Effects of Melatonin on Neuropathic Pain: A Systematic Review and Meta-Analysis



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Does melatonin improve pain, sleep and quality of life without significant adverse events?

INTRODUCTION

- Chronic neuropathic pain remains difficult to treat as current first-line therapies offer limited relief and poor tolerability.
- Sleep disturbance is a common feature of neuropathic pain and can amplify pain sensitivity and impair quality of life.

METHODS

- RCTs: melatonin vs placebo in neuropathic pain as adjunct or primary therapy
- Primary Outcome: pain intensity
- Secondary Outcome: sleep, quality of life, mood, adverse events
- Random-effects model; leave-one-out sensitivity; RoB-2 & GRADE

CONCLUSION

- Melatonin may be a well-tolerated add-on for sleep and quality of life, not a standalone analgesic.
- Further trials with standardized doses and pain etiologies are needed to clarify its therapeutic value.

Melatonin **did not reduce neuropathic pain**, but it **significantly improved sleep and quality of life**, without added side effects.

7 RCTs · 315 patients · 3–12 mg/day

Full abstract with forest plots

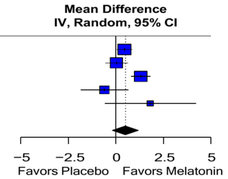
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RESULTS

Pain intensity: no significant difference (MD 0.50; 95% CI −0.18 to 1.17; p = 0.15)

Studies	Melatonin Mean	Melatonin SD	Melatonin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	MD	95% CI
Altiparmak 2018	4.10	0.94	40	3.65	0.94	40	27.6%	0.45	[0.04; 0.86]
Gilron 2025	1.18	1.18	30	1.15	1.18	30	24.8%	0.03	[−0.57; 0.63]
Shokri 2021	4.20	1.48	52	2.90	1.17	51	26.1%	1.30	[0.79; 1.81]
Varoni 2018	0.60	2.23	20	1.20	1.78	20	15.0%	−0.60	[−1.85; 0.65]
Yari 2024	2.91	2.68	12	1.10	2.67	8	6.4%	1.81	[−0.58; 4.20]
Total (95% CI)			**154**			**149**	**100.0%**	**0.50**	**[−0.18; 1.17]**

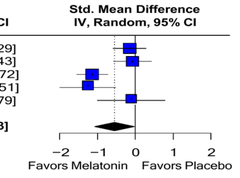
Heterogeneity: Tau² = 0.3894; Chi² = 15.59, df = 4 (P = 0.0036); I² = 74.3%
Test for overall effect: Z = 1.43 (P = 0.15)



Sleep quality: significantly better (SMD −0.55; 95% CI −1.07 to −0.03; p = 0.04)

Studies	Melatonin Mean	Melatonin SD	Melatonin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD	95% CI
Altiparmak 2018	3.20	0.52	40	3.30	0.76	40	22.7%	−0.15	[−0.59; 0.29]
Gilron 2025	26.50	2.57	30	26.70	2.57	30	21.6%	−0.08	[−0.58; 0.43]
Shokri 2021	3.63	1.28	52	5.04	1.18	51	23.1%	−1.14	[−1.55; −0.72]
Talaee 2021	0.20	0.65	17	1.40	1.15	17	17.5%	−1.25	[−2.00; −0.51]
Varoni 2018	29.30	21.00	12	31.60	20.10	8	15.1%	−0.11	[−1.00; 0.79]
Total (95% CI)			**151**			**146**	**100.0%**	**−0.55**	**[−1.07; −0.03]**

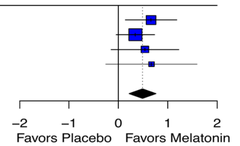
Heterogeneity: Tau² = 0.2632; Chi² = 18.49, df = 4 (P = 0.0010); I² = 78.4%
Test for overall effect: Z = −2.06(P = 0.04)



Quality of life: significant increase (SMD 0.49; 95% CI 0.22 to 0.76; p < 0.01)

Studies	Melatonin Mean	Melatonin SD	Melatonin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD	95% CI
Gilron 2025	68.10	2.40	30	66.50	2.38	30	27.2%	0.66	[0.14; 1.18]
Shokri 2021	70.09	9.57	52	67.16	7.16	51	48.6%	0.34	[−0.05; 0.73]
Talaee 2021	−0.55	0.97	17	−1.11	1.06	17	15.6%	0.54	[−0.15; 1.22]
Yari 2024	70.53	9.76	12	64.18	7.96	8	8.6%	0.67	[−0.26; 1.59]
Total (95% CI)			**111**			**106**	**100.0%**	**0.49**	**[0.22; 0.76]**

Heterogeneity: Tau² = 0; Chi² = 1.12, df = 3 (P = 0.7727); I² = 0.0%
Test for overall effect: Z = 3.53 (P < 0.01)



No significant difference in mood or adverse events (drowsiness, headache, nausea)