Spring 5-15-2020

Identification of and Treatment Options for Catatonia

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Bachelor of Science in Nursing, University of Wisconsin- Milwaukee

An Independent Study

Submitted to the Graduate Faculty

of the

University of North Dakota

in partial fulfillment of the requirements

for the degree of

Master of Science

Grand Forks, North Dakota

December

2019

Permission

Title: Identification of and Treatment Options for Catatonia

Department: Nursing

Degree: Master of Science

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Abstract

Catatonia is a severe neuropsychiatric syndrome that is typically responsive to treatment if recognized early and treated accordingly. This case review will review the treatment of a 57-year-old white male who has a long history of severe mental illness who was hospitalized due to self-injurious and aggressive behaviors. He has a diagnosis of Schizoaffective disorder, bipolar type with catatonia. M is civilly committed as mentally ill with a court order for psychotropic medication, has a permanent guardian, and an order for protective placement. He has various medical co-morbidities that complicate his clinical picture and treatment options. Symptoms of catatonia have been resistant to traditional treatment options. Alternative treatments and medication adjustments are required to stabilize M's condition and behavior to allow him to return to living in a less restrictive environment.

An overview of the literature recommends benzodiazepines as the first line treatment for catatonia. Alternative treatments and medications have proven to be effective in the treatment of catatonia when symptoms do not remit to benzodiazepines. The plan of care developed for the patient described in the case study below reflects a combination of the literature's recommendations for treatment of catatonia that is not responsive to benzodiazepines.

More education, to clinicians, regarding the use of screening tools and identification of catatonia will lead to improved patient outcomes. Early identification of catatonia improves treatment response and decreases medical complications associated with the disorder. Further research in the area of options for treatment resistant catatonia, would be helpful in cases such as M's.

Background

Catatonia is a neuropsychiatric condition that is characterized by an alteration in psychomotor functioning. Symptoms may range from inhibition to agitation. There are two types of catatonia which are retarded and excited. Patients experiencing retarded type catatonia are more likely to present with staring, mutism, rigidity, and catalepsy where individuals with excited type exhibit more impulsiveness and combativeness (Morrison, 1973). One may also experience a mixture of retarded and excited catatonia with symptoms waxing and waning. The prevalence of catatonia is up to 18% of inpatient psychiatric patients. Complications can include aspiration, weight loss, dehydration, pulmonary embolism, renal failure, cardiac arrest and death (Beach, Gomez-Bernal, Huffman, & Fricchione, 2017). When there are issues with mobility, incontinence of bowel and bladder may also occur creating concern regarding skin integrity. It is important to recognize and attempt to appropriately treat symptoms of catatonia to avoid these serious medical issues.

The history of catatonia dates to 1874 when Kahlbaum originally described the syndrome as a disease of its own. Before that, Kraepelin had considered catatonia as a subtype of dementia praecox or schizophrenia. Catatonia was considered a subtype of schizophrenia even in the Diagnostic and Statistical Manual of Mental Disorders III (Pelzer, van der Heijden, & den Boer, 2018). It was thought at the time to have poor prognosis and to be a chronic condition. In the Diagnostic and Statistical Manual of Mental Disorders IV, catatonia was no longer linked as a subtype of schizophrenia (Appiani & Castro, 2018). It has been found that catatonia may occur with other mental health diagnoses such as affective disorders like bipolar. Catatonia has also been associated with other psychiatric diagnosis as well as medical conditions. There were further changes to catatonia classification to improve recognition and treatment in the Diagnostic

and Statistical Manual of Mental Disorders V (Wilson, Niu, Nicolson, Levine, & Heckers, 2014). Prognosis of catatonia is considered good now, especially if recognized and treated early.

A diagnosis of catatonia should be considered any time there is a decline in responsiveness and psychomotor function. There are various rating scales available to assist in the detection of catatonia. The Bush-Francis Catatonia Rating Scale (BFCRS) is one of the more commonly used tools in clinical practice (Sienaert, Dhossche, Vancampfort, De Hert & Gazdag, 2014). The rating scale can also be used to determine treatment response by comparing pre and post intervention scores.

Case Report

M was admitted to the Wisconsin state hospital for his third admission after experiencing escalating confusion, uncooperative behavior and requiring an increased number of staff to care for him. He had been throwing things, throwing himself on the floor, banging his head, attempting to bite staff and tried to exit a moving vehicle on the way back from a medical appointment. He had been residing at a community based residential facility since previous discharge from the state hospital.

M was born and raised in Wisconsin. He attended college prior to experiencing his first mental health episode. Onset of illness was in 1983. He was treated with lithium and was stable for 30 years. He was productive and able to work during that time. Lithium was discontinued when he developed kidney impairment. He is single, has never been married and does not have children. He has three brothers, one who has been his power of attorney and is now his guardian. He denies any history of trauma. Denies any history of alcohol or other substance abuse.

M has medical issues that have complicated his clinical presentation. Upon admission, he had a foley catheter due to a recent diagnosis of a urinary tract infection and urinary retention. He was treated with a course of antibiotics. He has since required a foley catheter again due to urinary retention and a bifurcated urinary stream from urethral stricture. This was addressed and foley catheter was again discontinued. He has a parotid gland mass and is status post right renal cell carcinoma ablation. During his hospital course, he has had another renal ablation to remove remaining areas of malignancy. M has also had a right total hip replacement and a total thyroidectomy. M suffers from chronic kidney disease. Lithium had been restarted despite kidney impairment because symptoms were not adequately controlled with other medications. M become lithium toxic and subsequently, the lithium was discontinued prior to the present admission. He has a diagnosis of nephrogenic diabetes insipidus from long term lithium administration. Creatinine has been elevated but stable. M has lost a significant amount of weight over the past year, at least 50 pounds. This is likely due to poor intake. Medical issues did not appear to be followed up on as recommended at the residential facility.

M has been diagnosed with schizoaffective disorder, bipolar type with catatonia. He is considered to have a treatment resistant form of the disorder. The catatonia is a mixed type where he alternates between retarded and excited types. There has also been consideration that M has a form of frontotemporal dementia, but he has not been psychiatrically and behaviorally stable enough to do a full evaluation with neuropsychological testing. He has a history of initially responding to medication and then the medication appears to lose its effectiveness over time.

As stated previously, M was stable on lithium for several years until it was discontinued due to kidney impairment. Once discontinued, M began to experience more psychiatric symptoms. Multiple medication trials have been ineffective in controlling both his bipolar and

psychotic symptoms. He had serotonin syndrome in 2017 and has developed catatonia. Treatment of catatonia with lorazepam at high doses disinhibit him. He has previously been treated with Electro Convulsant Therapy (ECT) which was thought to be successful for a period but then became ineffective. He was prescribed clozapine during his last admission to the hospital and was at a therapeutic dose without adequate remission of symptoms. Past medications include aripiprazole, oxcarbazepine, divalproex, carbamazepine, cariprazine, haloperidol, olanzapine and asenapine. Medications were either ineffective or M experienced extrapyramidal symptoms that did not improve with the addition of Cogentin or Benadryl. Catatonia symptoms included M grabbing and swinging at others, laying in bed for long periods of time flipping his head side to side, and repeatedly saying things like "ba." Literature needed to be reviewed to find effective treatment options to treat M's resistant catatonia.

The current psychotropic medication regimen of memantine 10mg twice daily, phenobarbital 48.6mg twice daily, and zolpidem 10mg three times daily has alleviated many of M's symptoms of catatonia. He is also on lamotrigine 225 mg daily and gabapentin 300 mg every 6 hours as needed for agitation. He is relatively stable and has had a decrease in aggression despite continued periods of agitation. He continues to experience catatonia at times, but the episodes have become much less than at time of admission. This case study will review over treatment options in the literature for pharmacological agents that could alleviate symptoms of catatonia for this case study patient. Current medication regimen will remain unchanged as M awaits placement to an adult family home in the community.

Literature Review

Methods

A literature search was conducted on PubMed and PsychINFO electronic databases using the terms “catatonia,” “benzodiazepine,” “NMDA,” “zolpidem,” “treatment,” “amantadine,” “memantine,” “phenobarbital,” “barbiturates” and “electro convulsant therapy.” Results were filtered to include articles published within the past ten years. Articles were reviewed for being applicable to this case study. The results filter was expanded to a larger time period when there was not significant literature regarding the use of a treatment.

Catatonia Treatments

Benzodiazepines are considered the first line treatment for catatonia. It is also the most widely studied treatment of catatonia (Pelzer et al., 2018). Lorazepam is often the benzodiazepine of choice. Benzodiazepines will “correct deficient GABA-ergic function in the orbitofrontal cortex (Sienaert et al., 2014, p. 3).” Benzodiazepines are often effective in reducing symptoms of catatonia. In studies, benzodiazepines were effective in 70% of treatment cases and individuals with catatonia due to an affective disorder were more likely to have favorable response than someone with schizophrenia (Denysenko et al., 2018). Dosing of lorazepam varies from 2 to 16 mg per day and the medication may be administered by mouth or intramuscularly/ intravenously if the individual has difficulty swallowing (Pelzer et al., 2018). Lorazepam is usually well tolerated and high doses may be given with minimal sedation. It is a rather short acting medication and effects may wear off in approximately four hours after administration. Concerns regarding lorazepam include tolerance and addiction. It may also cause a paradoxical effect in some individuals or result in disinhibition at high doses. Benzodiazepine treatment

effectiveness should be observable within 3-4 days after initiation of treatment and benzodiazepines should be considered a short-term treatment. If there is not a noticeable reduction in symptoms of catatonia with benzodiazepine treatment, alternative treatments should be considered.

Zolpidem is similar in action to benzodiazepines as a GABA receptor agonist (Bastiampillai, McGovern, Lloyd, Lingappa, & Nelson, 2016) and may be considered as an alternative to lorazepam when there has not been successful response to lorazepam. There have been case studies where zolpidem has completely resolved symptoms of catatonia and has been used to treat chronic catatonia with three to four times a day dosing. Zolpidem has been used in both retarded and excited forms of catatonia (Thomas et al., 2007). Use of a zolpidem challenge test may be beneficial in patients. According to H. Javelot, Michel, Steiner, T. Javelot, and Cottencin (2015), zolpidem can be used as an important diagnostic tool. This can be done by giving a dose of Zolpidem to a patient exhibiting catatonic like symptoms and if symptoms improve, they likely are experiencing catatonia rather than another condition. Although it is not clear when Zolpidem should be used over benzodiazepines (Denysenko et al., 2018), it should be considered as a treatment option and could be considered a first line treatment in some situations.

Electroconvulsive therapy is considered a secondary treatment of catatonia. It may be beneficial in individuals who do not respond to benzodiazepine treatment. It may also be considered in situations where the patient's life is in danger. Complications regarding consent can arise regarding electroconvulsive therapy. Mental health commitments may contain an order for medication in acutely mentally ill but do not include an order for electroconvulsive therapy. It is more difficult to obtain a court order for electroconvulsive therapy and risk of the patient's life must be proven to gain an order when the patient is too ill to consent. This would likely be

the case in an individual with catatonia. Electroconvulsive therapy can cause serious side effects such as confusion, short term memory impairment, delirium and cardiac issues (Aboraya, Chumber, & Altaha, 2009). One study reported an 85% response rate to electroconvulsive therapy (Sienaert et al., 2014). Treatment response can usually be seen after one or two treatments, although some may require more treatment sessions. Treatment approach must be individually approached regarding frequency of treatments and total treatments required. There are a few case reports that address the use of electroconvulsive therapy to treat chronic catatonia. Many treatments were needed to achieve a response and symptoms often reemerged after treatments were stopped (Sienaert et al., 2014). Electroconvulsive therapy is an effective second line option for treatment of catatonia, but it does there are some concerns regarding risk profile. The risks versus benefits should be considered prior to electroconvulsive treatments.

Barbiturates, such as phenobarbital, can also be used in the treatment of catatonia. It has been found that drugs with anticonvulsant properties such as barbiturates, can help to relieve catatonic symptoms (Taylor & Fink, 2003). Throughout the research, there is not a lot of evidence regarding the efficacy of barbiturates to treat catatonia. They are often tied in with benzodiazepines when being discussed as treatment interventions. Taylor and Fink (2003), state that the use of barbiturates dates to 1930 for catatonia treatment. A patient was effectively treated with amobarbital at that time. According to a study done in 1992, barbiturates have a 50% response rate in individuals with catatonia. They are not used as much anymore due to their narrow therapeutic range. They have been replaced with benzodiazepines which are viewed as a safer alternative to barbiturates (Appiani & Castro, 2018). Although not a commonly used current treatment, barbiturates were used in the past for the treatment of catatonic symptoms.

This class of medications should still be considered for use if the individual has treatment resistant symptoms and other more common treatments have not been effective.

Glutamate antagonists or N-methyl-D-aspartic acid (NMDA) antagonists are an alternative treatment approach that have been used when benzodiazepines have been ineffective. Medications that are NMDA antagonists are amantadine and memantine. According to Denysenko et al. (2018), these medications may be used as augmentation in lorazepam resistant catatonia. They may increase dopamine in the frontal cortex and striatum. Although the exact mechanism of action is not completely understood, amantadine and memantine "seem to act by counteracting dysfunctional neurotransmission associated with catatonia" (de Lucena, Pinto, Hallak, Crippa, & Gama, 2012, p. 571). Both are usually well tolerated with minimal psychiatric side effects (Hervey, Stewart, & Catalano, 2012). Case studies have shown that NMDA antagonists are more beneficial in patients with schizophrenia rather than affective disorders. In one case study by Carpenter, Hatchett and Fuller (2006), a patient with catatonic schizophrenia had a rapid reduction in symptoms with the use of memantine. Memantine is more often used as an adjunct to a benzodiazepine and amantadine is more often used as monotherapy. Doses of Memantine range from 5 to 20mg daily and doses of amantadine range from 100 to 600mg daily (Beach, Gomez-Bernal, Huffman, & Fricchione, 2017). Glutamate antagonists should be considered in patients with catatonia if they are not adequately responding to benzodiazepine treatment and there are barriers, such as inability to consent, to receiving electro convulsant therapy. This class of medication appears especially effective in patients that have schizophrenia with catatonia.

Anti-convulsants, such as carbamazepine, topiramate and valproic acid, can also be used to augment the treatment of catatonia with lorazepam. Speigel et al. (2019) recommended a

change in the standard treatment protocol for catatonia. The proposal is to augment lorazepam with an anti-convulsant when the catatonia is not fully treated by lorazepam and when the etiology of catatonia is likely due to conditions other than schizophrenia or schizoaffective disorder. Response to valproic acid took longer to see treatment effects in one case study when there was no response to benzodiazepines (Daniels, 2009). The use of anticonvulsants as adjunct treatment for catatonia may also have some mood stabilizing effects on individuals with bipolar disorder.

Atypical antipsychotics may be considered in the treatment of catatonia although their efficacy is not completely understood. There are thoughts that the neurotransmitter actions of atypical antipsychotics could increase dopamine release in the prefrontal cortex, therefore improving catatonic symptoms (Daniels, 2009). There are concerns that atypical antipsychotic may also cause or worsen catatonia and can also cause neuroleptic malignant syndrome. It is believed that individuals with catatonia may be at increased risk of neuroleptic malignant syndrome so some believe that atypical antipsychotics should be avoided with catatonia (Daniels, 2009). Aripiprazole, an atypical antipsychotic, has D2 partial agonist actions and may therefore be more effective in treating catatonia than other atypical antipsychotics (Beach et al., 2017). Giving an atypical antipsychotic, in cases of catatonia, may also help improve psychotic symptoms in patients diagnosed with schizophrenia. Research does not strongly support the use of atypical antipsychotics in patients that don't have a diagnosis of schizophrenia. Alternatives should be attempted due to the increased risk of neuroleptic malignant syndrome in patients that are not diagnosed with a psychotic disorder.

There are several other treatments for catatonia that are being trialed and have been effective in some case studies. Transcranial Magnetic Stimulation (TMS) is a treatment that has proven effective in some case reports (Daniels, 2009). It was reported effective in four cases of high frequency stimulation of the dorso-lateral prefrontal cortex (Sienaert et al., 2014). The mechanism of action of TMS in unknown but it is thought to be like ECT by affecting the GABA-ergic pathways (Beach et al., 2017). Minocycline has been reported to be effective in patients diagnosed with schizophrenia with catatonia (Denysenko et al., 2018). Again, the mechanism of action is unknown but is thought to act like memantine in the treatment of catatonia by having anti-glutamatergic properties (Beach et al., 2017). Dantrolene and bromocriptine are also mentioned in studies as possible treatments for catatonia. They were used in combination with other treatments in cases of malignant catatonia (Denysenko et al., 2018). Although only trialed in one patient, there is a hypothesis that vagus nerve stimulation may be an effective long-term treatment for catatonia. In the single case, of a patient diagnosed with schizoaffective disorder, significant improvements in catatonia symptoms were present a year later with vagus nerve stimulation (Zilles, 2019).

Implications

It is imperative for both current and future psychiatric providers to stay up to date on treatment options for catatonia. There are several treatment options discussed that warrant further research. The more evidenced based treatment options available, the better able providers are to adequately treat catatonia. Providers should consider catatonia whenever they are caring for a patient with psychomotor slowing as catatonia is much more common than many believe. If identified as early as possible and treated effectively, patients with catatonia experience fewer medical complications and are more likely to have complete resolution of symptoms.

Combination treatment should also be considered if monotherapy is not effective in resolving symptoms.

Conclusion

The etiology of catatonia is not completely understood and there is a lack of research on the efficacy of interventions for treatment resistant catatonia. Further research is needed on treatment options, especially in non-traditional treatments. Providers also need more education to improve early identification of catatonic symptoms and the use of scoring tools to identify catatonia to aid in identification. Increased research and improved education on identification and treatment options will help improve the outcomes of individuals experiencing this debilitating disease.

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