A CASE OF MELATONIN INDUCED DEPRESSION IN AN ADOLESCENT WITH ASPERGER'S SYNDROME

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ABSTRACT

Melatonin is a commonly used drug in children with sleep difficulties and especially in neurodevelopmental disorders[1]. We are presenting a case of a16 years old young man with the diagnosis of Asperger's syndrome, who was treated with melatonin for his sleep difficulties but went on to develop depression.

INTRODUCTION

Melatonin is a hormone (N-acetyl-5 methoxytryptamine) produced especially at night in the pineal gland. Its secretion is stimulated by the dark and inhibited by light. Tryptophan is converted to serotonin and finally converted to melatonin which is an Indole. The suprachiasmatic nuclei (SCN) of the hypothalamus have melatonin receptors and melatonin may have a direct action on SCN to influence "circadian" rhythms[2]. When taken by healthy subjects at low doses melatonin appears to cause very few side effects in the short term (up to three months). A systematic review in 2006 looked specifically at efficacy and safety. Individuals with autism spectrum disorders (ASD) may have lower than normal levels of melatonin but the underlying cause of this deficit is unknown[3]. That may be the rationale for using melatonin for sleep difficulties in young people with ASD. Melatonin is generally considered to be a safe medication and frequently used in young people with sleep difficulties, however it can give rise some relatively serious but rare side effects. There is also some concern that melatonin might worsen symptoms in some people[4].

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CASE HISTORY

Our patient is a 16 years old young man, who is known to local Child and Adolescent Mental Health Services (CAMHS) for the last 4 years. He was referred to CAMHS due to behaviour difficulties and aggressive outbursts at the age of 12 and he was subsequently diagnosed with Asperger's syndrome the following year. There was no evidence of any co-morbid conditions, such as Attention Deficit Hyperactivity Disorder (ADHD), Tic Disorder and Depression or any anxiety disorder, which are often associated with Asperger's syndrome. Following the diagnosis, he received significant support in terms of individual therapy, anger management, behaviour management and parental support. Parents were also provided with the information about National Autistic Society (NAS) U.K and other parent support groups, and they used the services in order to enhance their understanding of his condition.

His birth history was unremarkable. He was bottle fed. His early development was fine except age appropriate social interactions. He was noted to have poor eye contact and was excluded from peer-play games. Establishing friendships was a major issue for him. He managed primary school but could not cope with the stresses and pressures of the secondary school and was referred to CAMHS by his General Practitioner (GP). There was no significant medical history. His immunisations were upto date and he was not known to have any drug or other allergies. He was the only child of the healthy parents with no family history of any significant mental health issues including depression/anxiety disorders.

His sleep difficulties started in his childhood and he reported to have early insomnia and intermittent night wakening for past seven years. He had a brief trial with Alimemazine tartrate, commonly known as, Vallergan, a sedating antihistamine, which was prescribed at the age of 8 by his GP. Medication was discontinued after 2-3 weeks because of lack of desired effect. When aged 16 he was commenced on melatonin for severe sleep difficulties. He was on melatonin 3 mg x nocte for one week, which was later increased to 9 mg by the end of 3rd

week. Few days after that an urgent appointment was arranged to see him due to concerns raised by his mother. Mother reported that he was withdrawn and quiet for the past 3 weeks. Other symptoms were poor appetite, increased agitation, tiredness with low levels of energy, refusing to go out and loss interest in fun activities, such as watching TV, spending time on internet, including face book. Inspite of very low mood, he didn't express any suicidal thoughts. Sleep was only slightly better. A clinical diagnosis of moderate to severe depression was made. Individual sessions with a clinical psychologist were arranged to offer cognitive behaviour therapy. The use of an antidepressant was not considered as first line treatment and family declined pharmacological intervention. There were no particular triggers to his depressive illness and there was no change to his school/home life was noted. Melatonin was discontinued as it did not appear to be significantly beneficial. Three days later after stopping Melatonin his mother contacted the CAMHS and reported a sudden improvement in her son's presentation as he was feeling better, his appetite returned and he was less agitated. He was seen in the clinic the following week, where he was noted to be relaxed with no signs of irritability or agitation. His mood was euthymic and according to his mother he was almost back to 'his usual self'. All depressive symptoms were resolved three weeks after stopping Melatonin. He had a brief period of contact with the clinical psychologist and focus of the work was around the sleep hygiene in order to improve the sleep but this had only minimal effect. He was discharged from CAMHS at the age of 17.

DISCUSSION

Sleep disturbances are a common problem in childhood, with a prevalence of about 25% in typical preschool and school-aged children[5] and are a major source of stress for children with a neurodevelopmental disability and their families.

The association of sleep problems with emotional, behavioral, and cognitive problems has been well established[6]. The prevalence of sleep problems has been reported to be even higher in children with developmental disabilities[7] including autism[8].

Melatonin-induced depression of locomotor activity in hamsters has been described but we could not find any reported case in human's [9]and we believe that our case report may be the first reported case of clinical depression associated with melatonin. Circadin, (prolonged-release melatonin tablet) according to summary of product characteristics [10], recognises altered and depressed mood and depression as its rare adverse reactions. The other side effects are labelled as uncommon, and are irritability, nervousness, restlessness, insomnia abnormal dreams, anxiety, migraine, lethargy, psychomotor hyperactivity, dizziness, somnolence, upper abdominal pain, dyspepsia, mouth ulceration, dry mouth and others. There is no mention of very common and common side effects, despite recognising that in clinical trials (in which a total of 1931 patients were taking Circadin and 1642 patients were taking placebo), 48.8% of patients receiving Circadin reported an adverse reaction compared with 37.8% taking placebo [10].

There is evidence to suggest that melatonin is used to treat various psychiatric symptoms including sleep difficulties in children. It is not licensed for this indication in children. There is a meta-analysis to support that there is no evidence that melatonin is effective in treating secondary sleep disorder or sleep disorder accompanying sleep restriction[3]. This case report highlights that though clinicians use melatonin commonly in children and adolescents, it should be used cautiously. The further research should be carried out about its efficacy and it is hoped that its true diagnostic and therapeutic niche will be defined.

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