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Case Report

Antipsychotics, Dysphagia, Aspiration Pneumonia, Bowel Obstruction and Related Surgeries in Adults with Severe Developmental Disabilities

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Abstract

Background: Dysphagia, aspiration pneumonia, constipation and bowel obstruction are serious side effects of antipsychotics, to which individuals with severe developmental disabilities (DD) are more prone.

Objectives: To examine antipsychotic treatments with such problems in severe DD, drug taper attempts, and outcomes for dysphagia and oral feeding.

Methods: We extracted cases from our IRB-approved Neuropsychiatry Clinical Database with dysphagia, aspiration pneumonia and/or bowel obstruction. Data includes age, race, gender, intellectual disability (ID) level, history of dysphagia/aspiration pneumonia/ bowel obstruction/surgeries for these including ostomy placement and feeding details. Also, antipsychotics at presentation and following dosing reductions and outcomes.

Results: Thirteen adults met the inclusion criteria: 7 males, 6 females. Median age was 59 years (range 29-69), all but 2 were < 65 years. One had borderline intellectual functioning and spastic quadriplegia; ID levels were: moderate in 1, severe in 7, and profound in 4. Nine of 13 (69%) had dysphagia; 8 with aspiration pneumonia (62%). Six of 13 (46%) had bowel obstructions. Seven of 13 (54%) had surgery for ostomies or bowel resection. All 13 received antipsychotics: olanzapine in 4: 40mg, 40 mg, 30mg and 25mg daily; clozapine in 3: 750mg (with paroxetine 20mg), 400mg and 375mg daily; quetiapine in 3: 800mg (with paroxetine 30mg), 600mg, 400mg daily; and risperidone in 1: 8 mg daily. Two received olanzapine with a selective serotonin reuptake inhibitor (SSRI) inhibiting CYP2D6: olanzapine 10mg with fluoxetine 80mg daily; olanzapine 20mg with sertraline 150mg daily. Four cases following antipsychotic and/or SSRI tapers showed improved swallowing on repeat video swallow and restoration of normal feeding, less thickened liquids (n=2) or gastrostomy-tube removal (n=2).

Conclusions: Individuals with severe DD receiving antipsychotics are prone to dysphagia, aspiration pneumonia, bowel obstruction and surgeries. Gradual taper of such medications, including of CYP2D6-inhibiting SSRIs may improve oral intake outcomes.

INTRODUCTION

Individuals with severe developmental disabilities (DD), including those who are minimally verbal (less than 20 words of expressive language), are prone to dysphagia and consequent coughing and choking when eating or drinking. The associated overflow results in leakage of food or liquids into their lungs, causing potentially life-threatening aspiration pneumonia. Studies found that 25-50% of children with central cerebral disorders such as cerebral palsy have clinical signs of dysphagia, and over half also experience severe constipation [1, 2]. This increased predisposition is likely due to impairments in the complex sensory and motor components required for swallowing and neurologically-related gastrointestinal motility problems.

Swallowing reflexes involve closely connected pathways between cortical extrapyramidal motor planning areas, centers controlling the brainstem and cranial nerves, and lower motor neurons. Dysfunction in any part of these systems occurring with cerebral disorders predisposes to dysphagia [1,2]. In addition, impaired coordination of brain-gut axis functions is thought to contribute to the increased incidence of gastrointestinal dysmotility disorders, dysphagia, and constipation. Additional factors that have been shown to contribute to dysphagia include

developmental impairments in oro-pharyngeal coordination [2]. Gut motility disorders are heterogeneous, with peripheral causes such as impairments in nerve or muscle tracts or central causes related to neurological, genetic, or hormonal dysfunctions [3]. Various environmental factors can worsen these problems, including medications used to treat aggression and self-injury, especially antipsychotics.

Antipsychotic-related dysphagia is documented in the general population without DD; however, published information on dysphagia-related complications of antipsychotics in those with DD is sparse. Dopamine blockade and resulting striated muscle spasm effects of antipsychotics are likely to contribute to swallowing difficulties in a dose-related manner. Other medications also worsen these effects, including muscle relaxants often prescribed for spasticity and benzodiazepines that may be part of antiseizure medication regimens or used for insomnia. Constipation and bowel obstruction resulting from antipsychotic treatments are thought to be mediated by pronounced, dose-dependent antagonism of cholinergic, histaminergic and serotonergic receptors [4]. Individuals with severe DD are known to be more sensitive to side effects of all medications, although the reasons for this remain to be elucidated. They also lack the capacity and autonomy to discontinue taking medications, causing adverse events.

Antipsychotics are frequently prescribed, often overprescribed, for persons with DD and especially severe DD to treat associated aggression, self-injury, and property destruction [5]. Factors contributing to such aggression include communication difficulties, higher seizure rates, and side effects secondary to antiseizure medication, including cognitive dulling and irritability, and impulsivity. Dysphagia and bowel obstruction are severe, dose-related side effects of typical and atypical antipsychotic medications that may occur in all ages but are more common in those with severe DD and in dementia. Signs of dysphagia associated with antipsychotic usage are well-documented and increase the potential for aspiration and subsequent pneumonia [6,7]. Such signs include coughing or choking when swallowing food or fluids, and fluid running from the nose when drinking. Individuals with DD often eat and drink too rapidly, have poor dentition, and do not chew food adequately, which increases choking and aspiration risks.

In addition, in January 2020, the Federal Drug Administration in the USA released a statement strengthening an existing warning that the atypical antipsychotic clozapine can produce severe constipation that, in rare cases, may progress to serious bowel complications, surgeries, hospitalizations, or even death if the problem is not diagnosed and treated quickly. Individuals with severe DD in residential facilities require close monitoring of their daily bowel movements, and many receive laxative polypharmacy and enemas for chronic constipation. Additionally, low-fiber diets, picky eating, and inadequate exercise often worsen constipation. Many individuals receiving antipsychotics and psychotropic medications still develop bowel obstructions and may require bowel resections for gangrene [8,9].

This study examines medication treatments and dosing in real-world psychiatry patients with severe DD, who developed dysphagia and/or bowel obstructions on psychotropic medication treatments. Such medications include but are not limited to, antipsychotics and selective serotonin reuptake inhibitors (SSRIs) that inhibit antipsychotic metabolism via the CYP2D6 hepatic enzymes, thereby increasing the effective doses of antipsychotics. Psychiatric prescribers and medical and surgical clinicians may overlook this interaction. The resulting higher effective antipsychotic dose and more significant dopamine blockade then increase the already elevated risks of individuals with severe DD to develop dysphagia, aspiration pneumonia, and bowel obstruction. In addition, we examined outcomes of antipsychotic and SSRI drug taper attempts as they impacted dysphagia, tube-feeding, and oral food intake in those patients whose guardians and multidisciplinary treatment team gave permission, as well as barriers to such tapers.

METHODS

Data Sources and Search Strategy

Methodology for systematic review and analysis began with a comprehensive case review and data extraction from our IRB-approved Neuropsychiatry Clinical Database for cases with keyword histories of "dysphagia," "aspiration pneumonia," and/or "bowel obstruction." Data extracted includes age, race, gender, intellectual disability (ID) level, minimally verbal status, history of dysphagia/aspiration pneumonia/ bowel obstruction/surgeries for these including ostomy (jejunostomy tube, gastrostomy tube, colostomy or bowel resection due to necrosis) placement and feeding details. Antipsychotic and SSRI medications and dosing were extracted from the time of presentation and at time of chart review, following any medication tapers or discontinuation, and outcomes of such problems along with any feeding improvements.

Selection Criteria and Quality Assessment

Inclusion criteria began with selecting bowel obstruction and dysphagia cases among adults with diagnosed intellectual disability. The 11 chronic inpatients resided in a state-run long-term hospital serving adults with developmental disabilities, while the 2 outpatients were treated in a university-affiliated psychiatric clinic. The lead author (JH) served as a treating psychiatrist for all of these patients with developmental disabilities and neuropsychiatric illness, taking over their management at what is described as baseline.

RESULTS

Thirteen adults met symptom inclusion criteria: seven males and six females. Median age was 59 years, with an age range 29-69 years. All but two were under 65 years old. Two were African American, and eleven were Caucasian. One had borderline intellectual functioning and spastic quadriplegia, while ID was moderate in one, severe in seven, and profound in four. All but 4 (69%) were minimally verbal. Nine of thirteen (69%) had dysphagia, of which 8 had a history of aspiration pneumonia (89% of those with dysphagia). Six of thirteen (46%) had a bowel

obstruction history; 2 had bowel resections, and one also had a colostomy bag following an upper ascending colectomy.

All 13 patients received moderate or high dose antipsychotics at baseline: olanzapine in 4: in daily doses of 40mg, 40 mg, 30mg and 25mg, clozapine in 3: dosed daily at 750mg (plus paroxetine 20mg), 400mg, and 375mg; quetiapine in 3: with daily doses of 800mg (plus paroxetine 30mg), 600mg, 400mg; and risperidone in 1: at 8 mg daily. Two receiving olanzapine were also treated with a selective serotonin reuptake inhibitor (SSRI) that inhibits CYP2D6, which markedly increased the effective antipsychotic dose: olanzapine 10mg plus fluoxetine 80mg daily; olanzapine 20mg plus sertraline 150mg daily (Table 1).

Four patients had their antipsychotic and/or SSRI gradually tapered and then showed improved swallowing on repeat video swallow studies and enjoyed restoration of normal feeding (n=2) of whom the gastrostomy tube was removed in one, or less thickened liquids (n=2). In other cases, either the guardians of chronic inpatients, or the hospital medical director, or treatment team members refused trial of medication taper, based on concerns of potential behavioral worsening. In one case, a 42-year-old female patient with spastic quadriplegia and borderline intellectual functioning described fears of repeat aspiration pneumonia if she were to try oral intake again. This was despite repeated discussions with her that her olanzapine had been tapered gradually, from 30mg daily to 2.5mg daily, and baclofen tapered from 120mg daily to 40mg twice daily. She also refused to have a repeat video swallow study. All patients with bowel obstruction histories continued to eat by mouth but were monitored closely regarding daily bowel movements and received laxative treatment and enemas if needed (Table 2).

DISCUSSION

All patients in this series presented with severe developmental disabilities accompanied by varying degrees of dysphagia, life-threatening aspiration pneumonia, and bowel obstructions or resections while being treated with antipsychotics. All received moderate or high doses of antipsychotics, in several cases, along with SSRIs that are potent CYP2D6 hepatic enzyme inhibitors, notably paroxetine, fluoxetine, and sertraline. Only one patient of the 9 with dysphagia did not have an aspiration pneumonia history, however, her dietary restrictions could be lifted following olanzapine taper from 25mg daily to 5 mg daily which improved her mood and quality of life significantly. Of the 8 others who did have aspiration pneumonia, such problems were recurrent in 2. Five of the 8 patients with a history of aspiration pneumonia were receiving gastrostomy tube feeding at the start of treatment and data collection, with no intake by mouth. The others had structured feeding routines requiring direct staff supervision of spoon-fed pureed foods, sips of thickened liquids and needing to swallow after each spoon or sip. Such close supervision reduces the individual's independence and quality of life, and requires intensive staffing.

All those with bowel obstruction histories continued their oral food intake along with laxatives and daily monitoring. A 32-year-old male had a permanent colostomy bag following an upper ascending colectomy, and he would repeatedly pull the bag off so that he would be allowed to take extra showers. The frequency of surgeries needed is also striking. Surgeries were for insertion and often re-insertion of ostomy tubes to enable feeding routes other than oral food intake and bowel resections for complications of bowel obstruction. Additional emergency room visits and revision surgeries are often needed in such patients due to wound complications of infection, ostomy loosening, tubes falling out or being pulled out by the person. These problems also increase burdens on medical and nursing services, especially if the patients have accompanying severe behavior problems such as aggression and self-injury compounded by their communication problems.

Table 1: Patients Presenting with Dysphagia

Subject #	Age	Race, Gender	ID Level	Asp. Pneumonia	Ostomy, Upper GI	Baseline Meds (mg)
1	60	WM	Sev	Present		olanzapine 40 daily, clonazapam 0.25bid
2	60	WM	Sev	Present		olanzapine 40 daily, clonazapam 1mg qhs
3*	65	WM	Prof	Present	Yes	quetiapine 800 daily, paroxetine 30 daily, clonazepam 0.5 hs
4	60	AAM	Sev	Present	Yes	**quetiapine 600 daily**, lorazepam 0.5 bid
5	62	WM	Prof	Present		**olanzepine 10 daily**, **fluoxetine 80 daily**, gabapentin 800 daily
6	42	AAF	BIF	Present	Yes	**olanzapine 30 daily**, tizanidine 12 daily, mirtazepine 60 daily, baclofen 120 daily
7	51	WM	Mod	Present	Yes	**olanzapine 20 daily, sertraline 150 daily**, carbamazepine 200 tid
8*	52	WF	Sev	Present	Yes	**clozapine 750 daily**, **paroxetine 20 daily**
9	47	WF	Prof			**olanzapine 25 daily**, hydroxyzine 25 bid

Blank spaces denote Negative or No; *Negative; Sev: severe; Prof: Profound; Mod: Moderate; BIF: Borderline Intellectual Functioning

Table 2: Patients Presenting with Bowel Obstruction

Subject #	Age	Race, Gender	ID Level	Surgery Lower GI Tract	Baseline Meds (mg)
3*	65	WM	Prof	Yes, bowel resection	quetiapine 800 daily, paroxetine 30 daily, clonazepam 0.5 hs
8*	52	WF	Sev	Yes, previous exploratory surgery for abdominal ileus	**clozapine 750 daily, paroxetine 20 daily**
10	69	WF	Sev	Yes, resections	**quetiapine 450 daily**
11	32	WM	Prof	Yes, resections, colostomy bag	**clozapine 400 daily,** lorazepam 3 tid, gabapentin 2800 daily
12	59	WF	Sev	Previous bowel obstruction and megacolon, no surgery	**clozapine 375 daily**
13	29	WF	Sev	Yes, recurrent bowel obstructions	**risperidone 8 daily,** clonazepam 1 daily

Blank spaces denote Negative or No Negative; Sev: severe; Prof: Profound; Mod: Moderate; BIF: Borderline Intellectual Functioning

Such feeding-related medical and surgical problems multiply patients' traumatic experiences and significantly lower their quality of life, as detailed in the results regarding the 42-year-old female patient with spastic quadriplegia and borderline intellectual functioning who was too fearful to try eating orally again. She described this as related to her past traumatic experiences with aspiration pneumonia. In addition, patients are of necessity removed from the pleasures of eating and drinking by mouth if feeding is changed via an ostomy tube. One minimally verbal male in the series, aged 51 years, frequently gestured using a calendar to ask when his next swallow study was since he understood that foods could be introduced once his antipsychotic was tapered more and if his swallowing improved. At study end, he was still receiving gastrostomy feeds morning and night but could eat pureed food at lunchtime, which improved his mood noticeably. He had been tapered gradually, first off sertraline 150mg daily, then off olanzapine 10 mg daily, which he tolerated well. If he continues to tolerate oral pureed lunch meals, these will gradually be expanded in accordance with his specialist.

Thus, following gradual taper of antipsychotics and/or SSRIs, dysphagia symptoms gradually improved for those patients in our study in whom it was tried. One other published case report describes quetiapine-induced dysphagia in a 40-year-old Caucasian woman with bipolar mood disorder and moderate to severe DD. Her dysphagia resolved following the cessation of quetiapine treatment. The authors emphasize that antipsychotic-induced dysphagia may go unnoticed or misdiagnosed, especially in patients with severe DD. Clinicians must be aware of this rare, reversible, potentially profound adverse side effect. Although the patient was changed to olanzapine and her dysphagia resolved, swallowing should be monitored closely [10].

Our results are comparable with other studies showing the reversal of dysphagia symptoms by tapering off the antipsychotics in patients in the general population without DD. A systematic review of 14 case reports of dysphagia occurring with typical antipsychotics and 22 cases with atypical antipsychotics found that reversal of dysphagia occurred after tapering off the offending antipsychotic [11]. The authors point out that dysphagia may occur without accompanying extrapyramidal side effects, thus making it even less likely to be identified as related to the antipsychotic. This is even more of a risk in those who are minimally verbal and thus unable to communicate. Another study retrospectively reviewed a group of 17 elderly hospitalized patients with dysphagia receiving antipsychotics in comparison with 51 matched controls without exposure to antipsychotics. Those with antipsychotic exposure scored significantly worse when rated on the Dysphagia Severity Rating scale ($p<0.01$). Higher antipsychotic doses were associated with lower swallowing function ($p=0.04$) [9].

Antipsychotics were tapered extremely gradually in our series, by the smallest dose possible at consecutive monthly intervals, to prevent rebound agitation; worsening may occur if tapered too rapidly, according to clinical experience. However, there is no study or evidence to guide the rate of taper attempts formally. Clinicians are encouraged to make working diagnoses as far as possible, even in those with severe DD, including attention deficit hyperactivity disorder (ADHD) in adults also by taking childhood psychiatric histories. Emerging evidence suggests that ADHD medications, including low-dose atomoxetine and amitriptyline treatment trials, may benefit those with impulsive aggression or self-injury even in the presence of severe DD, and thus be antipsychotic-sparing [12]. In addition, risperidone in low divided doses such as 0.5 mg three to four times a day may be the most effective and best tolerated antipsychotic for self-injury and aggression, with fewer dysphagia side effects, although higher doses again may be causative [5]. Seizures are extremely common in individuals with severe DD, and it is vital to review cases for behavioral worsening by antiseizure medications. Trials of adding an antiseizure medication such as lamotrigine may also be worthwhile in those with bizarre behavior accompanied by a suspicion of seizures such as staring spells or episodes of confusion reported by caregivers, especially if electroencephalogram is not feasible due to severe behavior problems [12].

Hunger is another well-described side effect of atypical antipsychotics, especially in high doses. One verbal patient in the series repeatedly named hunger as her biggest worry and complained to staff many times a day that she felt hungry, in spite of eating full meals. This concern is significant, especially in minimally verbal and communication-impaired individuals who cannot verbally communicate hunger feelings. Individuals with DD may try to take their peers' food and become aggressive or self-injurious if redirected, try to enter the refrigerator or pantry, and may get up at night to try and eat. In addition, they often try to eat and drink too rapidly, thus needing close staff supervision while eating or being fed to prevent aspiration. Several patients in the series were made to follow eating routines of one swallow, then one sip of fluid, and in one case, also cough before the next spoonful of pureed food. This is another stress on staff and a serious limit to patient autonomy.

As stated above, mechanisms of antipsychotic-induced dysphagia and subsequent aspiration pneumonia are likely due to receptor blocking effects of dopamine and serotonin receptors. Typical antipsychotic medications are potent dopamine-D2 antagonists, while atypical antipsychotics have lower binding affinity for dopamine-D2 receptors but higher affinity for 5HT2A serotonin receptors [13,14]. Dopaminergic changes in the extrapyramidal system likely modulate and regulate motor neurons involved in coordinating complex movements such as swallowing [11,16]. Dysphagia associated with these changes is documented for both typical and atypical antipsychotics [11,17].

The package insert for olanzapine lists swallowing difficulty as a severe possible side effect. However, all antipsychotics can cause dysphagia and constipation, not only in the elderly but in individuals of all ages (10). Those with dementia or more severe DD who are minimally verbal or have cerebral palsy are at much greater risk. In a 52-year-old female in this series, the surgery unit discontinued clozapine 750mg daily after she was admitted

for both paralytic ileus and aspiration pneumonia. While essential and life-saving, this resulted in marked restlessness and agitation when she was discharged. However, she later stabilized on divalproex after an emerging presentation of rapid cycling bipolar disorder, together with restarting clozapine at a much lower dose of 25mg twice a day, with risperidone 0.5mg three times a day, and lorazepam. She was able to have the gastrostomy tube removed and resume oral food intake following a normalized video swallow study. She also began working in the workshop, which she had not done before.

Studies report an increase in antipsychotic prescriptions for those with DD, based on increased rates of mental disorders among individuals with developmental disorders, including cerebral palsy [18]. Rates of polypharmacy (>2 antipsychotics) are also higher in those with CP only and CP with other neurodevelopmental disabilities compared with the general population [19]. In psychiatric inpatients, antipsychotic polypharmacy has been linked to significant adverse drug events, including gastrointestinal bleeding, falls, hypotension, extrapyramidal symptoms, respiratory depression, and suicidal behavior [20]. Few studies discuss the adverse effects of outpatient antipsychotic polypharmacy in those with DD. In addition, more studies are needed on dysphagia and bowel obstruction related to antipsychotic treatment in severe DD.

Limitations to the present study include the retrospective nature of the study and the association, but not proven etiology, between antipsychotic prescribing and dosage in those with severe DD and serious side effects. These include dysphagia, recurrent aspiration pneumonia, bowel obstructions, and related surgeries, including insertion of upper gastrointestinal ostomy tubes, bowel resections, and colostomy bags. Only a minority of patients in our series underwent a trial of gradual taper of antipsychotics and SSRIs; however, results in those who did are promising that such strategies are effective and should be attempted. If more literature becomes available on the topic in those with severe DD, guardians, and administrators may also be more open to such antipsychotic medication taper attempts.

CONCLUSIONS

Among the general population, individuals of all ages are at risk for developing dysphagia, aspiration pneumonia, constipation, and bowel obstruction with antipsychotic treatment, especially those with severe DD. The elderly and those with dementia are also more prone. Typical and atypical antipsychotics can be causative, related to their dopamine-blocking actions, in a dose-related manner. Treatment with antipsychotics and CYP2D6 enzyme-inhibiting SSRIs compounds the risk of these complications in this population. Gradual taper of such medications, including a cautious trial of taper of such SSRIs may improve oral feeding outcomes, independence, and quality of life. High doses of antipsychotics should be avoided in such individuals, while low dose risperidone in divided daily doses 3 to 4 times a day may be most effective and safe. Comorbidities such as attention deficit hyperactivity disorder should be clarified and treated with more appropriate non-stimulant ADHD medication trials in low doses if impulsive aggression and/or self-injury are present. Seizures are common in severe DD, making it vital to review cases for behavioral worsening by antiseizure medications, or also to try antiseizure medication for suspected seizures and bizarre behavior. Gradual taper of the offending antipsychotics and SSRIs may effectively improve oral feeding and quality of life.

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