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Original Article

Paediatrics Section

Sleep Disorders in Patients with Juvenile Idiopathic Arthritis as Characterised by Sleep Disturbance Scale for Children

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ABSTRACT

Introduction: Sleep disorders negatively impact a child's quality of life, behaviour and cognitive function. Sleep disturbances have not been widely studied in patients with Juvenile Idiopathic Arthritis (JIA) especially using the Sleep Disturbance Scale for Children (SDSC).

Aim: To characterise sleep disorders in JIA patients by using SDSC and determine its correlation with pain and disease activity.

Materials and Methods: In this cohort study, 30 patients each of active JIA and age and sex matched controls (age 6-15 years) were administered SDSC at enrollment and after six months of treatment (in JIA patients). The study duration was from November 2017 to March 2019. Pain severity and disease activity were assessed at baseline and after six month by Visual Analogue Scale (VAS) for pain and Juvenile Arthritis Disease Activity Score-27 (JADAS-27). Data at baseline between patients and controls were compared by unpaired t-test and between six months and baseline by paired t-test. Categorical variables were analysed by Chi-square test or Fisher's-exact test and correlation by Spearman correlation.

Results: Total SDSC score was higher in JIA patients at baseline (45.67±9.13 vs. 28.5±1.17) and decreased significantly after six months (29.73±3.17). Disorders of Initiating and Maintaining Sleep (DIMS), excessive somnolence, hyperhidrosis, arousal and sleep-wake transition were observed in 29, 18, 4, 1 and 2 patients, respectively. After six months excessive somnolence and hyperhidrosis were found in one patient each. Significant positive correlation was observed between total SDSC score, VAS for pain and JADAS-27 score.

Conclusion: SDSC scores revealed significant sleep disturbances in patients with JIA and a positive correlation with pain severity and disease activity.

Keywords: Childhood chronic arthritis, Juvenile arthritis disease activity score-27, Sleep problems, Visual analogue scale for pain

INTRODUCTION

The JIA is a common chronic, rheumatic disease in children, characterised by inflammation and pain in joints. Adequate amount of good quality sleep is essential for neuro-behavioural and cognitive development in children [1]. Sleep disorders have been reported to negatively impact child's health and result in behavioural problems like hyperactivity, attention deficit, irritability, distractibility, decreased day time alertness and performance, difficulty with social and emotional function and school absentism [1]. Disorders in sleep include difficulty in initiating or maintaining sleep, sleep latency or delay in falling asleep, fragmented sleep, disordered breathing, hyperhidrosis, disorganisation of sleep-wake pattern, sleep walking, sleep terror etc., [1,2].

Various methods to assess sleep disorders in children include actigraphy [1,2], polysomnography [1,3,4], sleep diary and questionnaires like Children's Sleep Habits Questionnaire (CSHQ) [5-8], SDSC [9,10]. Polysomnography requires the child to stay overnight in the laboratory which does not mimic the sleep in natural environment of child. Actigraphy though ideal, requires the instrument to be attached to the child's wrist for few days continuously which may not always be acceptable to younger children. Questionnaire based tools, being cheap and readily available, are commonly used in clinical practice to characterise sleep disorders in children.

The CSHQ is a 45 item questionnaire and thus is more time consuming whereas SDSC is a 26 item questionnaire and yields similar information about sleep disturbances [11,12]. Thus, SDSC is a more convenient tool to screen and characterise sleep disturbances in children. Moreover, SDSC have been reported to have a reliability of 0.71 and diagnostic accuracy of 0.91 [12].

Sleep disturbances like frequent limb movement, sleep fragmentation, sleep anxiety, sleep disordered breathing, parasomnia, daytime sleepiness, difficulty in falling asleep have been reported in JIA patients [3-8]. Moreover, sleep disturbance in JIA patients have been associated with pain and fatigue [13]. Most of the studies in JIA patients have used CSHQ as a tool to detect sleep disturbances. SDSC scale has been used very infrequently [3-8]. Moreover, no follow-up study has been reported in literature in which the association of disease activity scores in JIA with SDSC score has been studied. It was hypothesised that SDSC scale could characterise sleep disorders in patients with JIA and its score would decrease with reduction in disease activity scores.

Hence, this study was conducted with a primary objective to characterise sleep disorders in Indian children with JIA using SDSC and secondary objective to determine any correlation between SDSC score and pain and disease activity.

MATERIALS AND METHODS

This cohort study was conducted in a Tertiary Care Hospital in New Delhi, India from November 2017 to March 2019 after obtaining permission from the Institute's Ethics committee (IEC/PGIMER/RMLH/1696/17).

Study Population

The sample size was calculated on the basis of a previous study [5] in JIA patients which reported the mean sleep disturbance score of 47.8±6.2 as compared to 43.6±2.4 in controls. With an α error of 0.05, power of 90% and effect size of 1.75, sample size calculated was 26 per group. Hence, 30 consecutive patients of JIA, in age range 6-15 years attending Paediatric Rheumatology Clinic and equal number of age and sex matched healthy controls were enrolled in the study.

Inclusion criteria: For JIA group, presence of inflammation of one or more joints with swelling, tenderness or restricted range of motion [4]. Inclusion criteria for control group included children of hospital employees who were brought for innocuous things like medical check up for school purpose etc.

Exclusion criteria: Patients with psychiatric disorders, attention deficit hyperactivity disorder, medical problems like adenoids, obesity, upper respiratory infections, asthma, difficulty in breathing due to respiratory and cardiac disease and patients taking drugs which could affect sleep and patients with family history of sleep disorders were excluded from study.

Data Collection

Information collected included name, age, sex, subset of JIA, age of onset of disease, duration of disease, number of joints involved, number of active joints, physician's assessment of disease activity score, patient or parent global assessment of general well-being score, and treatment received.

These data were collected both at baseline and at six months. Examination was done to record the body mass index, active joints, and evaluate respiratory and cardiovascular involvement.

Evaluation of Sleep

Sleep was assessed by the SDSC [12]. It is a 26 item questionnaire that assesses the sleep behaviour and disturbance. Twenty six items on SDSC are grouped into six categories of sleep disorders:

(1) DIMS (7 items)

(2) Sleep Breathing Disorders (SBD) (3 items)

(3) Disorders of Arousal (DA) (3 items)

(4) Sleep Wake Transition Disorders (SWTD) (6 items)

(5) Disorders Of Excessive Somnolence (DOES) (5 items)

(6) Sleep Hyperhidrosis (SHY) (2 items)

The total score of SDSC scale ranges from 26-130 [12]. Each item of the scale has values 1 to 5, indicating the frequency of certain behaviour exhibited by children. 1 means "never," 2 means "occasional" while 5 means "always (daily)". Minimum and maximum score of each category of sleep disorders are- DIMS (7-35), SBD (3-15), DA (3-15), SWTD (6-30), DOES (5-25) and SHY (2-10).

The cut-off value of SDSC score, beyond which the presence of sleep disturbance in a child is considered, was 39 [12]. For categorisation of specific sleep disorder, as per SDSC, for the present study, minimum score of two multiplied by number of factor in that category of sleep disorder was taken as cut-off for that specific disorder viz., DIMS-14, SBD-6, DA-6, SWTD-12, DOES-10 and SHY-4. For each case and control, the total sleep disturbance score and individual category score was calculated.

Procedure

The caregivers (parents or guardians) of patients and controls were asked to fill SDSC questionnaire for children, after being thoroughly explained each item of the questionnaire [12]. The questionnaire was filled in presence of the first author at baseline and after six months of treatment for patients whereas the caregiver of controls filled the questionnaire only at baseline. Informed consent was obtained from caregivers and assent was taken, wherever necessary.

Evaluation of Disease Activity and Disease Related Pain

Disease activity in JIA patients was assessed by Juvenile arthritis disease activity score-27 (JADAS-27), a composite score of disease activity (range 0-57) [14] which included following four measures:

A. Physician assessment of disease activity: It was measured on a 10 cm VAS where 0 indicated no disease activity and 10 indicated maximum disease activity.

B. Patient or parent global assessment of general well-being: It was measured on 10 cm VAS where 0 indicated very good and 10 indicated very poor.

C. Count of joints with active disease.

D. Erythrocyte Sedimentation Rate (ESR)-3 mL of blood was drawn from a peripheral vein for estimation of ESR by Westergren method by an automated machine- Alifax Spa Padova-Italy. The ESR value was normalised to a 0-10 scale according to the following formula: {ESR (mm/hour)-20}/10

ESR values <20 mm/hour was converted to 0 and ESR values >120 mm/hour were converted to 120.

Severity of pain in joints was assessed by VAS (range 0-10), where 0 indicated no pain and 10 worst pain ever experienced.

Follow-up Evaluation of JADAS-27 and SDSC Score

The patients were followed-up in person every 4-8 weekly and assessed for compliance by seeking history from patient and parent and counting of strips and checking records for receipt of injections. JADAS-27 and SDSC scores were recorded at baseline and after six months.

STATISTICAL ANALYSIS

Continuous variables were presented as mean±SD and categorical variables were presented as absolute numbers and percentage. Data was checked for normality before statistical analysis. Normally, distributed continuous variables were compared using the t-test, whereas the Mann-Whitney U test was used for those variables that were not normally distributed. The SDSC score between patients and controls was compared using independent t-test and SDSC scores between baseline and at six months in patients were compared using paired t-test. Categorical variables were analysed using either the Chi square test or Fisher's-exact test. Spearman correlation was calculated between SDSC score of JIA patients and pain score and JADAS-27 at baseline and after six months of follow-up. For all statistical tests, p-value less than 0.05 were taken to indicate a significant difference. Statistical analysis was performed by the SPSS program for Windows, version 17.0 (SPSS), Chicago, Illinois.

RESULTS

The mean age of JIA patients was 11.42+3.22 years and controls 11.40±3.21 years (range for both patients and controls was 6-15 years). Two third (66.7%) of both patients and controls were males and one third females. None of the patients and controls was obese.

Of the 30 JIA patients, 11 (36.7%) were Systemic Onset JIA (SOJIA), 4 (13.3%) Enthesitis related JIA (ERA), 6 (20%) undifferentiated JIA, 5 (16.7%) polyarticular rheumatoid factor negative JIA and 4 (13.3%) extended oligoarticular JIA. Of these, eight patients were new, 10 were defaulters and 12 were relapsers. The defaulters were included as new patients. Patients who relapsed, required change of treatment.

Most of the JIA patients were on combination drug therapy. Intra-articular steroid was administered only once in four patients [Table/Fig-1]. The mean age of disease onset was 8.29±3.57 years (range-1.5-14 years). Mean duration of disease was 3.09±2.02 years (range-0.25-8 years).

Sleep Disturbance Score at Baseline and After 6 months Follow-up

At baseline, the mean total SDSC questionnaire score of patients was significantly more (45.67±9.13) than controls (28.5±1.17) (p<0.001) [Table/Fig-2]. All the enrolled patients had mean SDSC score of more than 39 suggesting presence of sleep disturbance in

Treatment profile	Cases N (%)
Naproxen + Intra-articular steroid	4 (13.3)
Methotrexate + Naproxen	5 (16.7)
Methotrexate + Prednisolone	4 (13.3)
Methotrexate + Sulfasalazine	1 (3.3)
Methotrexate + Leflunamide	1 (3.3)
Methotrexate + Prednisolone + Naproxen	3 (10.0)
Methotrexate + Prednisolone + Sulfasalazine	3 (10.0)
Methotrexate + Naproxen + Sulfasalazine	4 (13.30)
Methotrexate + Etanercept	1 (3.3)
Methotrexate + Prednisolone + Thalidomide	1 (3.3)
Methotrexate + Prednisolone + Etanercept	1 (3.3)
Methotrexate + Prednisolone + Tocilizumab	1 (3.3)
Methotrexate + Prednisolone + Leflunamide + Sulfasalazine	1 (3.3)
Total (N)	30

[Table/Fig-1]: Treatment profile of study population.

each patient whereas none of the controls had a score of above 39. Of the specific sleep disorder, DIMS, DOES, SWTD, SHY and DA was seen in 96.6%, 60%, 6.6%, 13.3% and 3.3% of JIA patients, respectively [Table/Fig-2].

Sleep disturbance scale for children score	Cases	Control	p-value
	Mean±SD (range)	Mean±SD (range)	
Disorder of initiating and maintaining sleep	18.27±3.11 (14-32)	8.87±1.04 (7-11)	<0.001*
Sleep breathing disorders	3.33±0.48 (3-4)	3.17±0.38 (3-4)	0.141
Disorder of arousal	3.27±1.46 (3-11)	3.17±0.38 (3-4)	0.718
Sleep-wake transition disorders	7.87±3.14 (6-20)	6.2±0.55 (6-8)	0.007*
Disorders of excessive somnolence	10.4±2.43 (7-17)	5.1±0.31 (5-6)	<0.001*
Sleep hyperhidrosis	2.53±1.28 (2-8)	2.1±0.55 (2-5)	0.096
Total score	45.67±9.13 (39-86)	28.5±1.17 (27-31)	<0.001*

[Table/Fig-2]: The Sleep Disturbance Scale for Children (SDSC) score in patients and controls at baseline.
*p-value-significant- <0.005; Student 't' test

After six months of follow-up, there was significant decrease in total SDSC score and specific sleep disorder score, p<0.001 [Table/Fig-3]. After six months, number of patients having DIMS, DOES, SWTD and SHY decreased significantly [Table/Fig-4]. SBD were neither observed at baseline nor after six month follow-up.

The data revealed that SDSC score for Dyssomnias (DIMS and DOES), Parasomnias (SWTD) and SHY decreased significantly after six months of follow-up [Table/Fig-3].

The Sleep onset time (time taken to fall asleep) was significantly more in JIA patients (2.18±0.80 hours) as compared to controls (0.13±0.05 hours), p<0.001. After six months, a significant decrease in sleep onset time was observed in JIA patients (0.38±0.19 hours, p<0.001).

Disease Activity and Pain

As compared to baseline, the mean number of joints involved, mean JADAS-27 score and mean Visual analogue score for pain decreased significantly after six months of follow-up [Table/Fig-3].

Relationship between Sleep Disturbance and Pain and Disease Activity

Statistically significant positive correlation was observed between total SDSC score and VAS for pain (r=0.403, p=0.027) and

Sleep disturbance scale for children score	Baseline	After six months	p-value
	Mean±SD (range)	Mean±SD (range)	
Disorder of initiating and maintaining sleep	18.27±3.11 (14-32)	9.60±1.59 (7-13)	<0.001*
Sleep breathing disorders	3.33±0.48 (3-4)	3.03±0.18 (3-4)	0.001*
Disorder of arousal	3.27±1.46 (3-11)	3.07±0.37 (3-5)	0.326
Sleep-wake transition disorders	7.87±3.14 (6-20)	6.20±0.48 (6-8)	0.003
Disorders of excessive somnolence	10.4±2.43 (7-17)	5.7±1.34 (5-11)	<0.001*
Sleep hyperhidrosis	2.53±1.28 (2-8)	2.20±0.48 (2-4)	0.039
Total SDSC score	45.67±9.13 (39-86)	29.73±3.17 (26-39)	<0.001*
Active joints	3.27±1.55 (1-6)	0.53±0.57 (0-1)	<0.001
JADAS-27	18.38±6.44 (1.3-25.7)	6.91±3.33 (4-14.5)	<0.001
ESR	43.17±14.02 (26-85)	15.40±6.93 (6-32)	<0.001
VAS score for pain	7.57±1.17 (5-9)	3.40±1.55 (2-7)	<0.001

[Table/Fig-3]: The Sleep Disturbance Scale for Children (SDSC) score and disease activity parameters in cases at baseline and after six months follow-up.
*p-value-significant- <0.005, JADAS: Juvenile arthritis disease activity score, VAS: Visual analogue scale; paired 't' test

Sleep disorders	Number of patients (%)	
	At enrollment	After six months
DIMS	29 (96.6)	0
DOES	18 (60.0)	1 (3.3)
SHY	4 (13.3)	1 (3.3)
SWTD	2 (6.6)	0
DA	1 (3.3)	0

[Table/Fig-4]: Sleep Disorders in JIA patients at enrolment and after six months of treatment.
DIMS: Disorder of initiating and maintaining sleep, DA: Disorder of arousal, SWTD: Sleep wake transmission disorder, DOES: Disorder of excessive somnolence, SHY: Sleep hyperhidrosis

JADAS-27 (r=0.412, p=0.024) at baseline. After six months of treatment, a positive correlation between total SDSC score and VAS for pain (r=0.510, p=0.004) and JADAS-27 (r=0.531, p=0.003) was also observed, suggesting that decrease in pain or disease activity contributed to decrease in total SDSC score and thus sleep disturbance in JIA patients.

Though the JIA patients were indulging in longer duration of screen exposure before sleep as compared to controls, the difference was not statistically significant (0.82±0.55 hours vs. 0.63±0.44 hours). But a significant difference in duration of screen exposure was noted in JIA patients after six months (0.28±0.28 hours), p<0.001.

DISCUSSION

Sleep disturbances lead to sleep deprivation, more so in chronic disease like JIA. Long term sleep deprivation affects the child's mood, cognitive function, reflexes, ability to do mathematical calculations, school performance and response to situations and ability to adapt to the chronic illness [15].

Studies have shown that JIA patients also suffer from sleep disturbances like difficulty in initiating sleep, sleep fragmentation, increased arousals/awakening, increased leg movements, anxiety, excessive daytime sleepiness, sleep disordered breathing, parasomnias etc., [3-8].

The present study revealed that patients with JIA had significantly higher sleep disturbance (SDSC) score than controls, higher

score for sleep onset time, disorder of initiating and maintaining sleep, excessive daytime somnolence and sleep wake transition disorder. On further analysis it was observed that DIMS and DOES were the common sleep disturbances in the enrolled patients. The finding of the present study were similar to earlier studies on sleep disturbances in JIA [4-10,13]. The study also revealed that with treatment, SDSC score decreased significantly after six month and marked decrease in the number of patients who had DIMS, DA and SWTD.

Unlike previous studies where SBD was a predominant disorder observed [5-7,13], it was not seen in the present study. SBD is an intrinsic dysommnia and arise from an abnormality of the patient that alters sleep process. Abnormalities may include psychological and organic causes like obesity, obstructive sleep apnoea, narcolepsy, enlarged adenoids etc., which were not present in our patients. The absence of SBD in the present study patients co1uld be due to patient selection or by chance [16,17].

Till date only two studies used SDSC to characterise sleep disorders in JIA patients. Of these one did not find any difference of SDSC score between JIA patients and controls [4], whereas the other reported sleep disorders in 39% of their patients and predominantly DOES and SHY [9]. The authors did not compare the SDSC score with controls. However, they reported improvement in sleep disorders with improvement in disease activity [9].

The Sleep onset time (time taken to fall asleep) was significantly more in JIA patients (2.18±0.80 hours) as compared to controls (0.13±0.05), $p<0.001$, suggesting disorder of initiating sleep and that was probably related to pain in joints. This was further supported by the observation that after six months, a significant decrease in sleep onset time and pain severity was observed.

Pain in joints in JIA is inflammatory pain through mediators [18,19]. It is possible that hypothalamus plays a role here, since sleep-wake cycle of circadian rhythm is regulated by hypothalamus and pain pathways also have a link with it [1,19]. Chronic widespread pain have been shown to be associated with poor sleep quality [18,20,21] and poor sleep may lead to accentuation of pain [22,23], thus adversely impacting the quality of patient's life. Disease activity is also believed to play a significant role in occurrence of sleep disturbances in JIA patients [6,10,13,19]. These was substantiated by the present study through observation of significant decrease of the SDSC score and individual sleep disorders score as the pain score and disease activity score decreased and a strong positive association between pain, disease activity and SDSC score.

The duration of screen exposure before sleep was longer in patients than controls at baseline which decreased significantly after 6 months of follow-up. It is possible that longer duration of screen time could also have been one of the reasons for sleep onset delay. Similar observation has also been reported in a previous study [24]. It is also possible that at enrolment, the JIA patients were indulging in viewing gadgets for a longer time to distract themselves from pain and the screen time decreased as the pain, disease activity and sleep disturbances decreased.

Limitation(s)

The present study was based on the use of a questionnaire (SDSC) for characterisation of sleep disturbance in JIA patients; hence recall bias inherent to any questionnaire is the limitation of this study. In addition, factors like intake of drugs like NSAIDs, steroids, psychological factors, environmental factors at home or school which could possibly have affected sleep were not accounted for.

CONCLUSION(S)

The SDSC can characterise sleep disorders in patients of JIA, both dyssomnias and parasomnias. Increased disease activity and pain in joints led to poorer sleep, thus more sleep disturbance in the form of DIMS (increase sleep onset time, sleep fragmentation), DOES (excessive daytime sleepiness), SWTD, DA and SHY and decrease in pain and disease activity led to improvement in SDSC score. Since sleep disturbances have both short term and long lasting impact on patient quality of life, function, mood, behaviour and school performance, it is suggested that screening of sleep disturbance of all JIA patients may be done at regular intervals. A variation in SDSC score may also guide a change in the treatment of JIA patients.

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