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## The Effects of Anticholinergics on Mental Health

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The Effects of Anticholinergics on Mental Health

by

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## PERMISSION

Title           The Effects of Anticholinergics in Mental Health  
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### **Abstract**

This study reviews the case of a 51-year-old female patient experiencing mood with manic behaviors. Concurrent history and use of medications with anticholinergic symptoms further complicate the case. Most notable of symptoms included dizziness, drowsiness and blurred vision. Research of patients at risk for anticholinergic burden or toxicity is well documented. Patients with mood disorders that suffer from psychosis often are treated by medications that have anticholinergic properties and extrapyramidal side effects. Anticholinergic use is further complicated by aging, as tolerance for the effects of medications decreases. Concurrent medical and psychiatric conditions, along with anticholinergic effects, can all present with similar overlapping symptoms making it difficult for the clinician to differentiate the underlying cause. Patient use of over the counter medication must also be considered by the provider. This has the potential to complicate the medical and mental health condition of the patient, adding another layer of complexity to the decision making of treatment options. Clinicians need to be aware of the risks, benefits, and use of anticholinergic medications and their effects on patients. Anticholinergics should be thoughtfully prescribed. Patients should avoid chronic use of anticholinergic medications. The literature demonstrates severe and unwanted side effects of anticholinergic medications. This can lead to issues with adherence to the plan of care and lead to severe complications or even death.

## Background

Many medications have anticholinergic effects. Clinicians have used these medications to treat illnesses, such as Parkinson's disease and chronic pulmonary disease. Clinicians have also used these medications for antipsychotic related parkinsonian symptoms. An aging population presents with a unique medical and psychiatric complexity today. Unfortunately, it's not that uncommon for patients to carry two or more disorders or illnesses. Comorbidity in mental illness can result from a medical illness and a mental health illness or vice versa. It can also result from two concurrent mental health disorders. The National Institute Of Mental Health (2019) describes comorbidity as the co-occurrence of two or more disorders. A study in the United States, found that those with a single disorder actually met diagnostic criteria for two or more disorders, this comorbidity was found to be as high as 45 percent The National Institute Of Mental Health (2019). Comorbidity creates unique challenges for healthcare professionals due to the overlap of mental illnesses or mental illness with a medical condition. It is essential that health care providers be aware of medical and psychiatric conditions, and medications in order to treat illnesses. Awareness can reduce adverse effects and improve adherence. Interactions from anticholinergic medications can be due to the compounded effects from multiple medications. Anticholinergic toxicity from medications is all too frequent and cases are often seen in the emergency department. Clinicians need to understand which classes of medications have anticholinergic properties to avoid toxicity and other complications UpToDate (2019). Many medications have anticholinergic properties. In this case report, we will look at antihistamines, such as diphenhydramine. I will review treatment options for possible unwanted anticholinergic

effects from olanzapine (antipsychotic) and lithium (antimanic) for treatment of a bipolar disorder. This paper will explore the process for decision making and treatment options for a patient that experienced the burden of anticholinergic effects.

### **Case Report**

The patient is a 51-year-old married female admitted for a manic episode. No significant prior history of mental illness. The patient carries a current diagnosis of bipolar disorder. The patient had brain surgery approximately six months ago and presented with a post-operative head wound that is healing. The patient has existing medical diagnosis including hypertension, unspecified hypothyroidism, morbid obesity BMI >40, non-traumatic subacute subdural hemorrhage, and hyperglycemia.

The patient is currently receiving the following scheduled medications levothyroxine, Lisinopril, lithium, lorazepam, melatonin, metoprolol, olanzapine, stool softeners, trazodone, and zolpidem. The patient is taking as-needed medications, that include diphenhydramine IM/oral, Tylenol. Lithium was started on admission to manage manic symptoms of bipolar disorder. Labs were normal with the exception of lithium, which was below therapeutic ranges.

On admission patient was paranoid with labile mood, elevated affect, and aggressive behavior. The patient was uncooperative at times during the interview. She presented as disorganized with loose associations, and her thought content wasn't reality-based. The patient has a short attention span and required redirection. Her speech was rapid and tangential. Language and motor function normal. She denied homicidal or suicidal ideations. A review of organ systems was negative. The patient was placed on a 72-hour hold and petitioned for commitment and court ordered treatment with antipsychotic medications.

The patient at the last visit was calm and cooperative, with no signs of aggression. The patient had organized thoughts, and speech was normal. The patient had marked improvement since admission.

What was interesting about this case is what happened over our last visits. She reported concerns with complaints of her sinuses were drying up, vision changes, hand tremors, and issues with cognition. Consultation was sought with the nurse practitioner and psychiatrist, to discuss these acute changes. The goal of the team was to understand the patient's symptoms. Medication changes were identified as a possible area of concern. Recent initiation of lithium, there was concern for possible anticholinergic burden due to recent exposure to olanzapine and diphenhydramine. with lithium recently being started as a concern. The patient's recent history of brain surgery was also an area of concern. Labs were unremarkable and vital signs were stable with the exception of blood pressure. Nursing was asked to recheck vitals. Lithium dose was left unchanged. Medication with anticholinergic properties were reviewed. Patient was adherent to olanzapine and as needed diphenhydramine. She was referred to internal medicine after consultation with my preceptor and attending psychiatrist. An additional complication was her known chronic use of over the counter anticholinergic medications. Patient reported frequent use of ranitidine and often used cold preparations for allergies and colds.

Lithium in elderly patients should be cautious used and dosing should start at low end of the range. Older patients generally do not tolerate lithium as well as younger patients and may respond and exhibit signs of toxicity. Lithium side effects include but are not limited to confusion, decreased memory, muscle spasms, dry mouth, hand tremor, excess thirst nausea, vomiting, vertigo, seizure, lethargy and coma. Patient changes in vision can represent medication adverse effects. Patients should be medically assessed for dehydration, renal issues,

cardiovascular and thyroid issues. However, autonomic changes such as vision changes typically present concurrently with lithium toxicity. Similarly, vision changes can be a side effect of lithium and generally subside with ongoing treatment RxList (2019).

Anticholinergics are another concern. The patient has a history of taking anticholinergic treatments and reported she finds them to be helpful with her allergies. Although atypical antipsychotics have a lower side effect profile compared to typical antipsychotics, there is still a concern for anticholinergic effects. Pupil and vision changes are a concern with patients taking anticholinergics, and anticholinergic effects left untreated can lead to serious medical complications (Lieberman III, 2004).

This patient takes olanzapine both scheduled and PRN and also has Benadryl ordered PRN. The medical issues are also concerning hypertension and brain surgery, both carrying risk for vision changes. Because this patient was experiencing had tremors during the day, a potential side effect from lithium. Olanzapine also being a concern for EPS. According to Lupu, Clinebell, Gannon, Ellison, and Chengappa (2017), cognitive deficits are relatively common to bipolar disorders. Patients should have neurocognitive assessments performed to determine the impact of anticholinergic agents.

### **Literature Review**

The case report above brought about thorough investigative research and review of the benefits and risks of anticholinergic effects in mental health patients. A search was conducted using the databases Pubmed, CINAHL Complete, and SAGE journals utilizing the search terms "anticholinergic effects" AND "mental health" or "burden." Limiters and filters included full-text articles and those published within the last eight years. CINAHL complete yielded 132



results, PubMed produced 48 results, in which 14 articles were reviewed. The articles reviewed and expanded search on their respective references found 11 articles to be most relevant.

While conducting research and investigating the effects of anticholinergic medications, it should be notable that there has been significant research performed and literature on the anticholinergic medications benefits and burdensome effects.

Anticholinergics are prescribed often for various conditions in the management of symptoms, such as conditions related to depression, psychosis, respiratory diseases, Parkinson's disease, nausea, vomiting, and allergies. High comorbidity in an aging population is more likely to be treated with anticholinergics and either be prescribed or obtained over the counter.

Anticholinergics affect the muscarinic acetylcholine receptors, these are distributed widely throughout the body, and there is a high potential to see effects on the peripheral and central nervous systems Ruxton, Woodman, and Mangoni (2015). The effects seen by anticholinergics can vary by degree and severity depending on pharmacokinetics and pharmacodynamics.

Peripheral effects consist of dry mouth, dry eyes, urinary retention, and cardiac disturbances such as tachycardia. Central nervous system effects include agitation, confusion, delirium, falls, and psychosis-like symptoms, including hallucinations and cognitive impairment. The patient discussed in this report began experiencing symptoms dizziness, blurred vision, hand tremors, and cognition issues relating to confusion, memory, and thinking issues. The normal aging process, along with anticholinergic use, can contribute to a higher likelihood of cognitive impairment, this can further complicate assessment and evaluation. The patient discussed is not considered "older," however, given her current condition, she presents as "older," and therefore, there may be an increased risk for anticholinergic burden.

According to Lupu, Clinebell, Gannon, Ellison, and Chengappa (2017), olanzapine has a lower EPS risk but poses a significant anticholinergic burden. This particular patient was prescribed Olanzapine and Benadryl, both with anticholinergic effects. Increased risk of falling is associated with both the use of olanzapine and trazodone Ruxton, Woodman, and Mangoni (2015). The patient's medical condition and multiple medications may affect acetylcholine receptors; furthermore, it should be noted that trazodone represented on some burden scales as an anticholinergic and for others not. To further complicate this picture, as discussed, the patient recently started lithium, and a side effect of lithium can be confusion. Confusion affects cognition, and this can be concerning as it overlaps with other areas. Toxicity was not necessarily a concern at this point, as indicated by lab reports.

Discontinuation of anticholinergics is an option when patients are experiencing any of the peripheral or central nervous system side effects. Discontinuation, however, comes at the risk of a potential relapse of Extrapyramidal symptoms. Extrapyramidal side effects (EPS) are often related to antipsychotic use. EPS can greatly and negatively affect patient's adherence. Typical antipsychotics typically carry a higher risk of these symptoms than do atypical medications. Atypical antipsychotics should be accompanied by an anticholinergic to gain positive outcomes with atypical use Gillies, Sampson, Beck, and Rathbone (2013). Olanzapine, an atypical antipsychotic, is taken by the patient on a schedule and PRN basis. The patient experienced hand tremors, a potential cause of lithium as well as olanzapine, and there are challenges in treating the individual. According to Desmarais et al. (2014), relapse rates of EPS after discontinuation of anticholinergics in patients on first-generation antipsychotics were between 10% and 77%, and for atypical it was much lower between 4% and 33%. Discontinuation of anticholinergics

with high relapse of EPS should draw attention to the importance of monitoring for EPS in patients taking antipsychotic medications.

Anticholinergics like Benadryl, Cogentin, and Artane are often prescribed to minimize the burdensome effects of EPS. A small study of 20 patients showed that 18 of the participants, when taken off anticholinergics, slowly showed positive effects on cognition and displayed no significant changes with movement disorders Desmarais et al. (2014). Drug-induced movement disorders, or EPS, include Dystonia, Akathisia, Tardive dyskinesia, and Parkinsonism. Dystonia, which is prolonged muscle contractions and maybe in the form of rhythmic jerks. Akathisia or motor restlessness is an EPS that is characterized by intolerance of inactivity, cannot sit still. Tardive dyskinesia, a disorder resulting in involuntary, repetitive body movements. Long term use of typical antipsychotics can cause a condition called pseudo parkinsonism, characterized by tremor, hypokinesia, rigidity, and postural instability. Treatment of bipolar disorder and schizophrenia often requires antipsychotics that have anticholinergics properties but have other undesirable effects, that make treatment challenging. Olanzapine does not have a high incidence of EPS at lower doses but has relatively moderate anticholinergic effects. The potential anticholinergic effects, EPS, and adverse actions of diphenhydramine, trazodone, and lithium, creates a more complex picture, especially in a patient with a TBI.

To better understand anticholinergic effects, it is useful to understand available scales and measures. A literature review assessing the suitability for observational studies of current anticholinergic scales and measures, found that it's valuable to quantify anticholinergic burden, especially when attempting to determine the relative risk vs. benefit of anticholinergic use Lozano-Ortega et al. (2019). In scoring anticholinergic medications, each medication is placed in a category. Some anticholinergic medications are scored further by dose. The findings show

that scales and measures with high levels of anticholinergic burden have been associated with high risk and severity of falls, drug-related adverse effects, cognitive issues, and all causes of mortality Lozano-Ortega et al. (2019). There are several scales available to assess anticholinergic burden. Clinicians should be aware of these scales. Anticholinergic scales include the activity scale, burden classification scale, cognitive burden scale, drug scale, loading scale, and anticholinergic risk scale. Most antipsychotics vary in the severity of their anticholinergic effects. When combined with other anticholinergic medicines, it can be challenging to attempt to evaluate the burden that such treatments place on the patient. Attempts with burden scales and measures are one way the other is using a blood sample and test the anticholinergic activity, which has proven to be expensive and complicated Kim et al. (2019).

The anticholinergic burden scale has excellent potential in quantifying the exposure of anticholinergic medication and is useful in assessing risk versus benefits of prescribing anticholinergic medications. There are prescribing strategies that can be effective in the treatment of mental illness. A multidisciplinary approach with clinician, pharmacist, patient, and nursing, to name a few, can benefit not only medication prescribing but also monitoring. According to Sathienluckana, Unaharassamee, Suthisisang, Suanchang, and Suansanae (2018), management strategies include avoiding or discontinuing any medication that would impair cognitive functioning, certainly the use of anticholinergics in the absence of EPS. There are other strategies, such as using antipsychotic depot. Long term injectables have shown not to have lower peak levels, and plasma levels remain stable; furthermore, it is not associated with the increased use of anticholinergics Pristed, Correll, and Nielsen (2017). Strategies with carefully developed plans can improve patient outcomes, quality of life, and adherence.

It is important to note that schizophrenia and bipolar disorder with the psychotic features are associated with cognitive impairment. Prescribing antipsychotics is a standard treatment found to be effective in these patients. As mentioned, antipsychotic medications can cause significant extrapyramidal side effects. Prescribing anticholinergics can help with unwanted and burdensome extrapyramidal side effects. Current treatment guidelines do not recommend prophylactic or chronic long-term use of anticholinergics with antipsychotics Ogino, Miyamoto, and Yamaguchi (2013). Benztropine (Cogentin) and Trihexyphenidyl (Artane) are commonly prescribed to block the excitatory cholinergic pathways. Anticholinergics are also a potent dopamine antagonist. Because of this, dopamine antagonist affects patient's behavior can change, and signs of agitation, mood elevation, and psychosis can occur. With regards to EPS, it is essential to address their effects as it can have lasting effects on the attitudes of patients toward medication use and adherence. Reducing drug-induced side effects makes the use of anticholinergics beneficial, but only to the point where anticholinergics properties maximize the reduction in extrapyramidal side effects and do not exert their own unwanted and troublesome effects. This balance can be challenging to strike, and often patients will have some symptoms from one or the other. A thorough discussion of the treatment strategies with the patient should take place. Monitoring and evaluating the response to medication and any potential adverse outcomes is imperative to support adherence, patient safety and quality of life. It is essential to establish a relationship with the patient so that the clinician understands what is being experienced to make better decision making with regards to treatment. According to Ogino, Miyamoto, and Yamaguchi (2013), "If EPS appears, clinicians should consider lowering the antipsychotic dosage or switching to an SGA with a lower risk of EPS. The risk-benefit ratio of anticholinergics may be optimized when used at the lowest effective dose, and with those

patients at highest risk for EPS." There are benefits to providing long-acting antipsychotics in that they offer increased stability by allowing the clinician to offer the lowest effective dose to control symptoms and reduce the potential for side effects.

In attempting to understand the patient's symptoms in this case report, it is essential to try and understand the effects that medications, specifically antipsychotics and mood stabilizers, can have on each other. Understanding these dynamics can contribute to the overall underlying information used in the decision-making process regarding future treatment decisions. Asking targeted questions aimed at isolating EPS can assist in the use or need for anticholinergic medications. Does a mood stabilizer potentiate or induce the effects of antipsychotic EPS? According to Tataru et al. (2012), studies to identify EPS induced interaction between antipsychotics and drugs used for mood disorders has shown to have mixed results. With lithium, there was no evidence when used with Haldol that EPS was potentiated or induced. EPS was potentiated or induced when selective serotonin reuptake inhibitors and during tricyclic antidepressant use. Tataru et al. (2012). Mirtazapine showed to reduce EPS in patients on antipsychotics. More studies would be needed to understand the relationships between specific medications across classes better. Understanding the compounded effects of polypharmacy is important to patient safety, care and outcomes. Clinicians should make every effort to limit polypharmacy and review the medication list and patient symptoms frequently to avoid unwanted side effects and complications related to treatment.

### **Implications**

In working with patients that have comorbidities in the form of a mental health disorder in addition to a medical disorder, it is vital that the clinician needs to perform a thorough initial

assessment, and frequent follow up assessments, coupled with careful medication management and review. Chronic use of anticholinergic medications should be avoided. Providers should consider alternative medication to medications that cause EPS. When possible and beneficial to the patient a medication change from a first generation to a second generation would avoid anticholinergic effects from treating EPS with medications such as Cogentin. Critical thinking is necessary to ensure that the treatment plan maximizes the stabilization of mental illness symptoms and simultaneously, minimizes or reduces the risk of the patient's medication side effects. Moreover, it is essential to rule out any medical condition that may be limiting the patient's quality of life. Failing to acknowledge or effectively care for patients with medication side effects can lead to detrimental outcomes. Health care providers must be aware that adherence to the treatment plan can have a negative impact, toxicity can occur, patient safety jeopardized, and ultimately impact the patient's overall health and wellbeing.

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