Case Report

PSYCHOTROPIC MEDICATIONS AND METABOLIC SIDE EFFECTS IN COMMON GENETIC SYNDROMES WITH INTELLECTUAL DISABILITY- CASE REPORT

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ABSTRACT

Multi-systemic genetic disorders are strongly associated with psychiatric illness and may require psychotropics for their management. The choice of psychotropics is primarily determined by medical comorbidities and adverse effects. A careful assessment of behavioural phenotype and metabolic monitoring for children on psychotropics should be followed to avoid adverse consequences. Hence, the need for monitoring of metabolic syndrome during routine clinical evaluation and the use of aripiprazole which demonstrated a good response with minimal adverse effects are highlighted with a description of cases of children with intellectual disability and neurodevelopmental genetic syndromes like Down Syndrome and Prader-Willi syndrome.

Keywords: Genetic syndromes, Aripiprazole, Down syndrome, Prader-Willi syndrome, metabolic side-effect.

INTRODUCTION

The rates of mental illness among people with Intellectual Disability (ID) are at least 2.5 times higher than in the general population.1 Health supervision for children with genetic syndrome by the Committee of Genetics of American academy of Paediatrics summarizes the assessments required from birth through adulthood.2 This includes periodic development and behavioural assessments during early childhood, and addressing issues related to sexuality and personal safety during adolescence.

Children with intellectual disabilities and communication difficulties may develop challenging behaviour that is severe and non-responsive to behavioural interventions and might require psychotropics for their management. Apart from the challenges encountered in the evaluation due to

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communication deficits, diagnostic masking and overshadowing, these are challenges often faced in clinical settings due to medical comorbidities. Management often requires a comprehensive plan to include developmental, behavioural and pharmacological interventions, and the choice of psychotropics is primarily determined by the medical comorbidities. The choice of psychotropics and the need for routine clinical evaluation of a child with ID and neurodevelopmental genetic syndromes like Down syndrome (DS) and Prader-Willi syndrome (PWS) are discussed in the context of the following case descriptions.

**DESCRIPTION OF CASES**

**Case 1:** Eleven-year-old male child with moderate ID, Attention Deficit and Hyperactivity Disorder (ADHD), and Down Syndrome presented with recent worsening in symptoms associated with increased irritability, aggression, self-injurious behaviour, and biological disturbance. After a detailed evaluation, the child was diagnosed with comorbid Bipolar Disorder-Not Otherwise specified (NOS). The child had ventricular septal defect, so cardiology opinion was obtained before starting Risperidone. The cardiologist had advised slow up-titration of psychotropics with monitoring of blood pressure and pulse rate. Hence gradual up-titration of Risperidone to 6mg per day was done under in-patient care. However, the child developed significant weight gain on Risperidone. He gained 6kgs weight from 35kgs to 41kgs within six weeks of starting Risperidone. Hence, cross titration of Risperidone with Aripiprazole was done. With Aripiprazole dose of 15mg per day, the child showed improvement in his behavioural symptoms, and there was no further weight gain noted. The child had paradoxical worsening with benzodiazepines, and there were limitations in providing medications on a required basis. A greater emphasis was laid on non-pharmacological interventions. Antecedent-Behaviour-Consequence analysis and reinforcements were employed to address self-injurious behaviour.

**Case 2:** A twelve-year-old male child with ID had presented to our outpatient clinic with behaviour problems in the form of tantrums and aggression. The child had been under regular psychiatric treatment with Olanzapine 10mg/day for more than two years. As the child had gained significant weight, the family had sought an opinion regarding further management. The child had almond-shaped eyes, hypogenitalia, and obesity. The presence of a typical behavioural phenotype of hyperphagia, skin picking, mood fluctuations, and temper tantrums led to a provisional diagnosis of Prader-Willi syndrome. The child’s baseline weight was within the normal limit of 50th percentile, which was increased to 90th percentile over one year. Olanzapine was tapered, and the child was started on low dose Aripiprazole 2.5mg twice daily for aggression and Clonidine 150mcg per day in divided doses for ADHD in combination with more intensive non-pharmacological interventions. The child’s behavioural problems improved within 3 to 4 weeks of treatment.

**Case 3:** A young adult male aged 24 years diagnosed with DS and ID presented with decreased interaction, biological disturbance, and muttering to self. Mental State Examination (MSE) was hampered by the expressive language deficits though the patient had only mild ID, and his comprehension was
good. A provisional diagnosis of Psychosis-Not Otherwise Specified (NOS) was considered. Baseline BMI was 29 amounting to overweight, and therefore the patient was started on aripiprazole. The patient showed symptomatic improvement with Aripiprazole 15mg per day over eight weeks, however social withdrawal persisted. Thyroid status was within normal limits. Serial observations revealed moderate to severe depressive symptoms, and the patient showed significant improvement after adding sertraline 50mg. Lifestyle modification was suggested, and the patient was referred to an occupational therapist for vocational rehabilitation. However, there were practical difficulties in the implementation of vocational rehabilitation or lifestyle modification with elderly parents.

DISCUSSION

The general psychiatrist needs to be aware of common genetic syndromes associated with ID, behavioural phenotypes, syndrome specific problem behaviours as well as common medical comorbidities to plan effective management. Studies have observed higher rates of obesity in individuals with DS, and prescribing psychotropics for this special population with a high cardio-metabolic burden is a challenge. Hence the metabolic monitoring schedule which includes monitoring of blood pressure, weight and calculation of BMI with waist measurements and investigations like blood sugar and lipid profile can be done in a child who is prescribed psychotropic drugs to avoid severe consequences.

Prader-Willi is also among the common syndromes often seen in a psychiatric setting. Although hyperphagia is considered a severe behaviour problem among children with this syndrome, studies have shown that food restriction had significantly reduced this potentially problematic behaviour. Therefore, behavioural interventions should actively include evidence-based interventions to address syndrome specific problem behaviours. Monitoring a child with genetic syndrome requires a holistic and multidisciplinary approach that addresses dietary, lifestyle, socioeconomic, medical, and genetic risk factors.

The choice of antipsychotic in treating the behavioural changes in children with genetic syndrome plays a vital role in preventing adverse consequences. In general, aripiprazole has a unique mechanism of action impacting dopaminergic and serotonergic neurotransmission with few side effects, and the efficacy and tolerability of aripiprazole in children and adolescents have been well demonstrated in many clinical studies. However, very few pilot studies are available, which has assessed the impact of aripiprazole on behavioural changes in children with a genetic syndrome. A recent review on psychotropic treatments in PWS indicated a poor literature base with few controlled trials and many case reports. Wolfgang Briegel had studied the clinical usefulness of aripiprazole treatment in PWS, and concluded that aripiprazole is effective in this distinct group of patients. In our patients also, aripiprazole has been demonstrated to be effective. The patients showed complete resolution of behavioural and psychotic symptoms. All the patients tolerated aripiprazole well and showed no further gain in weight. To sum up, aripiprazole might be a promising treatment approach in subjects with genetic syndromes like DS or PWS. However,
studies with larger samples are needed to evaluate the efficacy, benefits, and side effects of antipsychotics in this distinct group of patients. Special attention should be given to the metabolic side effects. Significant weight gain and thereby obesity, itself can act as an independent risk factor for the development of metabolic syndrome, especially in children. Hence the use of psychotropic medications in this population has to be done cautiously.  

CONCLUSION
Knowledge of common genetic syndromes associated with Intellectual disability, their key dysmorphic features, comorbid medical conditions, and existing guidelines for management is essential for psychiatric practice. The metabolic side effects may pose a challenge in the selection of psychotropics for the management of patients with genetic syndromes. Aripiprazole has shown a good response with minimal adverse effects in the subjects described in the case series, suggesting that aripiprazole could be a promising treatment approach for children with genetic syndromes.

Conflict of Interests
None

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