Evaluation of Melatonin Use in Acquired Brain Injury following Formulary Approval for Use and Monitoring

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Background

Melatonin is widely used for sleep disturbances following Acquired Brain Injury (ABI) due to a favourable side effect profile and low propensity for drug interactions.[1,2] However, there is a paucity of efficacy literature in ABI. Anecdotal experience suggested melatonin was initiated ad-hoc for extended periods, with limited capacity to objectively monitor benefit.

Aim

To evaluate an ABI formulary update for the use and monitoring of melatonin, including sleep-wake charting of sleep quantity and quality, and day-7 auto-review embedded into the medication management module of the electronic medical record (EMR).

Methods

A retrospective observational study assessing melatonin use amongst ABI patients was conducted at the Alfred Health neurorehabilitation unit between October 2020 and December 2021. Patients commenced melatonin for more than 7 consecutive days during their ABI admission were included.

DATA COLLECTION

SCREEN
inpatients admitted to Alfred Health's ABI rehabilitation unit between Oct-2020 to Dec-2021

REVIEW
patient EMR including admission histories, medication/ observation charts, discharge summaries, nursing and allied health progress notes

RECORD
study data using a custom REDcap data collection tool for secure storage and analysis

STUDY OUTCOMES

- Patterns of melatonin prescribing; duration (in days), dose at initiation, dose changes throughout admission and discharge dosing
- Documentation of sleep charts and sleep quality following melatonin initiation and dose changes
- Changes in Glasgow Coma Score (GCS) and delirium score (4-AT) following melatonin initiation
- Use of ancillary sleep and medications for behaviours of concern (BOC) in combination with melatonin.

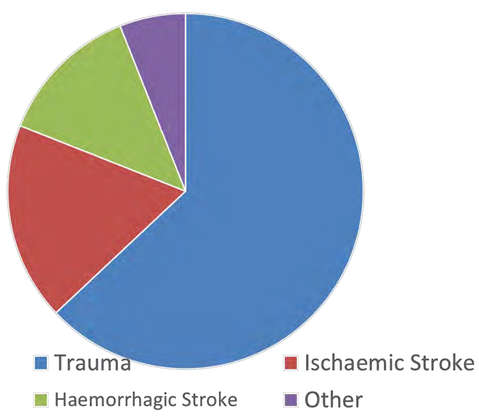
Data for study outcomes were collected two days prior to melatonin initiation (Day -2) and Day 0, Day 7 and between days 14-21 of melatonin commencement .

Results

There were 158 patients admitted to ABI rehabilitation during the study period, 53 patients (33.5%) commenced melatonin for ≥7 consecutive days and were included in the study.

Traumatic brain injury was the most frequent cause of ABI (Figure 1). For those experiencing traumatic brain injury, 70% were cleared of post traumatic amnesia (PTA) during their admission, with a median duration of 31 days PTA, indicative of a severely brain injured cohort.

Figure 1. Mechanism of acquired brain injury



Results

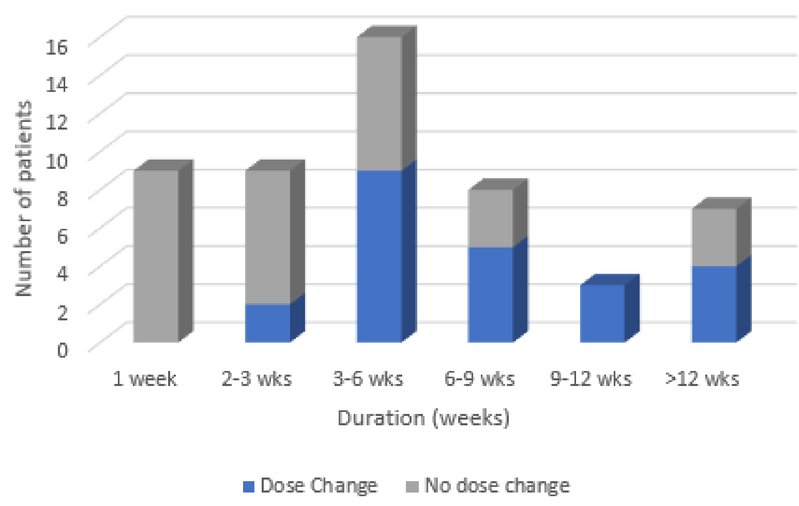
Table 1. Melatonin Initiation Characteristics (n=53)

Melatonin dose and formulation at initiation:			
2mg SR	**2mg SR + 3mg IR**	**3mg IR**	
44 (83%)	3 (6%)	6 (11%)	
Route of administration:			
PO	NGT	PEG	Other
50 (94%)	1 (2%)	2 (4%)	0

The most common melatonin regimen at initiation was 2mg controlled release (CR) daily (n=44, 83%), see Table 1.

At review 7 days following initiation, 21 (39.6%) patients had an increase in melatonin dose, three patients had a dose reduction and melatonin was ceased in nine (17%) patients. The overall median duration of melatonin therapy was 29 days (IQR 14-54), see Figure 2.

Figure 2. Duration of melatonin treatment and dose changes



At therapy initiation overnight sleep charts were recorded for all patients; 71% of hourly sleep observations were documented as 'asleep' or 'restful' (Table 2). Sleep quality was documented for 37 patients, 26 (70%) reported 'poor' sleep quality. On day 14-21, 78% of overnight sleep observations were documented as 'asleep' or 'restful'; three patients of 22 (14%) with sleep quality documented reported 'poor' sleep quality.

Table 2. Proportion of overnight sleep chart entries marked as "Asleep" or "Restful' following melatonin initiation

	n=50	n=53	n=46	n=22
Days post melatonin initiation:	**Day -2**	**Day 0**	**Day 7**	**Day 14-21**
Sleep chart entries marked as 'asleep' or 'restful', % (IQR)	60% (60-78%)	71% (63 –83%)	78% (64-81%)	78% (56- 89%)

Twenty-five (47%) patients had additional sedative(s) prescribed whilst receiving melatonin, zopiclone being the most common (n=21).

Discussion and Conclusion

- Data collected over the duration of the study provides insight into prescribing patterns of melatonin in ABI patients. The EMR auto-review at day-7 prompted the active re-evaluation of therapy, with a dose increase occurring for 40% and therapy cessation for 17% of the cohort.
- Formulary implementation resulted in improved monitoring of sleep quality, quantity and review of therapy efficacy. However, inconsistent sleep chart documentation is still a major limitation in assessing efficacy over time. Ancillary sleep medication use may be indicative of melatonin ineffectiveness.
- Practice changes resulting from these findings have included the EMR auto-review at Day-14 (rather than Day-7), and the expansion of the dosing and monitoring practices to the Aged Care Dementia and Delirium unit.
- This study provides a solid foundation to guide future prospective research into both melatonin use and treating sleep disturbance in the ABI setting.

References

1. Grima N, et al. Efficacy of melatonin for sleep disturbance following traumatic brain injury: a randomised controlled trial. BMC Medicine. 2018;16(1).
2. Osier N, et al. Melatonin as a Therapy for Traumatic Brain Injury: A Review of Published Evidence. International Journal of Molecular Sciences. 2018;19(5):1539.

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