Preoperative NMDA Antagonist Use and Phantom Limb Syndrome in Lower Extremity Amputations

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Purpose: In our country, approximately 150,000 people undergo lower extremity amputations annually. Phantom limb syndrome (PLS) follows amputations, causing debilitating neuropathic sensations. PLS commonly occurs after trauma/surgery, severely impacting patients' mental and physical functioning. Neuropathic agents may treat PLS, but do not prevent its development. Studies on postoperative N-methyl-D-aspartate (NMDA) antagonists for PLS management show mixed results. Current PLS studies lack statistical power, and literature on oral premedication before amputation is limited. This study was conducted to determine if premedication with NMDA antagonists can help reduce PLS and improve perioperative outcomes.

Methods: Using TriNetX and deidentified electronic health records, we selected lower extremity amputation (LEA) patients. We conducted a matched, case-control study for premedicated LEA patients (memantine, amantadine, or dextromethorphan within a 3-month preoperative window) versus standard care. Matched variables include age, gender, type II diabetes, neuropathy, depression, anxiety, Alzheimer's, Parkinson's, chronic pain, traumatic brain injury, spinal cord injury, and perioperative nerve block use. Outcomes were analyzed over a 5-year post-LEA period, including PLS development, acute postoperative pain, and postoperative nausea/vomiting (PONV).

Results: Each cohort had 750 patients after propensity score matching. Statistical analysis revealed a significant reduction in acute postoperative pain in patients premedicated with NMDA antagonists (Gross: 70, 115; 9.33% vs 15.33%, P = 0.0004); RR 0.609, 95% confidence interval: 0.460, 0.805, lower rates of PONV (Gross: 71, 117; 9.47% vs 15.6%, P = 0.0003); RR 0.607, 95% CI: 0.460, 0.800, and decreased PLS (Gross: 52, 175; 6.93% versus 23.3%, P<0.0001); RR 0.297, 95% CI: 0.176, 0.340.

Conclusion: Our study suggests preoperative NMDA antagonists may decrease pain outcomes post LEA. PLS had a 16.4% risk difference, meaning a 3.37 times higher risk without NMDA antagonist premedication. NMDA premedication also shows perioperative utility, reducing acute postoperative pain, nausea/vomiting. Future placebo-controlled, randomized trials on NMDA antagonist premedication for amputations are vital to confirm observed correlations.