Behavioral activation secondary to antidepressant use in an intellectually disabled woman

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INTRODUCTION

The under-appreciation for and potential lack of recognition of medication-related adverse effects in persons with intellectual disabilities (ID) can be a function of a variety of factors, including under-recognition of the prevalence of psychopathology in those with IDs compared to the general population, rating scales completed by the caregiver rather than the patient, low familiarity of healthcare needs by this special population, and lack of consensus criteria for diagnostic purposes.[1] Recognition and management of unintended medication-related effects may represent an area for clinical interventions and quality of life improvement for practitioners, especially pharmacists working with this population. We present a case of a woman with significant intellectual impairment who became increasingly agitated, aggressive, and self-injurious following initiation of an antidepressant.

CASE REPORT

The patient, MB, was a 30 year old white intellectually disabled woman (IQ level less than the 20-25 range) admitted to a state-operated long-term care facility secondary to aggression and an inability to participate in programs and unit activities. Screaming was the primary method of communication. No appreciable intelligible speech was present. The patient was able to point to preferred food choices and other preferred items. Staff assistance was needed for activities of daily living, such as personal hygiene and tooth brushing, as well as assistance at meal times.

The most recent information available for clinical team review was from her recent inpatient hospitalization for aggression which occurred 6 months prior to this placement. The previous long-term care facility was closed and records, including family history, were unavailable. Family contact was limited and had been sporadic. Based upon available data, the presenting behaviors were apparently present life-long. The diagnosis of Autistic Disorder (AD) was based on a review of the limited records available, interviews with staff who accompanied her, observation in the current environment, the continuing presence of impairments in social interactions (including interactions with peers), stereotyped and repetitive behavioral routines, and criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)[2]. Information available documented a history of self-injury (slapping and scratching with mild to moderate tissue damage), property destruction (breaking objects), and physical aggression (head butting staff and peers). Continued observational assessment regarding impairments in social interactions and the presence of stereotyped and repetitive behaviors were not inconsistent with the diagnosis of AD.

At the time of admission, her medication regimen included risperidone 6 mg, clonazepam 1 mg, naltrexone 50 mg, and a multivitamin daily. Within one week of admission, risperidone was decreased to 4 mg daily. The therapeutic rationale for this change included lack of a clearly defined indication, unidentified target behaviors, and to evaluate if akathisia was present and a possible contributing factor to observed agitation.[3] When seen in psychiatric clinic one month following admission, she was crying and disheveled. Staff reported the current presentation had been consistent throughout the month. Personal hygiene also was problematic. Staff reported the patient refused any assistance with bathing or oral care and became increasingly agitated around changing clothes.

The presentation of these features was considered as a component of the evaluation for a mood disorder. Mood disorders, particularly depression, in persons with impairments in verbal abilities and functioning, may present with more vegetative symptomatology. Clinician evaluation may include assessments for changes in functioning from baseline, particularly skills regression, appetite/weight, sleep, and aggression. Ghaziuddin and colleagues recommend screening for depression in persons with a diagnosis of AD with recent aggressive acts with concurrent changes in mood (irritability), sleep, and appetite.[4] Our patient presented with changes in mood (crying and increased irritability) and a decrease in functionality from baseline (poor personal hygiene). At that time, sertraline 25 mg once daily was initiated then titrated to 50 mg daily over the course of 2 weeks. When the patient was seen in psychiatric clinic 3 weeks after the increase to 50 mg daily, she was unable to stay seated, yelled, and screamed in a high pitch. Behavioral exacerbations also included head butting, shrieking, throwing objects, and dropping to the floor refusing requests to rise. Staff reported these behaviors presented approximately 6-7 days following the increase to sertraline 50 mg and were more intense than upon admission.

A determination of all factors that might impact a change in behavior was undertaken. To assess if environmental stressors were contributing to this change, a functional analysis was done by the unit psychologist. Persons diagnosed with AD have been found to be acutely sensitive to changes in their environment and/or routine and demonstrated marked distress over minor changes.[2] Environmental changes for this patient included discontinuation of participation in a vocational program. Other environmental interventions (decreasing stimulation, escorting to a private area) were unsuccessful, and the severity, duration, and frequency of the behaviors continued to increase. She became easily over stimulated. Behavioral exacerbations which may have been secondary to medical causes, such as constipation, dental pain, and urinary tract infections, were also assessed. Thus, behavioral changes secondary to environmental changes or a general medical condition were ruled out.

The effectiveness of the present medication regimen was evaluated and changes in behavior and/or medication correlated with behavioral data. Retrospective chart review established a temporal connection between initiation of sertraline and behavioral escalation, particularly following the increase to 50 mg. To determine if the behavioral exacerbations were secondary to a medication-mediated effect, the dose of sertraline was reduced to 25 mg for 1 week, then discontinued. Her behaviors markedly decreased within 1 week following the dosage reduction. No additional problematic behaviors, such as self-injury, aggression to people and/or property, and/or shrieking, were reported, and the patient was more redirectable. Personal hygiene was better, and the patient did allow some staff assistance. Screaming as a communication method returned to baseline levels.

With continued assessment of the patient and appraisal of these medication changes, the risk for an adverse drug-related event was evaluated using criteria for estimating the probability of adverse drug reactions (ADR) with the Naranjo ADR Probability Scale.[5] The impact of age, gender, concurrent medication use, the total daily dose of antidepressant, and psychiatric diagnoses were considered. The behavioral exacerbation effect was scored as 'probable' with a score of 8 out of a maximum of 12. Criteria for this instrument encompassed previous conclusive reports of the effect, improvement following discontinuation, inclusion of other causes, and a similar effect to the same or similar agent in a prior exposure.[5] All these factors were reviewed and evaluated in this patient. Use of an antidepressant, in this case sertraline, was considered the contributing cause for the behavioral changes.

DISCUSSION

In the general population, features of psychiatric illnesses are more readily identifiable, in part based on the therapeutic alliance with and information gleaned from the patient. The clinician also is able to gather information from and about the patient with an interview, administration of standardized assessment measures, or both. In a randomized trial of behavioral activation (identified as use of idiopathic functional analysis and contextual interventions), cognitive therapy and antidepressant use as treatment modalities in adults with major depression, researchers acknowledged that the "emphasis on the utility of function of thinking" has a "particularly important role in the treatment of depression."[6] Diagnostic overshadowing may represent one key factor to address in the ID population. This term has been used to refer to the clinician perception that behavioral problems thought to be secondary to IDs may actually be caused by a mental illness. Diagnostic overshadowing can therefore result in underestimating the clinical significance of the emotional and behavioral presentation and the deficits are inaccurately associated with a diagnosis of ID.[1]

Focusing on behavioral changes following the addition of an antidepressant, the potential for antidepressant-related agitation was further evaluated. Safer and Zito reviewed selective serotonin reuptake inhibitors (SSRI) trial results for adverse medication effects in pediatric populations. The authors also included findings from adult populations. Five categories were identified and included activation (with hyperkinesis and agitation), somnolence, insomnia, nausea and vomiting. For adults, activation/hyperactivity was an infrequently reported event although rates for agitation ranged from 4.5% to 5.9% in 18% (4 of 22) of placebo-controlled trials. [7,8-11] Agitation secondary to sertraline was reported by Reimherr and colleagues. Compared to amitriptyline and placebo groups, reported rates for the sertraline group were only slightly higher (15.4 and 11.3 vs. 12.1, respectively).[9] Information from the manufacturer included agitation among the most common adverse events associated with discontinuation (1%) in placebo-controlled clinical trials with major depressive disorder as the diagnosis (N=861).[12]

Two studies specifically addressed the use of sertraline in adults with diagnoses that included some degree of ID and a pervasive developmental disorders (including AD). McDougle et al. investigated sertraline for effectiveness and tolerability and found it was well tolerated. In the 12-week open label trial (N=42), there were 37completers. Three of the participants did not complete the trial due to increased anxiety and/or agitation. The researchers did not specify if these had a diagnosis of AD.[13] In a second trial, Hellings and colleagues sought to determine the benefits of sertraline for self-injury and aggression. Of the nine persons enrolled in the trial, five were dually diagnosed with AD. Increased agitation and self-injury necessitated discontinuation in one patient after 18 weeks. As with the previous trial, diagnostic criteria were not included.[14]

A diagnosis of bipolar disorder was considered in the patient presented above as well. Mood symptoms (abnormally/persistently elevated and/or expansive mood with a durational component), diminished need for sleep, and changes in appetite were absent. No cyclic nature was observed. Changes due to a general medical condition, as well as potential substance use were ruled-out, but the possibility of antidepressant-induced mania was considered.[2] This has been a topic of some debate as to whether the presentation of depressive symptoms may be part of an undiagnosed bipolar disorder or if use of antidepressants induces an adverse medication effect. Goldberg and Truman reported this effect for antidepressants may impact 20% to 40% of more susceptible patients with bipolar disorder.[15] A retrospective study by Koszewska and Rybakowski found bipolar patients who received tricyclic antidepressants were more likely to experience an antidepressant-mediated mood change compared to those prescribed an agent from another class (SSRI, bupropion).[16] Mood switching in bipolar depression was evaluated using adjunctive venlafaxine, bupropion and sertraline (N=174). Defining a 2-point or greater increase on the Clinical Global Impression for Bipolar Disorder (CGI-BP) mania rating scale as a cause for switching to hypomania or mania, 9% of the patients receiving sertraline (N=58) were considered to have switched.[17] Emergence of subthreshold hypomania and threshold switches with antidepressant augmentation in depressed patients with bipolar disorder was evaluated by Leverich et al. In trials with sertraline, brief hypomania was reported for 6.6% (5 trials of 76) in the acute phase (10-week trial) and 3.1% (1 trial of 32) in the continuation phase (up to 52 weeks). For recurrent brief hypomania, rates were higher in the continuation phase (5 trials of 32 or 15.6%). For the continuation phase, the total was 18.8%.[18] Based on findings reported in the literature, our patient's response to the addition of an antidepressant and dosage changes were considered the cause of the increase in agitation. Following discontinuation of the antidepressant, sustained agitation was not reported. Additional episodes of agitation were considered environmentally mediated.

Persons diagnosed with an ID face a number of challenges, as do the providers and clinical pharmacists participating in their care. The abilities of the individual to report any changes following modification in pharmacotherapy regimens, environment, or general health may be overlooked due to use of traditional screening instruments and lack of population-specific training for providers. Ongoing and systematic monitoring for medication related adverse effects in this population is imperative, due to a lack of self-reporting. The impact of a psychiatric pharmacist in facilities or with providers providing services for those with an ID may encompass identification of appropriate clinical interventions secondary to accurate diagnosis, evaluation for medication-related effects(both therapeutic and adverse effects), dosage adjustments required due to aging or other changes in physiology, and identification and prevention of medication errors.

CONCLUSION

Sudden and significant changes in behavior in a person with an ID, particularly if the person has limited verbal

skills, must be thoroughly evaluated. Medical and environmental causes must always be ruled out as potentially contributing. This case represents one example of the clinical challenges in recognizing and treating behavioral activation and/or medication-induced mania. Patients who experience these medication-related effects may be more at risk for mood disorders, and close monitoring for mood disorders is recommended. Working with patients with ID can be a challenging and rewarding area for psychiatric pharmacists.

CLINICAL PEARL

Consider antidepressant behavioral activation and/or antidepressant-induced activation in persons with IDs when environmental changes, general medical conditions, and other psychiatric disorders have been ruled out.

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