NICE National Institute for Health and Care Excellence

2021 exceptional surveillance of attention deficit hyperactivity disorder: diagnosis and management (NICE guideline NG87)

Surveillance report

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Surveillance decision

We will not update the NICE guideline on attention deficit hyperactivity disorder in relation to melatonin for the management of sleep disorders for this condition in children and adults.

Reason for the exceptional review

During development of NICE's evidence summary on melatonin for treating sleep disorders in adults who are blind, colleagues identified evidence about the use of melatonin in people with attention deficit hyperactivity disorder (ADHD) that may impact on recommendations in the guideline. After investigation, we identified 1 trial that fitted with the review protocol for the NICE guideline's inclusion criteria, which we then assessed for impact.

We were also made aware that melatonin has recently been licensed for insomnia in children and adolescents aged 6 to 17 years with ADHD, where sleep hygiene measures have been insufficient. The evidence for this licence authorisation (van der Heijden et al. 2007) was seen during development of the NICE guideline and is discussed in the section on information considered when developing the guideline.

Methods

The exceptional surveillance process consisted of:

- A consideration of evidence relevant to ADHD populations identified during development of NICE's evidence summary on melatonin for treating sleep disorders in adults who are blind.
- Searches of PubMed adapted from and updating the evidence summary searches focussed on identifying additional evidence about melatonin use with ADHD populations.
- Considering the evidence used to develop the guideline in 2008 and update it in 2018.
- Examining related NICE guidance and quality standards.

- Examining the NICE event tracker for relevant ongoing and published events.
- A search for ongoing research.
- Assessing the new evidence against current recommendations to determine whether or not to update sections of the guideline, or the whole guideline.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Search and selection strategy

We assessed 13 studies identified by evidence summary searches covering the period from bibliographic database inception to May 2021 that were related to ADHD populations (see search strategy in appendix E in the evidence review for the evidence summary on melatonin).

Additionally, we checked PubMed for any randomised controlled trials (RCTs) and systematic reviews about the use of melatonin in people with ADHD published after May 2021. We did not identify any additional relevant studies.

Overall, we included 1 relevant study from a total of 13 that met the review protocol inclusion criteria for the NICE guideline. This study is discussed in the next section.

Information considered in this exceptional surveillance review

The 2018 update of the NICE guideline included reviews of psychological efficacy and sequencing pharmacological treatments and pharmacological safety. Their protocols were developed by a multidisciplinary committee who identified quality of life (QoL), reduction of ADHD symptoms, improvements measured by the Clinical Global Impressions scale, and safety as critical outcomes.

Circadian rhythm disorders (CRD) are a cause of delayed sleep onset, and their symptoms and aetiology can overlap with those of ADHD. The treatment of CRDs can improve QoL in people with ADHD. Dim-light melatonin onset (DLMO) is a precursor to sleep onset, and advancing DLMO can stimulate earlier sleep onset and greater sleep duration.

We identified 1 RCT (van Andel et al. 2021), which reported melatonin advanced DLMO in adults (n=49) with ADHD and delayed sleep phase syndrome. Additionally, the study used the ADHD Rating Scale IV to measure melatonin's effect on ADHD symptoms. The authors note a 30% or more reduction on this scale is equivalent to remission and clinically relevant. The study reports sleep education (SE) plus melatonin (0.5 mg / day for 2 weeks) reduced self-reported ADHD symptoms by 12% (p=0.038) compared with SE plus placebo at 1-day post-treatment. Symptoms returned to baseline levels at 2 weeks post-treatment. In a substantially sized sub-group (n=36) with late-onset DLMO (after 9pm) who had higher baseline ADHD symptoms, reduction was not statistically significant (14%, p=0.062). The authors hypothesise this statistically insignificant reduction may be due to underpowering and that it may have been significant with a larger sub-group with late-onset DLMO. The study also reports that SE plus melatonin plus bright light therapy had no effect on ADHD symptoms compared with SE plus melatonin or with SE plus placebo.

Although the authors suggest a drop of 12% is clinically noteworthy it does not meet the 30% reduction the ADHD Rating Scale IV defines as remission. The results therefore do not demonstrate melatonin has a clinically significant effect on ADHD symptoms in the short term.

We identified British Association for Psychopharmacology (BAP) guidelines about the treatment of insomnia, parasomnias and CRD in children, young people, and adults. This recommends that melatonin can be used to advance sleep onset to normal values in children with ADHD who are not on stimulant medication. This is a consensus recommendation based largely on data extrapolated from RCTs of people with neurodevelopmental conditions. It notes that the long-term effects of melatonin are unknown and that sleep problems in childhood respond well to behavioural interventions.

Information considered when developing the guideline

The review of efficacy and sequencing from the NICE guideline included 1 RCT (van der Heijden et al. 2007), which did not demonstrate superiority of melatonin over placebo for QoL, ADHD symptoms and cognition. These outcomes were considered critical by the guideline development committee, and they were unable to make recommendations based on this study. This RCT is also used as evidence for efficacy for treating insomnia in paediatric populations in the specific product characteristics for melatonin tablets licensed in 2021.

The review of pharmacological safety from the NICE guideline included 1 non-comparative long-term study of melatonin (Hoebert et al. 2009) that reported no common adverse events.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

We will not amend the NICE guideline to add a recommendation about melatonin at this time. There is evidence that melatonin can advance sleep onset times in adults and children. However, evidence for its effect on QoL and ADHD symptoms is lacking or equivocal. We will continue to monitor the evidence-base about the use of melatonin in ADHD for emerging evidence.

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