

# Does Melatonin Improve Subjective Sleep Quality after Total Knee Arthroplasty? A Randomized, Placebo-Controlled Trial

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**INTRODUCTION:** Sleep disturbance is a common problem following total knee arthroplasty (TKA). Melatonin is a safe, inexpensive, over-the-counter sleep aid that has been shown to improve postoperative sleep quality in other surgical subspecialties. The objective of this study was to determine if exogenous melatonin improves sleep quality following primary TKA.

**METHODS:** A randomized, double-blind, placebo-controlled trial was conducted. One-hundred-seventy-two patients undergoing unilateral TKA for primary knee osteoarthritis were randomized to receive either 5mg melatonin (n=86) or 250mg vitamin C placebo (n=86) nightly for 6 weeks (Figure 1). The primary outcome was the Pittsburgh Sleep Quality Index (PSQI) at 6 weeks and 90 days postoperatively. Secondary outcomes included morphine milligram equivalents (MMEs) prescribed, adverse events, medication compliance, and 6-week and 90-day patient-reported outcome measures (PROMs). The sample size was sufficiently powered to identify a minimal detectable difference in PSQI of 2.0.

**RESULTS:** PSQI scores worsened at 6 weeks before returning to the preoperative baseline at 90 days in both treatment groups (Figure 2). There were no differences in PSQI scores between melatonin and placebo groups at 6 weeks (10.2±4.2 vs. 10.5±4.4, p=0.66) or 90 days (8.1±4.1 vs. 7.5±4.0, p=0.43). Treatment did not affect Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS-JR), Lower Extremity Activity Scale (LEAS), Visual Analog Scale (VAS) for pain, or Veterans Rand 12 (VR-12) Physical Component Score (PCS) or Mental Component Score (MCS) (Figure 3; p>0.05 for all PROMs). Poor sleep quality was associated with worse PROMs at 6 weeks and 90 days on univariate and multivariable analyses (Table 1; p<0.05 for all PROMs except 90-day LEAS), but melatonin did not modify these associations (Table 1; p≥0.05 for all interaction terms except 90-day VAS). There were no differences in MMEs prescribed, adverse events, medication compliance, or 90-day readmissions between treatment groups (all p>0.05).

**DISCUSSION AND CONCLUSION:** Exogenous melatonin supplementation did not improve subjective sleep quality or PROMs at 6 weeks or 90 days following TKA. Poor sleep quality was associated with worse physical function and pain. Our results do not support the routine use of melatonin supplementation after TKA.

Figure 1. CONSORT diagram

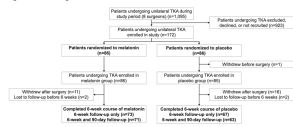


Figure 2. Changes in Pittsburgh Sleep Quality Index between study groups at 6 weeks and 90 days

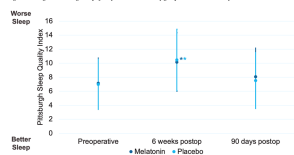


Figure 3. Changes in patient-reported outcome measures between study groups at 6 weeks and 90 days

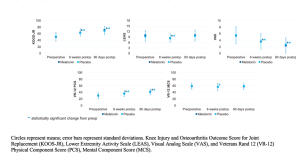


Table 1. Association between Pittsburgh Sleep Quality Index scores and patient-reported outcome measures at 6 weeks and 90 days between melatonin and placebo groups

Outcome	6 weeks		90 days	
	Standardized Coefficient	P Value	Standardized Coefficient	P Value
KOOS-JR	-0.14	0.888	-0.15	0.808
LEAS	-0.07	0.889	-0.07	0.776
VAS	-0.02	0.888	-0.01	0.889
VR-12 PCS	-0.01	0.889	-0.01	0.889
VR-12 MCS	-0.01	0.889	-0.01	0.889

\* indicates significant change from group

Circle represent scores over time represent standard deviation. Each figure and corresponding Outcome Score for Joint Replacement (KOOS-JR), Lower Extremity Activity Scale (LEAS), Visual Analog Scale (VAS), and Veterans Rand 12 (VR-12) Physical Component Score (PCS), Mental Component Score (MCS).