Sleep Medicine Reviews 26 (2016) 95–107

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

Sleep in patients with primary dystonia: A systematic review on the state of research and perspectives

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ARTICLE INFO

Article history:
Received 3 February 2015
Received in revised form
16 April 2015
Accepted 26 April 2015
Available online 9 May 2015

Keywords:
Sleep
Dystonia
Polysomnography
Self-report
Pathophysiology

SUMMARY

Patients with primary dystonia, the third most prevalent movement disorder, suffer from a markedly reduced quality of life. This might, at least in part, be mediated by non-motor symptoms, including sleep disturbances. Characterising and treating sleep disturbances might provide new inroads to improve relevant patient-centred outcomes. This review evaluates the state of research on sleep in patients with dystonia and outlines an agenda for future research. A literature search was performed in July 2014 using PubMed, Medline via Ovid, PsycInfo, PsycArticles via Proquest and Embase via Ovid. Search results were screened for eligibility by two independent raters. Peer-reviewed publications reporting on sleep in patients with primary dystonia were included. Of 1445 studies identified through the search strategy, 18 met the inclusion criteria. In total, the included studies reported on 708 patients diagnosed with focal dystonia (cervical dystonia or blepharospasm), torsion dystonia, and dopa-responsive dystonia. The results indicate that at least half of the patients with focal cranial dystonia suffer from sleep disturbances, but excessive daytime sleepiness is uncommon. Sleep disturbance is associated with depressive symptoms. The frequency and duration of dystonic movements is markedly reduced during sleep. Reduced sleep quality appears to persist after treatment with botulinum toxin that successfully reduces motor symptoms. The findings are limited by a high clinical and methodological heterogeneity. Future research is needed to i) further characterize subjective and PSG sleep in patients with different types of dystonia, ii) determine the aetiology of sleep disturbances (e.g., abnormal brain function associated with dystonia, side effects of medication, psychological reasons), and iii) test whether targeted sleep interventions improve sleep and quality of life in patients with primary dystonia.

Introduction

Primary dystonia is a neurological movement disorder characterised by involuntary muscle contractions causing twisting and repetitive movements or abnormal postures [1]. In contrast to secondary dystonia that has a known causation, such as head injury or a side effect of medication (tardive dystonia), the pathophysiological mechanisms of most forms of primary dystonia are unknown and the diagnosis is based on clinical observations [2]. Primary dystonia is considered the third most prevalent movement disorder after essential tremor and Parkinson's disease. Its exact prevalence is unclear due to a high variability in prevalence estimates between different studies. A recent review found that the prevalence estimates for patients with primary dystonia seeking medical attention were between 24 and 50 per million for early onset dystonia and between 136 and 430 per million for late onset dystonia [3]. Focal forms of primary dystonia are limited to a specific part of the body, such as the eyelids in blepharospasm or the neck in cervical dystonia (spasmodic torticollis), and typically begin in adulthood. Generalised forms of dystonia, in contrast, are often early-onset and involve several limbs and the trunk.

Various domains of quality of life, such as physical and social functioning and vitality, are impaired in patients with dystonia [4,5], which is, at least in part, attributable to the often disabling, disfiguring and stigmatising nature of this disorder. Botulinum toxin

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http://dx.doi.org/10.1016/j.smrv.2015.04.004
1087-0792/

Abbreviations

BDI	Beck depression inventory
BSP	blepharospasm
CD	cervical dystonia
EEG	electroencephalogram
EMG	electromyogram
ESS	Epworth sleepiness scale
L-dopa	levodopa
NMSQuest	nonmotor symptom questionnaire
PSG	polysomnography
PSQI	Pittsburgh sleep quality index
REM	sleep, rapid eye movement sleep
RLS	restless legs syndrome
SE	sleep efficiency
SSS	Stanford sleepiness scale
TST	total sleep time
TWSTRS	Toronto Western spasmodic torticollis rating scale

Glossary of terms

blepharospasm: form of focal cranial dystonia, involuntary muscle contractions of the eyelid

cervical dystonia: also called spasmodic torticollis, form of focal cranial dystonia involving the neck, causing an often painful involuntary turning of the head

cranial dystonia: different forms of focal dystonia localised in the head area

dopa-responsive dystonia: also known as hereditary progressive dystonia with marked diurnal fluctuation or Segawa syndrome, very rare form of generalised dystonia beginning in childhood or adolescence

dystonia: neurological movement disorder characterised by involuntary muscle contractions causing twisting and repetitive movements or abnormal postures

focal dystonia: dystonia symptoms are limited to one body area such as the neck in cervical dystonia

generalised dystonia: dystonia symptoms mostly begin in one limb and gradually spread to other limbs and the trunk

Meige's syndrome: includes symptoms of dystonia in several different facial muscles such as the eyes, jaw, tongue and mouth

torsion dystonia: very rare and severe form of dystonia typically beginning in childhood or adolescence

injection into the affected muscles is considered the first line treatment for cervical dystonia [6]. This treatment is well tolerated and of longstanding efficacy for the improvement of abnormal movement [6,7]. A limitation is that immune resistance may occur in some patients as a side effect of repeated injections [8]. Pallidal deep brain stimulation is a newer treatment option for patients with medically refractive dystonia [9,10]. Benefits of deep brain stimulation include substantial improvements of dystonia symptoms, disability and quality of life in previously treatment resistant patients [11]. A recent study found that treatment effects were maintained three and five year after surgery [12]. On the other hand, deep brain stimulation bears a risk of serious side effects. In a clinical trial of 40 patients with primary generalised or segmental dystonia [12], 49 new adverse events occurred between six month and five year after the brain stimulation treatment, 21 of which were rated serious and were almost exclusively device related. One participant attempted suicide shortly after the six-month visit during a depressive episode. As for non-serious adverse events, the most commonly reported side effect were dysarthria and transient worsening of dystonia.

Current treatment of dystonia tends to focus on the improvement of motor symptoms. The importance of non-motor symptoms including abnormal sensory phenomena, psychiatric symptoms, cognitive deficits, pain, and sleep disturbances is increasingly recognised; although their aetiology and treatment options are insufficiently characterised [13,14]. Non-motor symptoms have a large impact on the quality of life [15,16] and seem not to remit after botulinum toxin treatment and deep brain stimulation [14]. This underlines that targeted clinical assessment is necessary and treatments of non-motor syndromes need to be developed. Importantly, patients with dystonia consider sleep to be a prime determinant of their quality of life. There is a stronger link of quality of life with sleep than motor symptom severity in patients living with dystonia [5]. These findings fit within the broader context that sleep disorders are increasingly recognised as a frequent comorbidity of neurological disorders [17], with potential implications for early diagnosis, pathomechanistic insights, and treatment.

The aim of this review is to summarise the state of research, critically evaluate the methodological quality of existing studies, and highlight areas requiring future investigation. More specifically, we sought to identify research reporting on polysomnographically determined sleep, self-reported sleep and variables associated with sleep such as side effects of medication and depressive symptoms in patients living with primary dystonia.

Methods

Search strategy

A literature search was performed in July 2014 using PubMed, Medline via Ovid, PsycInfo, PsycArticles via Proquest and Embase via Ovid. No restriction of publication date was applied. To capture all relevant studies on aspects of sleep in different forms of dystonia, the following comprehensive set of terms was used for a search in all fields:

'insom*' OR 'sleep*' OR 'wake*' OR 'nap*' OR 'polysomnogr*' OR 'actigr*' OR 'fatigue*' OR 'nightmare*' OR 'hypersom*' OR 'apnea*' OR 'circadian*' OR '(restless leg*)' OR 'shiftwork*' OR 'bruxism*' OR 'drowsiness*' OR 'parasom*', linked to 'dystonia*' OR 'torticollis*' OR '(spasmodic dysphonia*)' OR '(musician* cramp)' OR '(writer* cramp)' OR 'blepharospasm*' OR '(Meige* syndrome)'.