Duloxetine Does Not Reduce Opioid Use Following Total Knee Arthroplasty: A Randomized Controlled Trial

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INTRODUCTION:

Duloxetine, a serotonin and norepinephrine reuptake inhibitor, may serve an analgesic role in multimodal pain regimens following total knee arthroplasty (TKA), particularly for patients with central sensitization, which may lower pain thresholds. This study evaluated the effect of duloxetine on opioid consumption, sleep, and outcomes following primary TKA.

METHODS:

A total of 241 patients were randomized to receive either 30 milligrams of duloxetine (n=126) or placebo (n=115) daily, starting one week prior to surgery and six weeks after surgery. Stratified randomization was based on presence (*n*=114) or absence (*n*=127) of central sensitization. As-treated analysis excluded 31 patients who did not adhere to the medication regimen (duloxetine *n*=108, placebo *n*=102). Daily morphine milliequivalents (MME), sleep duration, and quality were assessed for two weeks following surgery while KOOS JR and VAS pain scores were assessed at six weeks. *A priori* power analysis revealed that 100 patients in each cohort were required to detect a 2-point difference in VAS pain scores. Fourteen patients (5.8%) were lost to follow-up prior to 90 days, leaving 227 followed for a mean of 12.0 months.

RESULTS:

MME requirements (977.1 vs. 1,028.3; *p*=0.462) and sleep duration (6.6 vs. 6.5; *p*=0.726) at two weeks postoperatively, as well as KOOS JR (14.4 vs. 14.3; *p*=0.952) and VAS pain scores (2.6 vs. 2.4; *p*=0.482) at six weeks, were similar between groups. However, patients taking duloxetine reported higher well-restedness (6.9 vs. 6.4 out of 10; *p*=0.018). Among centrally sensitized patients, those receiving duloxetine reported being more well-rested (6.8 vs. 6.2; *p*=0.030). No significant differences in opioid requirements, sleep duration, or postoperative pain were observed in the centrally sensitized cohorts (all *p*>0.05).

DISCUSSION AND CONCLUSION:

Perioperative administration of duloxetine did not impact postoperative pain, opioid requirements, or sleep duration. However, improvements in sleep quality were observed, indicating potential utility in postoperative recovery.