

Supplementary Online Content

Bücheler F, Hackius M, Schreglmann SR, et al. Sodium oxybate for excessive daytime sleepiness and sleep disturbance in Parkinson disease: a randomized clinical trial. *JAMA Neurol*. Published online November 6, 2017.

doi:10.1001/jamaneurol.2017.3171

eTable 1. Baseline Characteristics and Final Dosages of Study Medications

eTable 2. Effect of Sodium Oxybate and Placebo on Daytime Vigilance, Nighttime Sleep, Parkinson Disease Symptoms

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Baseline Characteristics and Final Dosages of Study Medications

Abbreviations: UPRDS, Unified Parkinson's disease rating scale; ESS, Epworth sleepiness scale; PDSS-2, Parkinson's disease sleep scale-2; SO, sodium oxybate.

	All patients (n=12)	Placebo – SO (n=6)	SO – Placebo (n=6)
Baseline characteristics			
Age, y (SD)	62 (11.1)	57 (12.2)	67 (7.4)
Sex, M/F	10/2	5/1	5/1
Disease duration, y (SD)	8.4 (4.6)	6.7 (4.1)	10.2 (4.6)
Hoehn & Yahr St 2/3	4/8	3/3	1/5
UPDRS III in OFF at baseline (SD)	29.8 (11.5)	27.2 (7.8)	32.3 (14.6)
ESS at baseline (SD)	14.3 (2.3)	14.2 (2.6)	14.5 (2.3)
PDSS at baseline (SD)	17.6 (5.1)	18.5 (6.9)	16.7 (2.8)
Medical treatment, number of patients (average L-dopa equivalent dose, mg ± SD)			
L-Dopa	12 (610 ± 273)	6 (536 ± 206)	6 (683 ± 330)
Dopamine agonist	8 (168 ± 181)	4 (96 ± 95)	4 (240 ± 224)
Amantadine / COMT / MAO-B inhibitor	2 / 2 / 5	1 / 2 / 3	1 / 0 / 2
Total L-Dopa equivalent dose	778 ± 312	632 ± 177	923 ± 363
Study medications			
Final dose SO, g (SD)	4.8 (1.5)	5 (0.8)	4.7 (2.0)
Final dose Placebo, g (SD)	8.7 (0.6)	8.5 (0.8)	9.0 (0)

eTable 2. Effect of Sodium oxybate and Placebo on Daytime Vigilance, Nighttime Sleep, Parkinson Disease Symptoms

Abbreviations: MSL, mean sleep latency; MSLT, multiple sleep latency test; ESS, Epworth sleepiness scale; FSS, fatigue severity scale; PDSS-2, Parkinson's disease sleep scale-2; N1-3, superficial to deep non-rapid eye movement sleep; REM, rapid eye movement; AHI, apnea-hypopnea index; UPDRS, Unified Parkinson's disease rating scale; PDQ-39, Parkinson's Disease Questionnaire.

Baseline values, treatment outcomes and treatment-related changes (standard deviation) are given for each study medication separately (statistical post-hoc analysis with Wilcoxon signed ranks test for differences, * $P < .05$, ** $P < .01$, *** $P < .001$, left columns). Treatment effects (sodium oxybate versus placebo) as derived from linear mixed model analysis are given with confidence interval (CI) and corresponding P -values (treatment effect, right columns) for intention-to-treat (ITT) and per-protocol (PP) population.

1

	Sodium Oxybate (n=12)			Placebo (n=12)			Treatment effect			
	Baseline (SD)	Treatment (SD)	Change (SD)	Baseline (SD)	Treatment (SD)	Change (SD)	Effect ITT (95% CI)	P value (ITT)	Effect PP (95% CI)	P value (PP)
Daytime vigilance										
MSL in MSLT, min	3.1 (3.2)	5.3 (5.1)	2.2 (2.6)*	3.7 (2.8)	2.9 (2.9)	-0.7 (1.1)	2.9 (2.1-3.8)	0.002	3.5 (2.6-4.4)	0.0007
ESS	13.3 (2.5)	9.3 (2.9)	-4 (3.6)***	12.5 (2.2)	12.6 (2.6)	0.2 (1.5)	-4.2 (-5.3-[-3.0])	0.001	-5.2 (-6.4-[-4.0])	0.0002
FSS	4.1 (1.0)	4.1 (1.0)	0 (1.0)	4.3 (1.1)	4.2 (0.8)	-0.1 (0.9)	0.01 (-0.86-1.3)	0.97	0.1 (-0.3-0.6)	0.81
Nighttime sleep										
<i>Subjective measures</i>										
PDSS-2 complete	16.6 (3.6)	12.8 (4.7)	-3.8 (4.7)*	17.5 (5.2)	15.8 (3.3)	-1.5 (3.4)	-2.2 (-3.9-[-0.5])	0.21	-4.2 (-5.7-[-2.7])	0.01
PDSS-2 questions 1-3	5.3 (1.5)	3.7 (2.1)	-1.6 (2.3)	5.4 (1.7)	5.8 (1.5)	0.4 (1.3)	-2.0 (-2.8-[-1.2])	0.016	-2.8 (-3.6-[-2.0])	0.001
<i>Polysomnography</i>										
N1, min	62.7 (32)	44.2 (20)	-18.5 (29)*	74.2 (36)	77.9 (27)	3.7 (18)	-22.6 (-30.8-[-14.4])	0.03	-22.5 (-31.7-[-13.2])	0.03
N2, min	150.7 (38)	145.6 (43)	-5.1 (50)	138.5 (48)	133.0 (47)	-5.5 (36)	0.36 (-17.9-16.2)	0.98	12.9 (-5.1-30.8)	0.48
N3, min	60.0 (35)	119.0 (4)	58.9 (49)**	56.9 (42)	43.1 (32)	-13.8 (29)	72.7 (55.7-89.7)	0.0002	58.5 (41.9-75.2)	0.002
REM, min	38.4 (35)	28.4 (27)	-10 (25)	33.6 (20)	35.0 (34)	1.5 (32)	-11.5 (-23.2-0.3)	0.33	-11.2 (-24.1-1.8)	0.39
WAKE, min	104.9 (70)	83.7 (89)	-21.1 (45)	116.1 (44)	128.5 (67)	12.4 (61)	-33.5 (-55.8-[-11.3])	0.14	-31.9 (-54.7-[-9.0])	0.17
Arousal index, arousals/h	15.2 (5.3)	7.5 (2.9)	-4.6 (4.2)*	15.6 (9.9)	13.0 (5.2)	-2.4 (5.7)	-2.0 (-3.8-[-0.2])	0.27	-1.8 (-3.7-0.2)	0.38
Slow wave energy, mV ² *s	6.0 (4.0)	13.8 (8.9)	7.8 (7.4)	7.0 (7.2)	4.8 (4.2)	-2.3 (4.5)	9.9 (7.3-12.5)	0.0007	7.3 (5.3-9.3)	0.001
AHI, apnea/h	2.8 (3.4)	7.4 (8.3)	4.6 (9.2)	3.5 (4.0)	4.6 (5.1)	1.0 (5.4)	2.7 (0.2-5.2)	0.28	-0.1 (-1.7-1.6)	0.96
Parkinson's disease symptoms										
Morning UPDRS III OFF	29.6 (11.0)	26.7 (10.9)	-2.9 (4.4)	26.2 (8.9)	25.8 (8.7)	-0.3 (7.7)	-2.6 (-5.2-0.1)	0.34	-3.9 (-6.4-[-1.4])	0.14
PDQ-39	34.5 (15.9)	31.9 (14.5)	-2.6 (9.9)	34.2 (12.2)	28.4 (12.4)	-5.9 (8.6)	3.1 (-0.5-6.8)	0.39	1.3 (-2.6-5.2)	0.74

2

3