechanical tests confirmed the development of neuropathic pain after CCI. All individual drugs and dexmedetomidine combination with either tramadol or amitriptyline were effective in reducing mechanical allodynia and hyperalgesia. Dexmedetomidine, amitriptyline, tramadol, amitriptyline+dexmedetomidine, and tramadol+dexmedetomidine combination did not produce any sedation/motor impairment (P > 0.05). LIMITATIONS: Although the combination of these drugs improved the CCI model of neuropathic pain in this study, an additional interpretation of the underlying mechanism(s) will be needed to confirm these findings. CONCLUSION: The combination of these drugs appears to be more effective in increasing the pain threshold after peripheral nerve injury, when compared with the administration of either of amitriptyline or tramadol alone and should be considered as a possible alternative to decrease side effects of individual drug therapy.

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