Study Objectives:

Pain is the number one presenting complaint in the Emergency Department (ED) yet evidence remains that pain continues to be undertreated. We proposed a study comparing low dose ketamine in combination with morphine to morphine alone for treatment of acute pain in the ED. We hypothesized that low-dose ketamine in combination with morphine will provide superior analgesia to morphine alone when used for acute pain in the Emergency Department with an acceptable side effect profile.

Methods:

This was a prospective double blind placebo controlled study. Patients 18 years or older were eligible presenting to the ED with acute pain and the treating physician decided to use morphine. Those with headache or head injury, eye injury or eye pain, nontraumatic chest pain, or pregnant patients were excluded. Study drug/placebo (0.3 mg/kg of ketamine or equal volume saline) was administered to subjects no more than 30 minutes after the initial dose of morphine. Subjects rated on the Visual Analog Pain Scale (VAPS) at 0, 30 and 60 minutes after study drug. Total morphine used was at the discretion of the treating physician and determined by chart review. The study was powered to detect a clinically relevant reduction in mean pain of 1.5 on the 11 point VAPS (2-tailed alpha = 0.05 using Man-Whitney test) assuming initial mean pain score of 7.0 with a standard deviation of 2.6. Final sample size estimate was 54 patients per arm. Random effects linear regression, accounting for repeated measures per individual, was used to compare pain scores between placebo and treatment at 0, 30, and 60 minutes.

Results:

During enrollment, one subject was observed to have a severe dysphoric reaction and the study was temporarily suspended. An interim analysis was performed to identify serious complications. For the ketamine group, none were deemed “very concerning” but 4 patient’s reactions were considered “mildly concerning.” Seventeen patients were randomized but one received an unblinded dose of ketamine with 7 patients receiving ketamine and 9 placebo. Mean pain score at 0 minutes did not differ between placebo and ketamine [7.3 vs. 6.9; mean difference: 0.4 (95% CI: -1.7, 2.5)] but differed significantly at 30 minutes [7.7 vs. 3.7; mean difference: -3.9 (95% CI: -6.4, -1.5)]. This difference did not persist at 60 minutes [6.8 vs. 4.9; mean difference: -1.9, 0.3]). Total morphine did not differ between the placebo and ketamine [9.0 vs. 10.3 mg; mean difference: 1.3 (95% CI: -4.5, 7.1)].

Conclusion:

Preliminary analysis suggests a clinically significant decrease in pain score at 30 minutes for those patients who received ketamine in combination with morphine compared to morphine alone. Despite the lower pain scores, there was no appreciable difference between groups in the amount of morphine they received. Although none of the side effects to ketamine were very concerning, four of the seven subjects who received ketamine had significant adverse effect.