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Implications of Psychotherapy and Low-Dose Medication Following First-Episode Psychosis

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Abstract

Schizophrenia, a mental disorder characterized by hallucinations, delusions, and disorganized thoughts and speech, is typically treated using antipsychotic medication and therapy. Randomized trials focusing on schizophrenia have provided evidence that early intervention, which entails talk therapy combined with low-dose antipsychotic medication directly following onset of psychosis, is most effective in treating symptoms. The literature review detailed in this paper is intended to help better understand the relationship between low-dosage antipsychotic medication, pair with regular psychotherapy, and how that relationship can help patients to adhere to treatment for long-term remission.

Background

Elyn R. Saks first experienced mental illness at the age of eight years old, and was diagnosed with schizophrenia while she was attending Yale Law School in the early 1980's. When she experienced her first episode of psychosis, she was forcibly restrained and forced to take medication. Thirty years later, she has learned to live with her diagnosis by utilizing tools that include antipsychotic medication, regular therapy, and a strong support system that consists of close friends and family. She is now an Associate Dean, and Orrin B. Evans Professor of Law, Psychology, Psychiatry, and the Behavioral Sciences at the University of Southern California (Saks, 2013).

Schizophrenia is often associated with personal suffering, family burden, disability, and premature death, as well as societal costs. Schizophrenia is a serious mental illness that is characterized by hallucinations, odd behavior and speech, delusions, and incoherent thoughts. Recently, a randomized trial was conducted to provide evidence that early intervention, which entails talk therapy combined with low-dose antipsychotic medication directly following onset of psychosis improves symptoms and functioning over that of traditional care (Kane, et al., 2016). While there are comprehensive first-episode psychosis programs that highlight low-dose antipsychotic medications, as well as psychotherapy, vocational and educational recovery, and family education and support, few studies have been done to compare multimodal team-based approaches with usual first-episode care provided to first-episode patients (Kane, et al.,2016).

Traditional first-episode psychosis care consists of antipsychotic medication. This medication, and lack of adherence to long-term treatment by patients, is a primary issue when preventing relapse (Chien, et al., 2016). People with schizophrenia typically struggle with poor

medication adherence, which leads to inadequate control of symptoms. Adherence therapy (AT) is a kind of intervention that seeks to minimize patient's psychiatric symptoms by enhancing adherence to treatment plans (Gray, et al., 2016); AT is essentially a form of cognitive-behavioral therapy. There has been research on non-adherence to antipsychotic medication by first-episode psychosis patients to examine the relationship between behaviors and attitudes, though attitudes do not necessarily translate into behaviors (Hui, et al., 2016).

Therapy and medication are often combined and used as treatment for patients experiencing psychosis. Usually persons experiencing psychosis due to schizophrenia have some kind of experience with occupational therapy, but few are submitted to traditional forms of psychotherapy. Prior research suggests that patients and doctors have differing opinions on goals for such treatment in patients experiencing psychosis, which may compromise a patient's adherence to treatment plans (Moritz, et al., 2016). If doctors and patients agree on the purpose and focus of treatment regimes, as well as what symptoms are most important to treat, therapy and medication may be more tailored to specific patient needs.

Other factors when determining efficacy for patients and treatment adherence is early detection and the age of the patient around the time of onset. Combined intervention strategies are being used to improve early detection and quality of care in adolescents and young adults in the early phases of psychotic disorders (Lambert, et al., 2016) and there are various studies being conducted to examine the intervention's' cost-effectiveness. Psychotic episodes of schizophrenia usually first occur in adolescence and early adulthood, an important time when developing a sense of self, independence, relationships, and life plans. The onset of symptoms can be incredibly traumatic to the individual and may cause considerable mental trauma (OREYGEN,

2002). Younger patients diagnosed with schizophrenia are also less likely to experience adverse consequences and socio-economic problems due to their illness compared to adults that have received various treatments throughout their lifetime (Targum, et al., 2016).

Understanding Schizophrenia

Symptoms of schizophrenia typically arise at different ages for males and females; males exhibit symptoms typically between the ages of 18 and 25 years-old, while females exhibit symptoms later on, between ages 25 and 35 years old (Ochoa, et al., 2012). People with schizophrenia experience both positive and negative symptoms. Positive symptoms are symptoms that are "added" to a person's reality. Positive symptoms include delusions, hallucinations, disorganized thoughts or speech, and abnormal motor functions. Negative symptoms are reduced abilities, such as neglected personal care and hygiene, lack of emotion, or lost of interest in activities that used to bring pleasure (Mayo Clinic Staff Print, 2016). While the causes of schizophrenia are complex and not entirely understood, they are likely a result from the combination of family history, environmental factors, and neurochemistry. The neurotransmitters dopamine and glutamate have been found in excess in brains of individuals diagnosed with the disorder. Antipsychotic medications are thought to help control dopamine levels within the brain, helping to minimize symptoms.

Schizophrenia is usually diagnosed through a psychiatric evaluation, using DSM-5 assessment of symptoms (Mayo Clinic Staff Print, 2016). Brain imaging, using Positron emission tomography (PET), a three-dimensional imaging technique, can also provide insight into schizophrenia and possible treatments (Kirino, et al., 2016). PET scans monitor chemicals

and activity in the brain, and can help to diagnose a number of brain diseases and disorders (Mayo Clinic Staff, 2014). PET scans can detect minor but dynamic changes in a person's brain, helping to map the neurochemical responses schizophrenia is associated with (Kirino, et al., 2016).

Psychosis symptoms can often go untreated, especially if diagnosis is inaccurate at the time of the first episode. The complications if left untreated can be dramatic: suicide or suicide attempts, anxiety disorders, depression, substance abuse, social isolation, homelessness, health and medical issues, and sometimes aggression (Mayo Clinic Staff Print, 2016). Due to these complications, people diagnosed with schizophrenia have a life expectancy of 12 to 15 years less than those who have not been diagnosed with the disorder (Burgemeester, 2013).

Early Onset and Detection

While males and females present symptoms at different ages, the peak age of early onset of psychosis symptoms is between ages 12 and 29 years-old (Lambert, et al., 2016), but typically before the age of 18 (Kumperscak, 2013). Younger patients diagnosed with schizophrenia, or early onset schizophrenia (EOS) experience fewer unfavorable repercussions of the illness. Older patients, however, experience a lifetime of changing treatments, as well as socio-economic struggles related to their illness (Targum, et al., 2016). These age-related differences in experiences regarding psychosis treatment can influence the trajectory of therapy and adherence. Onset, severity, and trajectory of the illness are influenced by environmental and biological factors, while the intensity of episodes and rates of relapse are dependent upon psychosocial factors (Kumperscak, 2013). Environmental factors indicative of EOS can include maternal

malnutrition, fetal infection, and lack of fetal oxygen.

There have been advances in identifying individuals who are at clinical high risk (CHR), even before the onset of symptoms. In the brain, *N*-methyl-D-aspartate receptors, specifically in the cortical parvalbumin-containing interneurons (PVIs) were implicated in the positive and negative symptoms of psychosis, as well as the individual's levels of cognitive functioning (Barron, et al., 2017). Schizophrenia is twice as likely to occur in individuals with a relative with EOS, ten-fifteen times higher in fraternal twins, and fourty to fifty times higher occurrence among identical twins and someone with both parents who have been diagnosed with schizophrenia (Kumperscak, 2013).

Diagnosis of EOS can be difficult, and is often misdiagnosed. A child diagnosed with EOS can likely have another mental illness that is not schizophrenia. Symptoms of schizophrenia must be present for at least one month's duration. According to the Diagnostics and Statistical Manual of Mental Disorders (DSM-5), individuals must have experienced at least one of the following symptoms: hallucinations, delusions, or disorganized speech, with a total of two symptoms which might also include catatonic behavior or negative symptoms. Individuals may also experience levels of functioning that are below the levels experiences before symptom onset (Kumperscak, 2013). EOS individuals have a tendency to also fail to meet appropriate levels of social, academic, interpersonal, or occupational development.

Non-Adherence

People with schizophrenia have a high-frequency of non-adherence to medication and treatment. Treatment discontinuation is evident in approximately 74% of patients (Kingdon &

Turkington, 2006). Emotional abuse specifically can increase the chances of non-response to medications intended to treat psychosis (Misiak, et al., 2017). Non-adherence is most prevalent in males with schizophrenia (Hui, et al., 2016). Individuals who have been diagnosed with schizophrenia and its spectrum disorders have a 70-90% instance of relapse (Chien, et al., 2016). Non-adherence to antipsychotic medications for long-term maintenance is highly indicative of relapse and hospitalization (Chien, et al., 2016). Along with frequent hospitalization, non-adherence is also associated with severe positive symptoms, poor social support and connectedness, as well as substance abuse (Hui, et al., 2016). There is roughly a 47% instance of substance or drug abuse comorbidity within the schizophrenic population (Morrison, 2009).

There are various domains for non-adherence: patient-, medication-, and environment-related. (Hui, et al., 2016). Patient-related non-adherence stems from a patient's attitude towards medication, lack of insight into their mental illness, and substance abuse or self-medicating for psychosis symptoms (Abdel-Baki, et al., 2012). Medication-related non-adherence involves the efficacy of the prescribed antipsychotic medications, adverse side-effects, and weight gain (Abdel-Baki, et al., 2012). Environmental-related non-adherence can be a result of low levels of family and social support, and lack of therapeutic alliance (Abdel-Baki, et al., 2012). The development of therapeutic alliance, or a connection with a therapist, leads to patients remaining in psychotherapy in the long-term.

Understanding cognitive functions can also help with early detection and intervention to reduce the burden and risk of non-adherence after onset (Barron, et al., 2017). Having poor insight into the mental illness or not acknowledging the symptoms of schizophrenia can cause a person to relapse. Often times, patients stop taking antipsychotics when their acute symptoms

subside, and they can take days, weeks, or even months to experience the symptoms again, making it difficult to draw the connection between medicating and symptom subsidiation (Tartakovsky, 2016). Individuals with schizophrenia often have inconsistent routines, which can result in forgetting to take medication as well.

Medications

Antipsychotic medication is the primary treatment option for psychosis and individuals who experience schizophrenia (Hui, et al., 2016). While there are two primary generations of antipsychotic medications, the second-generation results in fewer side effects (Chien, et al., 2016). Second-generation, or atypical, antipsychotics include Aripiprazole (Abilify), Clozapine (Clozaril), and Olanzapine (Zyprexa). First-generation antipsychotics have significant side effects, and can often result in tardive dyskinesia, which is a movement disorder that in some cases be irreversible (Mayo Clinic Staff Print, 2016). First-generation medications include chlorpromazine, fluphenazine, haloperidol, and perphenazine. Second-generation antipsychotics can also be administered orally or injectable. Long-acting injectable (LAI) antipsychotics are more effective than oral antipsychotics for adherence and relapse prevention (Kim, et al., 2012). LAI should only be considered when a patient becomes non-adherent to treatment at any point, and should not be administered after first-episode psychosis. Interesting enough, though second-generation antipsychotics have fewer side effects associated with them, there is not an increased level of adherence among those patients who have been prescribed them. PET studies performed on psychosis patients have revealed that when 65-80% of dopamine receptors are blocked in the brain with the use of antipsychotic drugs it may increase a person's response to

clinical treatment (Kirino, et al., 2016).

Antipsychotic polypharmacy (APP), which is the prescription of two or more antipsychotic drugs to a patients at one time, is strongly advised against (Kadra, et al., 2016). APP, however, has roughly a 10-30% prevalence, especially in the male population diagnosed with psychosis. While APP is typical with second-generation antipsychotic drugs, the side effects can be extreme, resulting in a higher rate of non-adherence (Kadra, et al., 2016).

Pharmacological treatment can leave roughly 60% of psychosis patients with residual symptoms, even when a patient is compliant (Kingdon & Turkington, 2006). Injectable medication can increase adherence in patients with schizophrenia (Tartakovsky, 2016). If a patient misses an appointment for their injectable antipsychotics, their doctor or treatment team can intervene at an early stage, and potentially stop relapse all together.

Therapies

Treatment as Usual

There are various treatments that are typically applied to people with schizophrenia. Treatment as usual (TAU) consists primarily of medication, psychological consultation, home visits, mental health assessments, and brief education about the disorder (Chien, et al., 2016). Psychosocial intervention is also sometimes prescribed to patients, and includes therapies such as individual or family, social skills training, vocational rehabilitation, and supported employment (Mayo Clinic Staff Print, 2016). In extreme cases, when patients are nonresponsive to TAU treatments, electroconvulsive therapy (ECT) may be administered. Though this is the typical treatment provided to patients, none of these interventions are the most effective, at least when

used singularly.

Adherence Therapy

Adherence therapy (AT) may provide insight into the mental illness, as well as enhance motivation and management of the illness (Chien, et al., 2016). AT is based on a combination of motivational interviewing (MI) and cognitive behavioral therapy (CBT) (Gray, et al., 2016). AT aims to give the individual awareness of the mental illness, an understanding of the need for treatment and maintenance, as well as the ability to recognize events as pathological (Chien, et al., 2016). Adherence therapy can be used along with TAU in order to increase maintenance to treatment (Gray, et al., 2016).

A single-blind, randomized trial study was conducted over a period of 52-weeks to observe the long-term effects of regular AT (Gray, et al., 2006). The study sought to find evidence of adherence to talk therapy, as well as adherence to medications prescribed to combat psychosis symptoms. The conclusion of the study was that there was no significant difference in adherence to talk therapy. Rather, AT was found to be most useful for antipsychotic medication adherence.

Cognitive-Behavioral Therapy

Cognitive- behavioral therapy (CBT) is a specific type of one-on-one talk-therapy that is used as a treatment for various mental illnesses, including depression, anxiety, personality disorders, and schizophrenia (Zorumski, 2012). CBT is spread out over a period of time, usually consisting of 12 to 20 sessions, with follow-up sessions as needed. There are various stages of CBT the patient and therapist go through in order for it to be most effective. The first stage is assessment, where the patient explained their experiences and symptoms in depth to the

therapist. Next is the engagement stage, when the therapist helps the patient to understand the purpose and process of CBT, as well as reevaluate any negative beliefs the patient may have towards therapy or medication (Tartakovsky, 2016). The ABC model is used throughout treatment in order to help gauge experiences and symptoms of schizophrenia appropriately, and is used to organize confusing experiences (Kingdon & Turkington, 2006). The ABC model assesses the Activating Event, Beliefs of the patient, and Consequences of an experience. Goal setting is also an important stage of CBT, because it allows the patient and therapist to set realistic goals pertaining to the course of treatment. For example, a patient may have a relationship with a spouse or family member, so one of the goals of CBT might be relationship quality (Tartakovsky, 2016). Normalization is used to help reduce feelings of anxiety following a psychotic episode or experience. Collaborative analysis is a stage where having a trusting relationship between patient and therapist is pertinent. This analysis helps to review possible triggers and interferences that lead to the onset of an experience. Alternative explanations are developed by the patient as a coping strategy for experiences, and helps to dissociate symptoms from reality.

In regards to psychosis, CBT has the potential to improve both positive and negative symptoms. CBT uses special cognitive techniques to help correct inaccurate thoughts and emotions by promoting a comparison to observable truths, or reality (Zorumski, 2012). MI is also used in CBT to help link in the patient's mind that adherence to treatment will decrease the chances of relapse (Tartakovsky, 2016). This not only helps the individual acknowledge that they are experiencing symptoms, but also helps to separate these from what is actually happening. CBT is most effective in treating psychosis when it is combined with medication, and is

marginally more effective than any singular treatment option (Zorumski, 2012).

There is often times a reluctance to use CBT when trauma is evident in patients diagnosed with schizophrenia, especially in EOS individuals (Morrison, 2009). Trauma and PTSD are often found to be comorbid with psychosis, but CBT can address these disorders, while also counteracting the symptoms schizophrenia presents. Social unease and anxiety disorders can also be dealt with through CBT by challenging those thoughts consciously (Morrison, 2009). CBT has also proven effective to help increase an individual's resilience against their mental illness.

Analysis

A report was published in The American Journal of Psychiatry in April of 2016, that detailed a study conducted with schizophrenia patients submitted to a program that kept antipsychotic medication dosages low and focused on patient-to-counselor talk therapy (Carey, 2015). The Early Treatment Program (ETP) study is a part of the Recovery After an Initial Schizophrenia Episode (RAISE) stratagem implemented by the the National Institute of Mental Health (NIMH) (Kane, et al., 2016). RAISE focused on the development and execution of first-episode treatments in the United States health care system (Mueser, et al., 2015). The RAISE- ETP is known as NAVIGATE, and is a multimodal team-based approach provided in routine mental health treatment settings intended to help first-episode people reach functional and psychological health (Mueser, et al., 2015).

The study in 2016 chose thirty-four community mental health treatment centers in the U.S., in 21 different states. All sites, to be considered for the study, were required to have

experience in treating people with schizophrenia, early intervention interests following first-episode psychosis, sufficient staff to implement the experimental design, be able to recruit enough patients to participate, and reassurance that the experiment would be completed. NAVIGATE uses four primary interventions, being personalized medicine management, resilience-focused individual therapy, family psychoeducation, and supported employment and education (Kane, et al., 2016). The study lasted for two years, from 2010 to 2012, and was comprised of shared decision-making between therapist and patient, taking into consideration patient treatment preferences. Patients were randomly assigned to either community care (TAU) or NAVIGATE; there were 181 and 223 patients in each group, respectively (Kane, et al., 2016).

After the 2 year study was complete, the results concluded that NAVIGATE patients remained in treatment longer than community care patients (23 months average versus 17 months). NAVIGATE patients also had higher scores on the Quality of Life Scale, had increased levels of interpersonal relations, engagement in activities, and experienced decreased hospitalization rates and levels of depression (Kane, et al., 2016).

Implications

The results of the NAVIGATE study are important to consider moving forward, especially within the healthcare system. The current period between first-episode psychosis and treatment is about a year and a half (Carey, 2015). While this may not seem like a long period of time, the study shows evidence towards the importance of intervention as early as possible, and notes that the ideal window of intervention is within three months of first-episode. One of the main hindrances patients currently face when seeking treatment is cost. While medical insurance

covered some of the treatment costs of the NAVIGATE study, like therapy and medication management, government supplements are needed to make this treatment option viable across the country (Kane, et al., 2016). Prior to publication of the study, Congress had allocated $25 million of federal funds to the Substance Abuse and Mental Health Services Administration (SAMHSA) to use for first-episode interventions, including supported employment and education (Smith, 2014). Since 2014, states have been gradually combining SAMHSA funds with state funds in order to provide adequate early intervention and treatment for psychosis patients (Kane, et al., 2016).

It would also be of importance to use the talk therapy and medication management aspects of the study for long-term treatment plans. While patients showed greater improvements over the two years following smaller doses of antipsychotic medications combined with talk therapy (WebMD Archives, 2015), the positive results of NAVIGATE did not maintain themselves after five years. Using this evidence, it could be concluded that continuous and consistent treatment would need to occur for optimal success. Similar to adherence therapy that helps to maintain consistent adherence to medications, constant one-on-one therapy sessions along with smaller doses of medication could help patients achieve higher overall satisfaction and happiness.

Conclusion

Schizophrenia is a difficult mental illness to diagnose and treat effectively. The research reviewed here suggests that early intervention following first-episode psychosis can be most helpful for many people with schizophrenia. Similarly, there are various therapies that have proven to minimize symptoms of schizophrenia, the most effective being low-dosage second

generation medication paired with regular talk therapy. This helps to increase the chances of adherence to therapy and medication, and also helps the patient maintain a normal life.

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