VRAAG 5B: Sleep

Primaire studies

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
Edalat-Nejad 2013	• Design: cross-over RCT • Funding/CoI:The Vice Chancellor of the Arak University of Medical Sciences • Setting: University hospital, Iran • Sample size: N=82 • Duration: 12 weeks	• Eligibility criteria: Inclusion criteria: age >18 years, ability to give informed consent, duration of HD >3 months, PSQI score ≥5 and adherence to regular and steady dialysis program or medication that interfere with melatonin secretion; Exclusion: known major illness (malignancy, active infection and uncontrolled heart failure), pregnancy, iron deficiency anemia, poor control diabetes mellitus (hemoglobin A1c >7.5), current use of melatonin or known allergy of melatonin, acute medical or surgical condition that required hospitalization or operation throughout the study and dementia or psychotic disorder as diagnosed by researchers that interferes with patient's participation in this trial • *A priori* patient characteristics: intervention vs. control ○ Age mean 58y (SD 14y) ○ Male 53% ○ Diabetics 43% ○ Vintage of 6-296 months	Melatonin 3 mg + Theanine 10 mg Vs Placebo	Sleep quality: CRITICAL OUTCOME PSQI global score at 6 weeks: 6.99 (SD 3.42) vs 8.91 (SD 4.30), p=0.000 Components of PSQI: Sleep duration 1.00 (SD 0.98) vs 1.60 (SD 1.05), p=0.000 Sleep disturbance 1.03 (SD 0.42) vs 1.15 (SD 0.43), p=0.045 Sleep latency 1.46 (SD 0.90) vs 1.24 (SD 0.81), p=0.087 Daytime dysfunction 1.22 (SD 0.79) vs 1.37 (SD 0.79), p=0.167 Sleep efficiency 1.16 (SD 1.19) vs 1.72 (SD 1.08), p=0.005 Subjective sleep quality 0.79 (SD 0.53) vs 1.41 (SD 1.04), p=0.000 Use of sleep medications 0.32 (SD 0.68) vs 0.43 (SD 0.61), p=0.289 Quality of life: CRITICAL OUTCOME No information	Level of evidence: unclear risk of bias • No information on randomisation procedure; information on blinding limited to description of identical tablets; dropout rate 17%
Koch 2008 Koch 2009	• Design: cross-over RCT • Funding/CoI: not reported • Setting: not reported, but likely in the Netherlands • Sample size: N=24 • Duration: 18 weeks	• Eligibility criteria: Inclusion criteria: patients between 18 and 85 years and on stable haemodialysis (>3 months on haemodialysis with adequate dialysis efficacy) were included. Exclusion criteria: prior use of melatonin, use of hypnotics that could not be stopped during the study, and severe psychological or neurological	Melatonin 3 mg Vs Placebo	Sleep quality: CRITICAL OUTCOME **Based on actometer after 5 or 11 weeks:** (all values are medians and IQR) 1. On day of dialysis: Sleep onset latency (min): 15.5 (27.8) vs 44.5 (43.3), p<0.05 Sleep efficiency (%): 73.1 (27.5) vs 67.3 (30.7), p<0.05 Actual wake time (%): 19.4 (13.6) vs 20.0 (28.6) Actual sleep time (min): 387.5 (155.6) vs 376.7 (118.6), p<0.05 Fragmentation index: 3.1 (0.7) vs 4.5 (1.1),	Level of evidence: unclear risk of bias • No information on randomisation procedure, no information on blinding other than the statement the trial was double blinded, dropout 16%

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		disease. • *A priori* patient characteristics: intervention vs. control ○ Age median 71 (IQR 14.3) ○ Male 70% ○ BMI median 24.5 (IQR 4.7) ○ Dialysis duration median 19 months (IQR 20)		p<0.05 2. On following night: Sleep onset latency (min): 28.5 (22.6) vs 36.0 (31.9), p<0.10 Sleep efficiency (%): 69.2 (30.6) vs 65.0 (22.1), p<0.1 Actual awake time (%): 28.2 (23.7) vs 24.8 (14.2) Actual sleep time (min): 386.8 (169.7) vs 351.0 (119.7) Fragmentation index: 3.0 (1.2) vs 3.9 (1.3) **Based on sleep questionnaire** (all values are medians and IQR) 1. On day of dialysis Daytime napping (min): 0 (37.5) vs 30.0 (48.8) Sleep onset latency (min): 15.0 (12.5) vs 45.0 (90.0), p<0.05 Wake periods (min): 25.0 (22.5) vs 30.0 (25.0), p<0.05 Sleep time (min): 480 (120.0) vs 345.0 (180.0), p<0.05 2. On following night Daytime napping (min): 22.5 (35) vs 12.5 (30) Sleep onset latency (min): 15.0 (21.2) vs 40.0 (100), p<0.05 Wake periods (min): 30.0 (17.5) vs 30.0 (2.5), p<0.05 Sleep time (min): 435 (86.3) vs 420 (180.0) Quality of life: CRITICAL OUTCOME No information	
Russcher 2013	• Design: RCT • Funding/CoI: Dutch Kidney Foundation • Setting: 5 large regional hospitals in the Netherlands • Sample size: N=67 • Duration: 12 months	• Eligibility criteria: Inclusion: stable haemodialysis patients aged 18 to 85 years with a haemodialysis history of at least 3 months and adequate dialysis efficacy, suffered from subjective sleep problems at baseline according to the Epworth Sleepiness Scale (ESS) questionnaire and their mean sleep onset latency measured by means of actigraphy was longer than 15	Melatonin 3 mg Vs Placebo	Sleep quality: CRITICAL OUTCOME **Based on actometer** 1. On day of dialysis Sleep efficiency at 3 months: 7.6% difference (95% CI 0.77-14.4) Actual sleep time at 3 months (min): 49 difference (95% CI 2.1-95.9) 2. On following night: no significant differences At 6, 9 and 12 months: no significant differences	Level of evidence: high risk of bias • Block randomisation, unclear allocation concealment, unclear blinding, 37% dropout rate

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		min Exclusion: current melatonin use, known hypersensitivity to melatonin, severe psychological or neurological disease, unstable angina pectoris, NYHA class IV hear failure, pregnancy, participation in another clinical trial 1 month prior to the start of the study • *A priori* patient characteristics: intervention vs. control ○ Age mean 65.5 (11.7) vs 64.4 (12.0) ○ Male 58%vs 65% ○ BMI 26.3 (4.4) vs 25.6 (5.4) ○ Vintage 30.6 (27.3) vs 28.3 (22.5)		Quality of life: CRITICAL OUTCOME **MOS SF-36** Vitality at 12 months: -1.9% difference (95% CI -12.6-8.7) Physical functioning at 12 months: -11.4% difference (95% CI -21.8- -1.1) Mental health at 12 months: 9.3% difference (95% CI -0.1-18.7), p=0.052 Emotional role at 6 months: 14.6% difference (95% CI -0.6-29.8) Emotional role at 12 months: 29.8% difference (95% CI -1.4 -61.0) Physical role at 12 months: -22.2% (95% CI -49.2-4.8) Social functioning, bodily pain, general health, last year's health: no significant differences	