474981 - PROPRANOLOL DECREASES PAIN PERCEPTION IN HEALTHY VOLUNTEERS

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Introduction: The potential usefulness of beta-adrenergic antagonists in the treatment of acute pain has been suggested by studies using the beta-1-receptor antagonist esmolol as an adjunct agent in perioperative management. Here, we investigated if the lipophilic mixed beta blocker propranolol reduces nociceptive pain in healthy subjects.

Methods: Local REB approval was obtained for this study. Twenty male volunteers took part in a randomized, double-blind, placebo-controlled crossover trial. Painful heat stimuli were applied to the volar forearm before (Time 0), between 5 and 20 min (Time 1), 25 and 30 min (Time 2), and 35 and 40 min (Time 3) after drug administration. Heat stimuli were applied using a 9 cm² thermode (Medoc TSA-II NeuroSensory analyzer, Medoc Ltd Advanced Medical System, Israel) at a temperature of 45 - 49 °C to elicit pain of 70/100 on a VAS before drug administration. Temperatures were held constant for each subject throughout the study. Following a 20 minute rest period, propranolol 0.3 mg/kg or normal saline were injected intravenously. ECG, oxygen saturation and blood pressure were recorded throughout the experiments and VAS ratings acquired at Time 0, 1, 2, and 3. Heart rate and VAS data were analyzed using ANOVA for repeated measures, followed by simple contrasts.

Results: The main effect of time was significant for the propranolol condition [$F(2.1, 38.3)=8.82, P=0.001$], indicating that propranolol had a significant analgesic effect. The pain ratings were reduced from a mean of 70.2 (SD=2.9) at Time 0 to a mean of 62.3 (SD=8.4, $P<0.001$) at Time 1. The reduction was maintained at Time 2 ($M=64.6, SD=9.3, P<0.01$) and Time 3 ($M=65.1, SD=9.7, P<0.05$). There was no difference of pain scores at Time 1, 2, and 3. The main effect of time was not significant for the saline condition ($F(2.4, 43.3)=8.82, P=0.1$). The heart rate results mirrored those of the VAS scores [main effect of time: $F(2.4, 43.7)=39.2, P<0.001$ in the propranolol condition and $F(2.4, 43.7)=1.38, P=0.26$ in the saline condition]. For further analysis, subjects were subdivided into propranolol responders and non-responders according to their heart rate response. The responders showed a trend for a greater decrease of VAS ratings following propranolol administration compared to the non-responders [$F(1, 17)=3.4, P=0.08$].

Discussion: Our findings show that propranolol reduces pain induced by experimental heat stimuli in healthy volunteers. The reduction of pain ratings was accompanied by a reduction in heart rate as expected following propranolol. Heart rate responders showed a non-significant trend for a greater effect of propranolol on pain perception compared to non-responders. It remains to be clarified if the analgesic effect of propranolol is independent of its effect on heart rate.

References: none