Melatonin in Youth: N-of-1 Trials in a Stimulant-Treated ADHD Population (MYNAP): A Nested Randomised Clinical Trial

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INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder, affecting 5% of children worldwide. First line treatment is stimulant medication but can lead to adverse events such as initial insomnia (characterised by prolonged sleep onset latency (SOL)).

METHODS

Multi-center, parallel triple-blinded RCT nested in a series of N-of-1 trials

68 participants 6 to 17 years with DSM-IV/V diagnosis of ADHD on stimulants with SOL of ≥45 min, ≥3 nights/week, for ≥1 month as confirmed by parent or guardian (65 completed the trial phase with analyzable data)

- Recruitment via a national ADHD database and physician referral
- Remote trial; melatonin/placebo delivered to participants
- Data were collected via online sleep diaries (RedCap)

Upon recruitment, participants implemented optimal sleep hygiene (SH) measures for 2 weeks then underwent three pairs of treatment/placebo periods for a total of 6 weeks.

Weight-based dosing (before bedtime):

- 3 mg of sublingual melatonin to children < 40 kg
- 6 mg to sublingual melatonin to children ≥ 40 kg

RESULTS

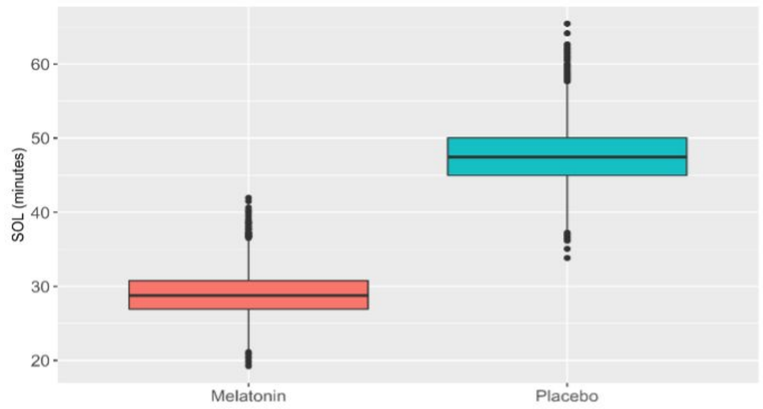

Fig. 1 SOL (mins): On melatonin, SOL was significantly less (average decrease of 18.7 minutes, 95%CI 14.0-23.7; posterior probability 0.94, strong evidence of statistical significance) than on placebo. 40/65 (61.5%) children reduced SOL by 15.9 to 84.3 mins; 24/65 (36.9%) had no significant effect; and one increased SOL by 36.7 minutes). On melatonin, 32/65 (49.2%) children had SOL <30 mins (clinical cut-off) vs 1/65 (16.9%) of children on placebo (p= 0.0002)

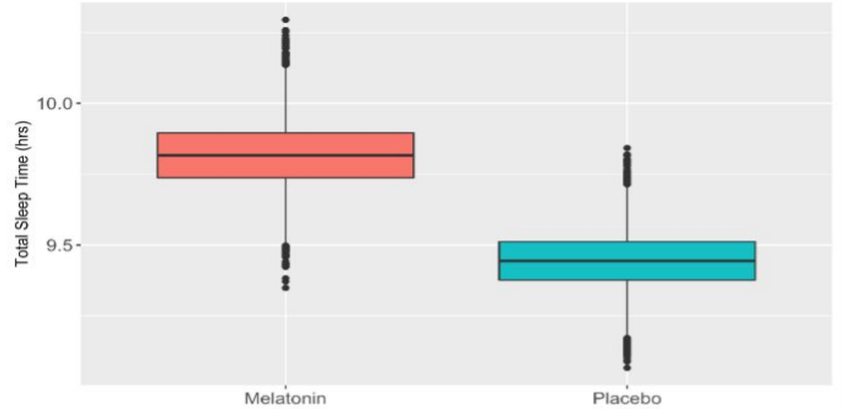

Fig. 2 Total Sleep Time (hrs): Mean difference in sleep duration was 0.37 hrs (95% CI 0.24-0.50; posterior probability 1.0, very strong evidence of statistical significance).

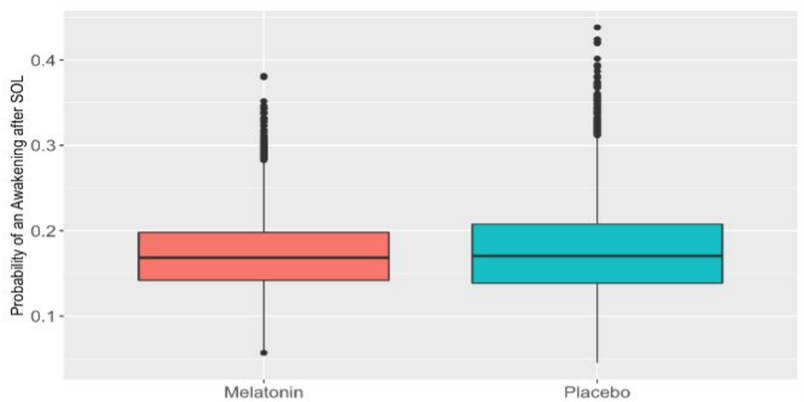

Fig. 3 Probability of Awakening after SOL: There was no significant difference (mean difference 0.004, P = 0.54) in probability of awakening after sleep onset.

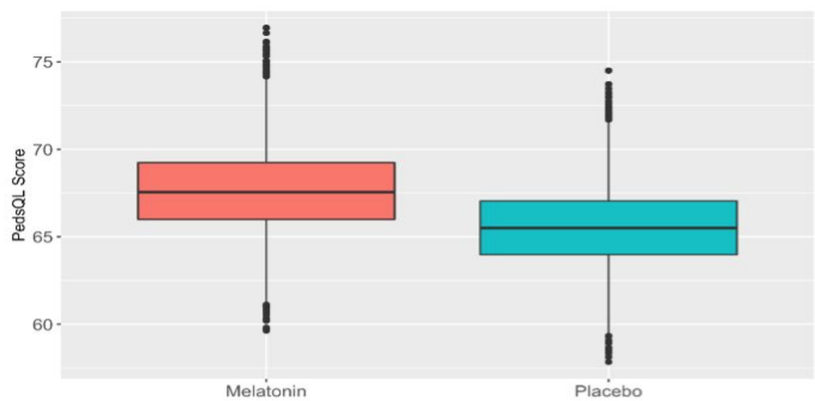

Fig. 4 PedsQL Score: Mean difference for PedsQL was 2.1 (95% CI 0.2-4.0; posterior probability 0.98, strong evidence of statistical significance).

CONCLUSIONS

- Melatonin assisted 61.5% of children with ADHD on stimulants with insomnia. Clinicians and parents can use this response rate to guide therapeutic decision-making
- There were no serious adverse events and 3 minor unrelated adverse events

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