Pharmacological and non-pharmacological interventions for non-respiratory sleep disturbance in children with neurodisabilities: a systematic review

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Scientific summary

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Background

Sleep is essential for physical and mental functioning and well-being. Difficulties with sleep initiation, sleep maintenance and sleep scheduling result in disturbed sleep not only for the individual, but often for other family members as well. Non-respiratory sleep disturbances in children with neurodisabilities (NDs) are more common and more severe than in children with typical development. However, sleep disturbance is rarely a diagnostic criterion; rather, it co-occurs with a diagnosis of a ND. Non-respiratory causes of sleep disturbance among children with NDs include behavioural factors (e.g. parenting), damage or disorders affecting circadian rhythms, hyperarousal, pain, seizures, anxiety and the presence of medical technologies. Many children have more than one sleep difficulty and the aetiology of sleep disturbance is often multifactorial. Sleep disturbances are associated with poor cognitive, physical and/or emotional outcomes for children and parents and result in increased demands on services. Help with sleep is a high priority for parents, practitioners and other stakeholders. However, support is patchy and approaches to managing sleep disturbance are variable and inconsistent. Interventions include pharmacological and non-pharmacological approaches. Pharmacological interventions act on the physiological processes of sleep and/or the timing of the sleep–wake cycle. All are prescribed 'off-label'. Non-pharmacological interventions include parent-directed psychoeducational interventions, chronotherapy, phototherapy, dietary changes and sensory interventions. Evidence on intervention effectiveness is particularly limited for some of these approaches. Importantly, the evidence on pharmacological and non-pharmacological interventions, and across all types of NDs, has never been subject to a single review.

Objectives

- Assess the clinical effectiveness and safety of different intervention approaches to sleep disturbances for children with NDs and, when possible, to:
  - Examine whether or not the clinical effectiveness of an intervention differs for different types of ND, different causes of sleep disturbance and different types of sleep disturbance.
  - Review and evaluate evidence regarding the use of more than one intervention approach, sequentially or in combination, to manage a specific cause of sleep disturbance.
  - Review and evaluate evidence regarding the impact of the setting and/or skills/qualifications of practitioners on intervention effectiveness.
- Assess evidence regarding the acceptability and feasibility of sleep disturbance interventions.
- Describe the settings in which sleep disturbance interventions are being delivered, and by whom.
- Make recommendations, when appropriate, with respect to the management of sleep disturbance among children with NDs generally and/or with respect to particular NDs.
- Identify and describe interventions that look promising and are of relevance and/or feasible to the NHS but that have not been robustly evaluated.
- Make recommendations regarding priorities for future primary research on this topic.

Methods

We undertook a systematic review of pharmacological and non-pharmacological interventions for non-respiratory sleep disturbance among children aged 0–18 years with NDs.

In February and March 2016 (updated in February 2017) we searched Applied Social Sciences Index and Abstracts, The Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Conference Proceedings Citation Index, Cumulative Index to Nursing & Allied Health, Database of Abstracts of Reviews of Effects, EMBASE, Health Management Information Consortium, MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, PsycINFO, Science Citation Index, Social Care Online, Social Policy & Practice, ClinicalTrials.gov, World Health Organization International Clinical Trials Registry Platform and UK Clinical Trials Gateway. The Social Care Online, Social Policy & Practice, Health Management Information Consortium, Conference Proceedings Citation Index and PsycINFO all provide some coverage of reports and other unpublished documents, so the available grey literature are represented in the search results. The reference lists of relevant systematic reviews and included studies were also scanned. There were no limits on date, language or study designs. Studies of children and young people with NDs experiencing non-respiratory sleep disturbances were included. Studies of NHS-relevant pharmacological and non-pharmacological interventions targeted at improving sleep in any setting with and without a comparator were eligible. For pharmacological interventions, only randomised controlled trials (RCTs) were included. For non-pharmacological interventions, RCTs and other study designs, with and without a comparator, were eligible. Qualitative and quantitative studies of parents' or children's experiences of receiving a sleep disturbance intervention were included. Key study characteristics and results were extracted and quality assessed independently by two researchers. When possible, a meta-analysis was undertaken and, when feasible, subgroup analyses considering previous interventions and NDs were undertaken. When meta-analysis was not possible, a narrative synthesis approach was adopted. Qualitative and quantitative data on parents' or children's experiences of receiving a sleep disturbance intervention were collated into themes or topic areas. A descriptive narrative of these findings was produced.

Results

A total of 39 studies were identified: 25 RCTs and 14 before-and-after studies (one with a control group). Sample sizes varied (range 5–244 participants). Thirteen RCTs investigated a pharmacological intervention, namely the use of oral melatonin. Twenty-six studies investigated non-pharmacological interventions. Nine of these evaluated parent-directed tailored interventions, eight evaluated parent-directed non-tailored interventions and two evaluated non-comprehensive parent-directed interventions. A further seven studies evaluated other non-pharmacological interventions: dietary interventions, $n = 2$; alternative medicine, $n = 1$; exercise-based interventions; $n = 1$; weighted blankets, $n = 1$; faded bedtime with response costs, $n = 1$; and light therapy with a daytime activities programme, $n = 1$.

With the exception of one study, all studies were rated as having a risk of bias. Findings from the pharmacological interventions suggest that there was evidence of benefit with melatonin compared with placebo. There was a statistically significant increase in diary-reported total sleep time (TST), which was the most commonly reported outcome, with melatonin compared with placebo [pooled mean difference 29.6 minutes, 95% confidence interval (CI) 6.9 to 52.4 minutes; $p = 0.01$]; however, the statistical heterogeneity was extremely high (97%). For the single melatonin study that was rated as having a low risk of bias, the mean increase in TST was 13.2 minutes and the lower CI included the possibility of reduced sleep time (95% CI –13.3 to 39.7 minutes). It is difficult to draw conclusions as regards the clinical effectiveness of the non-pharmacological interventions, owing to the limited number of RCTs, the variation and range of outcome measures and the risk of studies being underpowered to detect an effect.

Sixteen of the interventions included in the clinical effectiveness review were also investigated in terms of their feasibility and/or acceptability and/or the parent/clinician views of the intervention. These outcomes are referred to as 'family experience' data; however, such data were limited. The majority of studies used quantitative methods to investigate family experiences of non-pharmacological interventions with the exception of one study, which reported on difficulties with administering medication.

Conclusions

The evidence on the management of sleep disturbances in children with NDs is limited and largely of poor quality. There is some evidence of benefit for melatonin compared with placebo. The extent of this benefit is uncertain and so it is not possible to make recommendations for practice. There is a range of non-pharmacological interventions for sleep disturbance. The clinical effectiveness of these interventions is unclear, owing to the limited number of RCTs, the heterogeneous nature of the interventions and outcomes used and the insufficient power in studies to detect any effect.

Implications for health care

It has not been possible to draw conclusions about the clinical effectiveness of pharmacological or non-pharmacological interventions owing to the quality of research and the lack of available evidence.

Recommendations for research

- The development of a core set of outcome measures would facilitate the evaluation of future assessments of the impact of pharmacological and non-pharmacological interventions for sleep disturbance.
- Further exploration of existing tools, practices and strategies to identify sleep problems in children with ND disorders in routine practice would be beneficial.
- Trials comparing slow-release and fast-release melatonin may be useful.
- Further investigation of combined or sequential use of melatonin (or other pharmacological interventions) and parent-directed interventions is suggested.
- Trials evaluating parent-directed interventions are needed. They should include an exploration of intervention feasibility and acceptability. Interventions addressing sleep initiation should be prioritised.
- Evaluations of low-intensity parent-directed interventions – evaluated to date in children with recognised sleep disturbance – as preventative interventions are recommended.
- Research that maps current practices and explores families' understanding of sleep disturbance, and their experiences of obtaining help, is suggested in order to inform developments in service provision.
- All studies should seek to include a health economics evaluation.

Study registration

This study is registered as PROSPERO CRD42016034067.

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