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Aripiprazole Induced Micturition Difficulty and Urinary Retention in a Female Adolescent with Disruptive Mood Dysregulation Disorder

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ABSTRACT

Side effects of aripiprazole are due to an extension of its mechanism of action in addition to its effect on alpha 1 adrenergic receptor and a weak antagonist action at H1 receptors. Urinary retention is a peripheral anticholinergic side effect of aripiprazole but rarely reported. Aripiprazole has direct blockade effect on local alpha 1 adrenoceptors and consequently leads to improved sphincteric tone. The effect of aripiprazole on hypodopaminergic in the central pathways [possibly in the basal ganglia] that supposedly controls the micturition reflex is the basis behind the off label use of aripiprazole as a treatment option for clozapine induced enuresis. Further studies are required to elucidate the exact pathophysiology involved and medications that could be beneficial in treating this side effect.

INTRODUCTION

There has been reports of urinary incontinence [clozapine, risperidone] and retention [olanzapine, chlorpromazine, loxapine, thioridazine, SSRIs] with both typical and atypical antipsychotic use in some literature, but rarely with aripiprazole. Aripiprazole [Abilify] is an atypical antipsychotic commonly classified as a third generation antipsychotic and a dopamine partial agonist. It is U.S. Food and Drug Administration approved for schizophrenia, bipolar disorder, an adjunct in the treatment of depression, autism related irritability and acute agitation associated with schizophrenia and bipolar disorder. It is used off label in behavioral disorders in children, adolescents and in patients with dementia. It works via its partial agonist/modulatory action at dopamine 2 [D2] and 3 [D3] receptors. Its action as a partial agonist at serotonin type 1A [5HT1A] and blockade of serotonin types 2A, 2C and 7 may also be relevant at clinical doses. Side effects are due to an extension of its mechanism of action in addition to its effect on alpha 1 adrenergic receptor and a weak antagonist action at H1 receptors leading to its anticholinergic and sedative side effects respectively. Difficulty urinating with attendant bladder distention and urinary retention is a peripheral anticholinergic side effect of aripiprazole but rarely reported.

CASE REPORT: Miss K.R., a 17-year-old African American female with a history of Fetal Alcohol Syndrome [FAS] and borderline Intelligent Quotient [IQ] with a history of Disruptive Mood Dysregulation Disorder [DMDD], Major Depressive Disorder [MDD] with psychotic features, and Post-Traumatic Stress Disorder [PTSD] was admitted on the child and adolescent unit for attempted suicide by overdose on Tylenol and stain remover. She was started on 2.5 mg daily of aripiprazole for mood dysregulation and 15 mg daily of citalopram for depressed mood and subsequently on 1 mg at bedtime of Prazosin for PTSD related symptoms. Aripiprazole was increased to 2.5 mg twice daily and eventually a total of 7.5 mg daily. Citalopram [Celexa] was gradually increased to 20 mg daily because of persistent complaints of depressed mood and suicidal thoughts. Day 10-15 on admission she started complaining of inability to urinate with lower abdominal fullness without dysuria, frequency or flank pain. No fever or worsening anxiety was reported by patient. This persisted for several days with conservative management. Various other causes of her urinary symptom like obstructive, infective, inflammatory and neurologic were all ruled out in this patient. Urinalysis was negative, Complete Blood Count [CBC] was within normal limits, so was the Comprehensive Metabolic Panel [CMP]. No evidence of Extrapyramidal side effects was

present in this patient. Post void urinary volume was greater than 350mL. Aripiprazole was cut down to 5 mg daily with no improvement of symptoms necessitating complete withdrawal of the medication. Within a couple of days after the discontinuation of aripiprazole, patient's urinary symptoms completely abated.

Selective Serotonin Reuptake Inhibitors [SSRI] have less evidence in the literature to cause urinary retention, besides, with the discontinuation of aripiprazole in this patient, her symptoms abated. There have been reports of the combination of Citalopram and Aripiprazole leading to urinary retention. She continued to be free of urinary retention with the continuation of the SSRI Celexa. It would have been good to re-challenge patient with the same medication, however, patient declined any thought of that and insisted medication be added to her list of medication allergy.

The effect of aripiprazole on hypodopaminergic in the central pathways [possibly in the basal ganglia] that supposedly controls the micturition reflex is the basis behind the off label use of aripiprazole as a treatment option for clozapine induced enuresis, this could also explain the pathophysiology of urinary retention in patients on aripiprazole. Aripiprazole has direct blockade effect on local alpha 1 adrenoceptors and consequently leads to improved sphincteric tone. Literature also suggests that dopamine cross activates both central and peripheral alpha 1 adrenoceptors which ultimately improves the sphincteric tone. There are reports linking antagonism at the serotonin 1A receptors to bladder dysfunction, hence aripiprazole exerts its urinary side effect by 5HT1A partial agonism as well. Summarily, the 5HT1A receptors play a huge role in the control of bladder contractions while the alpha 1 adrenergic receptor is believed to promote the contraction of the neck of the bladder, urethra and prostate to enhance bladder outlet resistance.

This case highlights the highly disabling urinary side effect of second generation antipsychotics, in this case, Aripiprazole and the need for physicians to consider discontinuing the medication if necessary regardless of patient's symptomatic response. Physicians need to be aware of this rare side effect of Aripiprazole. Further studies are required to elucidate the exact pathophysiology involved and medications that could be beneficial in treating this side effect.

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None reported

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