**Melatonin In Acute Mania Investigation (MIAMI-UK) - preliminary results from an RCT.**

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Introduction: Melatonin (MLT) is used as a hypnotic in slow release form (Circadin), licenced in the UK for > 55 years. This is the first double-blinded RCT to investigate MLT augmentation for hypomania or mania in a general adult bipolar sample as previous studies were in rapid cycling bipolar patients or in young manic patients with insomnia. We aimed to investigate whether Circadin can treat manic or hypomanic symptoms during relapse and improve sleep and over-activity.

Methods: Participants were in- or outpatients with bipolar disorder. Participants were recruited but only randomised when their Young Mania Rating Scale (YMRS) score was =/> 20, to Circadin 2mg/day or matching placebo, taken 1-2 hours before bed for 21 days. Ratings included the YMRS, Altman Self Rating Mania Scale (ASRMS), Leeds Sleep Evaluation Questionnaire (LSEQ), QIDS-C and SR (for depression). Activity counts of the actigraph were stored in 1 minute epochs, allowing 22 days of continuous use, analyzed with Cambridge Neurotechnology Ltd. Actiwatch Sleep Analysis software.

Results: Sixty one bipolar patients were recruited and 41 (22 female; aged 18-62; mean age 41.0) randomised. Of the 41 patients, 13 were inpatients throughout the study, 18 outpatients and 10 had a mixed in and outpatient stay. The primary endpoint, YMRS at 21 days, showed no difference between circadin patients and the placebo group ($p=0.4470$). Fewer patients had ASRMS≥10 at day 21 in the Circadin group ( $p=0.0500$). For the depression scales the proportion of patients improving with a self-report measure QIDS-SR ≤5 at 21 days was statistically significantly greater on circadin ($p= 0.0462$) but the clinican rated version QIDS-C was not ($p=0.4301$). There were no LSEQ differences between Circadin and placebo at 21 days.

Conclusions: Although these findings are preliminary, an initial perspective is that the self-report measures of mood may be more sensitive to some mood parameters than the clinician rated scales. This dissociation between measureable symptoms and signs could be an emerging difference in the patients' perception of recovery while using a slow release preparation of a natural neuro-hormone, with possible relevance to stabilisation in general, but will need replication in a larger sample size.
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