Psychiatria Danubina, 2021; Vol. 33, No. 4, pp 580-582 https://doi.org/10.24869/psyd.2021.580 *Case report*

MELATONIN FOR RESTRICTIVE REPETITIVE BEHAVIOURS IN A YOUNG ADULT WITH AUTISM: A CASE REPORT

Onur Tuğçe Poyraz Fındık[1] & Funda Gümüştaş[2]

[1]*Child and Adolescent Psychiatry Department, Marmara University Pendik Research and Training Hospital, Istanbul, Turkey*

[2]*Child and Adolescent Psychiatry Department, Istanbul Medeniyet University Faculty of Medicine, Istanbul, Turkey*

received: 6.5.2021; revised: 1.7.2021; accepted: 7.7.2021

* * * * *

INTRODUCTION

Restricted and repetitive behaviours (RRB), one of the core symptoms of autism spectrum disorders (ASD), can have a detrimental effect on daily life functioning of individuals with ASD and their families (Gabriels et al. 2005). There are relatively few studies in the field of management of RRB in individuals with ASD. Current evidence has indicated that psychotropic agents are either partially beneficial or not on RRB in ASD (Yu et al. 2020).

Melatonin is a neurohormone secreted at dark phase by the pineal gland, and modulates circadian rhythms including the sleep-wake cycle (Gagnon & Godbout 2018). Evidence indicates that melatonin can be secreted from other structure including gastrointestinal (GI) tract, lungs, bone marrow and placenta. Melatonin has also been shown to influence the immune system, GI motility and the reproductive system (Gagnon & Godbout 2018, Wang et al. 2021). Some studies showed the lower melatonin levels in individuals with ASD compared to neurotypical controls, and suggested an association between a deficit in melatonin production and autistic behaviours (Rossignol & Frye 2011, Tordjman et al. 2012). Accordingly, a more recent study pointed out that melatonin might be an effective treatment option for RRB in an animal models of ASD (Wang et al. 2020). Here we report a case of youth with ASD with long-term and treatment resistant RRB, and the effectiveness of melatonin on his behavioural outcomes.

CASE PRESENTATION

Our patient was a 18-year-old male diagnosed in early childhood with ASD. He had a repetitive behaviour with tearing his clothes for the last 1 year. He was firstly punching a hole in his clothes with his finger and beginning to tear the whole clothes on him from that hole in a few seconds. Despite all the efforts of his family to prevent him, he made unwearable 2 or 3 clothes a day on average. This behaviour was always happening at home, not outside or at school. A precipitating factor could not be determined. His family was frustrated and financially exhausted due to his clothing expenses.

Developmental history and behavioural problems

He was second in birth order, born six weeks premature, with a low birth weight and stayed in an incubator. He had a housewife mother of 44 years of age, and a low-paid worker father of 44 years of age. His parents had a nonconsanguineous marriage, and he had a brother with attention deficit hyperactivity disorder (ADHD). His medical history included ventricular septal defect, asthma, and strabismus. He had an operation for strabismus in early childhood. All his developmental milestones were delayed. He had a delay in walking until the age of 5, because of cooccurring some motor coordination deficits. Also, he had a delay in onset of toileting skills until the age of 7, and speech until the age of 4. He had serious problems in social development. He had poor eye contact and failed to develop reciprocal interaction with his peers and others. He had been receiving special education with a diagnosis of ASD since the age of 3. His sensory sensitivities, specific interests and stereotypes changed over time, but they were dominant symptoms in his clinical course until his adolescence. He was prescribed risperidone at the preschool period. He was diagnosed with comorbid ADHD within his primary school period and used immediate release methylphenidate and risperidone (0.5 mg/day) until secondary school with low improvement in his ADHD symptoms.

During his adolescence, his behavioral problems and the need for psychopharmacological intervention for those were minimal. He was able to acquire reading skills but no writing. He had clapping stereotypes and an excessive interest in music. Melatonin (3 mg/day) was started at the age of 15 for his sleep problems. Melatonin was continued for 1 year and his sleep improved. Even if melatonin was discontinued, he did not experience sleep problems again.

He firstly started to collect feathers from clothes by the age of 17, and then continued by tearing his clothes

in a repetitive nature. The repetitive behaviours were not accompanied by a different behavioural problem such as aggression, irritability, or sleep problems etc. During interviews, he was appearing disinterested, making little eye contact, and speaking minimal for answering to questions. Blood tests including full blood count, electrolytes, TFT, liver and renal function tests were normal. Aripiprazole was prescribed, gradually increased, and used at 20 mg/day for 3 months. There was a minimal improvement in the clothes tearing behaviour at the beginning of the treatment, but the response did not continue, and the repetitive behaviour rapidly increased again. Sertraline was added to aripiprazole but discontinued by his family due to aggression, irritability, sleep problems and emotional lability at the second month. Risperidone (1 mg/day) was added for 1 month. Within this period, irritability and emotional lability were improved, but he was excessively tearing clothes, and slightly difficulty falling asleep. Risperidone was discontinued. Melatonin (3 mg/day) was prescribed for his sleep difficulty and aripiprazole was continued. With the supplementation of melatonin, a sudden reduction in his clothes tearing behaviour was striking. He only tore clothes a few times in the next two months, or even not at all in the last 1 month. Now the aripiprazole dose has gradually moved into the taper phase. The patient's caregiver provides informed consent allowing for the use of his clinical data in the case report.

DISCUSSION

This report illustrates a case of ASD where his problem behaviours were not severe, social interaction, academic and daily life skills could be improved, but there was a deterioration for RRB by time. Melatonin decreased RRB, which did not respond to an antipsychotic and selective serotonin reuptake inhibitor (SSRI).

Treatment of RRB still continues to be a challenging issue. A recent meta-analysis showed that antipsychotics, especially risperidone and aripiprazole, had a small statistically significant effect on RRB, while antidepressants, oxytocin, omega-3 fatty acids, methylphenidate, naltrexone, atomoxetine, secretin, NAC, and vitamin D were not found any effect to reduce RRB (Zhou et al. 2021).

It has been demonstrated that sleep problems are associated with decreased social interaction, increased stereotypes and behavioural problems in individuals with ASD (Mannion & Leader 2014). Exogenous melatonin supplementation has been shown to improve sleep problems in ASD, and contributed to decrease problem behaviours in those with ASD suffering from sleep problems (Gagnon & Godbout 2018, Rossignol & Frye 2011). However, to the best of our knowledge, there is no study in literature examining the effect of melatonin on problem behaviours of individuals ASD without sleep problems.

Some studies suggested associations between RRB and anxiety symptoms, sensory sensitivities (Gagnon & Godbout 2018). Recently, exogenous melatonin has been suggested to be effective agent for anxiety, pain, migraine, irritable bowel syndrome, improved working memory, reduced systemic responses to stress, antioxidant and anti-inflammatory, in addition to its sleep modulation effect (Gagnon & Godbout 2018, Srinivasan et al. 2012, Wang et al. 2021). Melatonin may have been beneficial through many different mechanisms such as sleep modulation, sensorial regulation or effect of anxiety relief associated with RRB. It might be inferred that sleep disturbance may not play a mediating role for his RRB in our case since the absence of sleep disturbance until SSRI use (approximately 6 months period). There are need studies to confirm its effects on RRB and to determine which mechanisms are effective.

Despite the fact that here we provide a case report, our outcomes aim to call attention to possible treatment option with melatonin for RRB, in line with an animal study of Wang et al. (2020). Further studies are needed to determine the continuity of the effect, the need for dosage adjustment, and whether there is a subgroup for suitable for this effect.

Acknowledgements: None.

Conflict of interest: None to declare.

Contribution of individual authors:

All authors made equal contribution to this case report in terms of drafting, writing, obtaining the patient' s consent, and revising the paper.

References

1. *Gabriels RL, Cuccaro ML, Hill DE, Ivers BJ, & Goldson E: Repetitive behaviors in autism: Relationships with associated clinical features. Res Dev Disabil 2005; 26:169-181*
2. *Gagnon K & Godbout R:Melatonin and comorbidities in children with autism spectrum disorder. Curr Dev Disord Rep 2018; 5:197-206*
3. *Mannion A & Leader G: Sleep problems in autism spectrum disorder: A literature review. Rev J Autism Dev Disord 2014; 1:101-109*
4. *Rossignol DA & Frye RE: Melatonin in autism spectrum disorders: a systematic review and meta-analysis. Dev Med Child Neurol 2011; 53:783-792*
5. *Srinivasan VC, Lauterbach E, Yu Ho K, Acuña-Castroviejo D, et al.: Melatonin in antinociception: its therapeutic applications. Curr Neuropharmacol 2012; 10:167-178*
6. *Tordjman S, Anderson GM, Bellissant E, Botbol M, et al.: Day and nighttime excretion of 6-sulphatoxymelatonin in adolescents and young adults with autistic disorder. Psychoneuroendocrinology 2012; 37:1990-1997*

7. *Wang B, Zhu S, Liu Z, Wei H, Zhang L, He M, et al.: Increased Expression of Colonic Mucosal Melatonin in Patients with Irritable Bowel Syndrome Correlated with Gut Dysbiosis. Genomics Proteomics Bioinformatics 2021; 16:S1672-0229(21)00018-8. Epub ahead of print. PMID: 33607299*
8. *Wang HB, Tahara Y, Luk SHC, Kim YS, et al.: Melatonin treatment of repetitive behavioral deficits in the Cntnap2 mouse model of autism spectrum disorder. Neurobiol Dis 2020; 145:105064*
9. *Yu Y, Chaulagain A, Pedersen SA, Lydersen S, et al: Pharmacotherapy of restricted/repetitive behavior in autism spectrum disorder: a systematic review and meta-analysis. BMC psychiatry 2020; 20:1-11*
10. *Zhou MS, Nasir M, Farhat LC, Kook M, Artukoglu BB, Bloch MH: Meta-analysis: pharmacologic treatment of restricted and repetitive behaviors in autism spectrum disorders. J Am Acad Child Adolesc Psychiatry 2021; 60:35-45*

Correspondence:
Onur Tuğçe Poyraz Fındık, MD
Child and Adolescent Psychiatry Department,
Marmara University Pendik Research and Training Hospital
Fevzi Çakmak Mah. Muhsin Yazıcıoğlu Cad. No: 41, Pendik-Istanbul, Turkey
E-mail: onurtuuce@hotmail.com