Juvenile Idiopathic Arthritis and sleep disorders – a co-morbid nightmare

Dr Teresa Ward, from the University of Washington, is researching the reasons why Juvenile Idiopathic Arthritis (JIA) children are more vulnerable to suffering from poor sleep health and sleep disordered breathing, a co-morbidity that can negatively affect child and family health outcomes.

Juvenile arthritis is an extremely painful and debilitating disease and can even affect children as young as two years of age. Juvenile Idiopathic Arthritis (JIA) is the most common rheumatic disorder affecting an estimated 12,000 children under the age of 16 in the UK alone. However, the underlying cause and processes are poorly understood.

Symptoms can range from mild to severe and can include joint inflammation, pain, morning stiffness and mobility restrictions. As a result, some children are limited in the physical activities they can participate in, leading to anxiety, frustration, and emotional distress. JIA peaks between one to four years or six to 12 years, depending on the type of JIA, and 20% of children experience long-term pain, impacting their lives well into adulthood.

There are seven subtypes of JIA (oligoarticular JIA [four or less joints]; rheumatoid factor positive or negative polyarticular JIA [five or more joints]; systematic JIA; enthesitis-related arthritis; psoriatic arthritis; and undifferentiated JIA), defined on the basis of the clinical and laboratory features present in the first six months of illness.

Dr Ward, an expert on sleep health, has investigated the intriguing relationship between JIA and the prevalence of sleep disordered breathing, such as Obstructive Sleep Apnoea (OSA). Research conducted by Dr Ward and her team indicated that OSA is more common in six to 11 year olds afflicted with JIA compared to typically developing control children. However, many questions remain unanswered: What is the prevalence of OSA in JIA? Why is OSA more prevalent in JIA patients? When does OSA emerge in these children? Does OSA treatment improve the quality of life of JIA sufferers?

IMPACT OF SLEEP DISORDERED BREATHING

Sleep, like diet and exercise, is essential for maintaining good health. During sleep, the body performs many fundamental functions including hormone rebalancing, cell repair and memory consolidation. It is particularly important for children and adolescents to get adequate sleep, as it is crucial for their physical and intellectual growth and socio-emotional development.

Obstructive sleep apnoea in children is a serious public health concern. Its timely diagnosis and treatment is important, as OSA is associated with adverse health outcomes (cardiovascular morbidity, obesity) and increased use of healthcare resources. OSA is a common sleep disorder, affecting 1–4% of typically developing children, but the prevalence of OSA in JIA is unknown. Obstruction of the upper airway leads to irregular breathing, hypoxia (reduced blood oxygen levels), snoring and fragmented sleep. The peak time of OSA is between the ages of two and six. During this period the tonsils and adenoids are comparatively large in relation to the airway, and can cause partial blockage.

Poor sleep health secondary to an underlying sleep disorder such as OSA and/or poor sleep habits has negative health consequences, including an inability to concentrate, restlessness, excessive daytime sleepiness, mood disturbances, and behavioural issues (e.g., hyperactivity). In fact, children displaying these symptoms can be misdiagnosed with attention deficit hyperactivity disorder.

JIA AND SLEEP DISORDER CO-MORBIDITY

Research conducted by Dr Ward and her team has shown that 40% to 50% of school-age children with JIA suffer from OSA, in comparison to healthy controls. Polysomnography, otherwise known as 'sleep study', is the gold standard to diagnose OSA, and this was used in her studies of JIA (involving 221 participants). During sleep, the patient's brain waves, blood oxygen level, carbon dioxide, heart and breathing rate, arousals from sleep, and the number of times a patient stops breathing are recorded and analysed. Importantly, none of these JIA patients had been referred to a sleep clinic for OSA evaluation. This is likely due to sleep not being routinely screened and assessed for in

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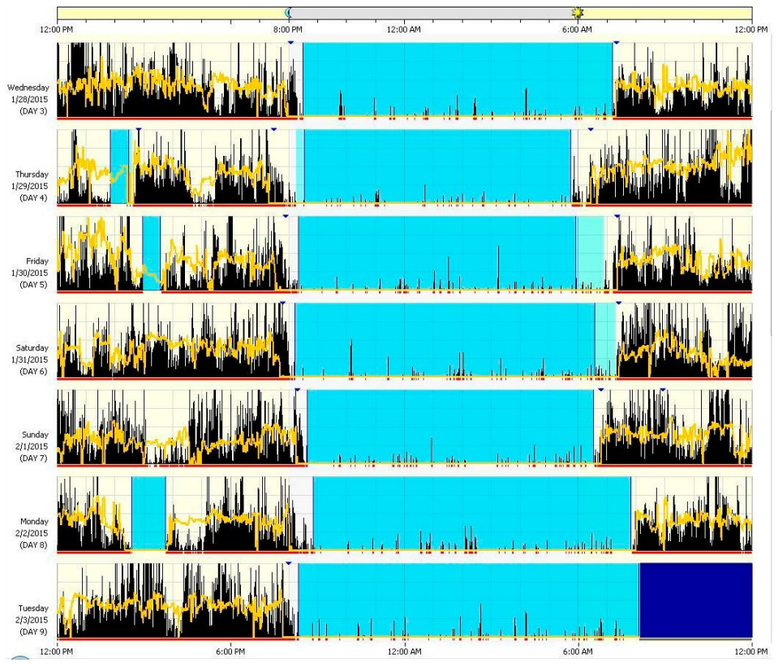
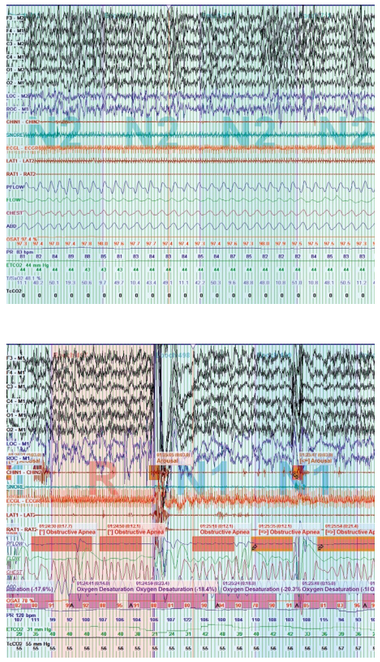


Actigraphy showing sleep fragmentation



Contrast in polysomnography readings between normal breathing (top) and OSA (bottom)

paediatric primary and specialty care clinics. Additionally, children and their parents may not be aware of their child's sleep symptoms, thus needing a prompt from healthcare providers during clinic visits.

Dr Ward recently conducted studies to examine how OSA impacts the quality of life and fatigue in JIA. She compared JIA children with OSA to JIA children and typically developing control children without OSA, and found that JIA children with OSA had increased fatigue and impaired quality of life compared to JIA and typically developing controls without OSA. Quality of life and fatigue are important health outcomes for clinicians who manage JIA patients. Dr Ward's findings highlight that OSA extends beyond sleep to affect children's physical, emotional, and overall wellbeing. Further, JIA children with OSA also showed a slower mean reaction time and reduced attention span in comparison to JIA and typically developing controls without OSA.

WHY ARE JIA PATIENTS MORE VULNERABLE TO OSA?

Although there is no definitive answer, Dr Ward's research may help explain why JIA patients are more prone to OSA. JIA children have a high prevalence of arthritis in the temporomandibular joint (TMJ), which is a risk factor for OSA. The TMJ (or 'jaw joint') is connected to the temporal bone and mandible (or lower jaw), and TMJ arthritis may impair mandibular growth, restricting breathing and resulting in OSA development. However, more research is required to confirm this.

POTENTIAL TREATMENTS AND BIOMARKERS

JIA and OSA can be treated independently – JIA patients respond to a combination of anti-inflammatory and disease-modifying drugs, whereas OSA patients who are children are treated with surgery (removal of tonsils and/or adenoids) or use of ventilation therapy. However, more research is needed to determine whether or not these therapies resolve OSA in JIA.

Dr Ward and her team have conducted a small pilot study on the use of urinary protein biomarkers to examine if urine proteins were expressed differently in JIA children with OSA from JIA children without OSA and typically developing controls without OSA. The preliminary findings suggest that JIA children with OSA excrete different proteins than JIA and control children without OSA. Additional research is needed with a larger sample to confirm and validate why certain proteins may be more abundant in JIA with OSA relative to JIA and typically developing controls without OSA. The use of biomarkers as a potential diagnostic tool for OSA is novel, and may be more cost effective and less labour intensive than the current method of polysomnography.

Finally, Dr Ward is also exploring the possibility of developing a web-based self-management sleep promotion intervention for children suffering from poor sleep health (e.g., unhealthy sleep habits such as lack of a bedtime routine or media use before bed]) that is not related to an underlying sleep disorder, like OSA. Although paediatric sleep clinics can improve sleep health, waiting lists are long and currently there is a lack of paediatric providers trained in sleep medicine. Therefore, a low-cost, accessible and convenient web-based platform that encourages children and their parents to change certain behaviours and develop self-management skills to improve their sleep health, will be of great benefit, and may also improve disease management and health outcomes in children living with JIA.

Q&A

How was the relationship between JIA and sleep disordered breathing discovered?

In 2006, during my two-year post-doctoral fellowship I had an opportunity to examine data on sleep quality in JIA. Our findings showed that JIA children had fragmented sleep secondary to obstructive sleep apnoea, which we did not expect. We hypothesised that sleep fragmentation would be secondary to pain.

Why is poor sleep and sleep disordered breathing common in JIA patients?

Poor sleep is common in JIA likely due to multiple factors including underlying disease mechanisms, pain, poor sleep habits, and sleep disorders (OSA, periodic limb movements). Although poor sleep is common, we do not know the prevalence of OSA in JIA because few studies have used polysomnography, the gold standard technique to diagnose OSA, in JIA. Of the few studies that used polysomnography, OSA and periodic limb movements have been found. Additional research using the gold standard polysomnography is needed to better understand the prevalence of OSA in JIA.

What is the long-term impact for JIA patients, whose sleep disorder is undiagnosed?

Unrecognised and untreated sleep disorders, like obstructive sleep apnoea, may contribute to pain, fatigue, and health-related quality of life in JIA. The presence of OSA – a treatable condition – with JIA places children at increased risk for poor disease management, increased health care costs, and poor clinical health outcomes, including health-related quality of life, fatigue, pain, and physical and psychosocial function.

Why might the protein biomarkers be more abundant in JIA with OSA patients compared to JIA and typically developing control children without OSA?

Right now we are unsure, but recent findings suggest that systemic inflammation, as reflected in urinary proteins, can be induced by episodes of low oxygen levels, increased carbon dioxide, and arousals from sleep that characterise OSA. The kidney is sensitive to the effects of intermittent low oxygen levels that result in activation of the sympathetic nervous system and the renin-angiotensin system. Such inflammation represents a mechanistic finding that could lead to additional studies linking how the physiologic perturbations seen in OSA result in alterations in protein expression that distinguish JIA children with OSA from JIA without OSA and healthy control children without OSA.

How can these biomarkers be used clinically?

Development of reliable non-invasive clinical biomarkers capable of distinguishing JIA children with OSA, from those with only JIA, to healthy control children without OSA would provide new knowledge about the underlying mechanisms of OSA in children with and without JIA and enable early screening and diagnosis of OSA in JIA children.

Additional research using the gold standard polysomnography is needed to better understand the prevalence of OSA in JIA

MORE INFO:

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- www.sleepreviewmag.com/2016/09/school-nursing-center-focuses-enhancing-sleep/
- www.seattletimes.com/author/teresa-m-ward-maida-lynn-chen/
- https://nursing.uw.edu/research/programs/sleep-research/

Detail

RESEARCH OBJECTIVES

Dr Ward's research focuses on improving sleep health and health outcomes for children with and without chronic conditions such as arthritis, asthma or chronic pain. Throughout her research, she has been particularly interested in the effect of poor sleep health on caregiver–child dyad interactions, symptoms, health outcomes, and the underlying mechanisms that might predispose some children to develop sleep disordered breathing. Focusing on these, she hopes to determine unique and essential information for clinical practice to detect sleep disorders more quickly and effectively, and improve the sleep health and quality of life of those affected.

FUNDING

NIH: National Institute of Nursing Research (P30 NR016585; R01NR01734; P30 NR011400); University of Washington, School of Nursing Research & Intramural Funding Program

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BIO

Dr Teresa Ward is an Associate Professor at the University of Washington who has dedicated her time to improving the lives of children with chronic conditions affected by sleep disorders and poor sleep health. She works within the Family and Child Nursing department teaching both undergraduate and graduate students in the use of physiologic and behavioural sleep measures.

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