

Popular Treatments for Patients with Schizophrenia

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## TREATMENTS FOR SCHIZOPHRENIA

### Abstract

The purpose of this literature review was to analyze five articles regarding various treatment methods for people with schizophrenia. Cetin (2015) provided an overview of the popular treatments of the past, present, and future. The second, third, and fourth studies presented examined popular psychopharmacology medications and compared the efficacy of them. Lammers et al (2013) compared risperidone long acting injection with first generation antipsychotics. Percinel et al (2014) focused on the efficacy of the only FDA approved second generation antipsychotic, clozapine. Kokurcan (2019) compared clozapine with long acting injectable and oral antipsychotics. All found a decrease in undesirable symptoms, but the drugs came with side effects. The final article discussed the benefits of combining CBT with psychopharmacology. By understanding the consequences of the treatments, further experimentation can be done to find a treatment method with little to no harmful side effects for those who suffer from schizophrenia.

*Keywords:* Schizophrenia, cognitive behavioral therapy, psychopharmacology, treatment, clozapine, risperidone long acting injection

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Schizophrenia is a serious psychotic disorder that affects people throughout the entirety of their lives and requires continuous treatment. Much research has been done about the psychopathology, symptoms, and treatments of schizophrenia, but a consensus on the latter has not yet been reached. There currently exists numerous treatment methods and medications for those who suffer from schizophrenia, but more research is being done to determine the best method. Current methods typically include drug therapy with first-generation antipsychotics (FGA) and second-generation antipsychotics (SGA), the latter more preferred for its decrease in potential life threatening side effects compared to the former. Another form of antipsychotics that are common in the treatment of schizophrenics are long-acting injectable antipsychotics of the second-generation formulation, which can be used for patients who prefer to consume fewer pills. While drug therapy seems to be the favorable course of treatment, certain researchers conducted studies that show the effects of cognitive behavioral therapy (CBT) on the positive and negative symptoms which are common amongst schizophrenics, indicating that psychosocial approaches are an important aspect of the treatment process. Discussed below are the results of different experiments that aim to identify the pros and cons of various treatment approaches.

### **Literature Review**

Mesut Cetin (2015) analyzed the functionality and side effects of FGAs and SGAs on patients with schizophrenia. Cetin did this by examining the common historical, present, and future treatments and how they react with the brain's neurotransmitters. Both FGAs and SGAs focus on eliminating the positive symptoms of schizophrenia, but do so in different ways. FGAs act on dopamine pathways in the brain and cause extrapyramidal symptoms (EPS), while SGAs

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also work on antagonists in the dopamine pathways, but cause an insignificant amount of EPS, if any at all. This inevitably led to the abandonment of FGAs. A NIMH-funded CATIE study was conducted in 57 centers in the United States and showed that while SGAs are preferred to FGAs, an emphasis mitigating the metabolic side effects of SGAs was necessary to prevent negative symptoms in patients. A large concern among physicians was weight gain and patients who were already overweight were limited in their use of SGAs and a social support system that helped the patient monitor their weight was recommended. Suicide is more of a modern concern among schizophrenia patients and clozapine became the first FDA approved SGA, largely for its anti-suicidal effects. Various psychosocial approaches were developed and combined with pharmacotherapy, but the latter remains the dominant form of treatment among physicians. Cetin (2015) also discussed the results from a broad meta-analysis that compared the effectiveness of 15 different antipsychotic drugs. The results from that experiment, showed that 100% of the drugs had a significant impact on the delusions and hallucinations patients experienced when compared to placebos. With this, Cetin (2015) concluded that it is imperative for patients to be treated with antipsychotic drugs. There is a consensus on the necessity of using antipsychotic drugs, but the use of injectable antipsychotics, specifically risperidone, is still being debated. Benefits among researchers has not been concurred upon, and the varied results between patients do not help in solving this debate. This analysis provides information on a variety of techniques and concludes that the use of FGAs is preferred when able to mitigate the metabolic and psychosocial side effects.

Risperidone long acting injection (RLAI) is a popular treatment technique for schizophrenia, however, as mentioned in “*Treatment of Schizophrenia: Past, Present, and Future,*” (Cetin., 2015), there is not much research available on the effectiveness of RLAI, in

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comparison to other forms of drug therapy. “*Risperidone Long-acting Injection in Schizophrenia Spectrum Illnesses Compared to First Generation Depot Antipsychotic in an Outpatient Setting in Canada*” (Lammers, Zehm, & Williams., 2013) showed data collected by retrospective chart review to compare the effects of RLAI and first generation antipsychotic injection (FGAI).

Included were patients on the schizophrenia spectrum that started depot therapy and have had at least 3 injections of a depot antipsychotic. Researchers collected data on the current dosages, age, weight, gender, time since diagnosis, and comorbidities. To determine if common side effects such as tardive dyskinesia (TD) or EPS were occurring, the Abnormal Involuntary Movement Scale and Simpson Angus Scale scores were recorded in cases where necessary. The results were manipulated in a way that would help determine the probability of treatment discontinuation and hospitalization after a period of 18 months. The retrospective chart review showed high levels of continuation of both RLAI and FGAI (77% and 86%, respectively,  $p = 0.22$ ) and low levels of hospitalization (14.3% and 12.7%, respectively,  $p = 0.09$ ). In terms of side effects, RLAI has a significantly lower incidence of EPS (17%,  $p < 0.001$ ) in comparison with FGAI (52.9%,  $p < 0.001$ ). Evidence of lower instances of TD were also seen, but the differences were not of statistical significance. There were no significant differences between treatments continuation and hospitalization rates in patients receiving RLAI or FGAI, but the lower rate of side effects in patients using RLAI is promising for future research.

There are numerous antipsychotic drugs on the market for treating schizophrenia, but clozapine is the first FDA SGA approved drug and is commonly used when patients show a resistance to other antipsychotics. Ipek Percinel, Kemal Utku Yazici, Hatice Serpil Eremis, Burcu Ozbaran, Sezen Gokcen Kose, Joanna Zemla, Tugba Donuk, & Bulent Idris., 2014 analyzed the efficacy of clozapine treatment in five different case, four with early onset

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schizophrenia (EOS) and one with very early onset schizophrenia (VEOS). *“The Role and Efficacy of Clozapine Treatment in Early Onset and Very Early Onset Schizophrenia Cases: Discussion of Five Cases”* focused on five adolescents with schizophrenia and the ongoing concerns on the side effects of clozapine. The prevalence of side effects for all cases were measured using the Extrapyramidal Symptoms Rating Scale (ESRS). The level of functionality as well as psychotic symptoms were evaluated using the Global Assessment of Functioning Scale (GAF) and Scale for the Assessment of Negative/Positive Symptoms (SAPS/SANS), respectively. Percinel et al (2014) found in four of the five cases, patients had a positive response to clozapine, while the only patient with VEOS, had a decrease trend in leukocyte and neutrophil counts as well as an increase in the complaint of symptoms which resulted in the discontinued use of clozapine treatment. In the four cases with EOS, clinical improvement and increase in functionality was observed. A concern amongst the cases observed was the significant increase in the risk of neutropenia in adolescents treated with clozapine (16%) compared to adults (3%), which was seen specifically with the patient with VEOS. This study determined that in cases where there are little to no risk factors among adolescents with schizophrenia, clozapine might be a promising option.

Schizophrenia affects all patients differently, thus, treatment typically corresponds to the patient’s current needs with some patients requiring a combination of drugs. Ahmet Kokurcan (2019) did a cross-sectional study at a university hospital in turkey and compared the clinical characteristics of schizophrenic patients taking clozapine alone, with those taking combined treatment, specifically, long acting injectable and oral antipsychotics. The assessments were similar to the ones used in Percinel et al (2014), SAPS/SANS, GAF, with the addition of the Calgary Depression Scale for Schizophrenia (CDSS) and Yale-Brown Obsessive Compulsive

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Scale (YBOCS). The sample consisted of 84 patients taking clozapine and 178 under combined therapy. Results of the experiment showed the severity of the negative symptoms was significantly higher in clozapine users ( $35.90 \pm 13.10$ ,  $31.98 \pm 12.38$ ,  $p = 0.019$ ) and clozapine patients had more hospitalizations ( $p < 0.05$ ). However, when examining those taking combined therapy, GAF scores were significantly higher ( $p < 0.05$ ). This shows that patients taking clozapine have more severe clinical symptoms, especially when looking at negative symptoms and depression, and although not significant, clozapine slightly improves positive symptoms.

As seen in the articles above, pharmacotherapy alone is typically inadequate in alleviating the positive and negative symptoms of schizophrenia. However, a CBT approach to schizophrenia has been found to be beneficial in treating psychosis when combined with pharmacotherapy. In “*Response Rates in Patients with Schizophrenia and Positive Symptoms Receiving Cognitive Behavioral Therapy: A Systematic Review and Single-Group Meta-Analysis*,” (Bighelli, Huhn, Schneider-Thoma, Krause, Reirmair, Wallis, Schwermann, Pitschel-Waltz, Barbui, Furukawa, & Leucht., 2018), the first meta-analysis was done examining the response rates of patients with schizophrenia to their overall and positive symptoms. 33 randomized controlled trials of 1142 patients with schizophrenia receiving CBT were analyzed and significant results were found. 44.5% of patients reached a minimum of 20% of reduction of overall symptoms and 13.5% reached the minimum of 50% reduction of overall symptoms. In regards to positive symptoms, similar results were found; 52.9% has a minimal improvement in positive symptoms and 24.8% were categorized in the much-improved reduction of positive symptoms. Other factors such as treatment duration, number of sessions, and age were not significant factors in response rates. Bighelli et al (2018) concluded that combining CBT with pharmacotherapy would prove to be beneficial in reducing the overall and positive symptoms

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associated with schizophrenia.

### **Discussion**

The five discussed articles have the ultimate goal of improving treatment options for those suffering from schizophrenia. Attempting to live with the symptoms caused by schizophrenia is a challenge and there needs to exist a medication that can adequately provide relief for these patients without creating new life threatening symptoms. As a generalization, pharmacotherapy, specifically with drugs like clozapine and RLAI, is held to be the dominant form of treatment. The first four mentioned studies showed the necessity for the addition of psychosocial therapy and the final study described confirmed the benefits of CBT in the reduction of symptoms.

The study done by Cetin (2015) emphasized the preference of SGAs in comparison with FGAs for the lack of more serious side effects. SGAs were still limited in their use because of the metabolic side effects associated with them. The findings from this study corresponded with the findings from the study done by Percinel et al (2014) which examined the efficacy of clozapine treatment in five cases. Both studies agreed on the fact that clozapine is the best course of treatment for patients who have a low risk of symptoms. The latter study had its limitations which would affect its ability to be generalized. Percinel et al (2014) focused specifically on adolescents and on five individual cases who have only been diagnosed with schizophrenia a year before the study took place. Although clozapine was proven effective in reducing symptoms, the low number and young audience cannot be generalized to adults with more advanced stages of schizophrenia. Speaking further on the limitations of this experiment was the fact that the only patient with VEOS had to stop the treatment because of concerns from parents. More research needs to be done to support the findings of this experiment, preferably a

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double-blind, placebo controlled study with a much larger sample size.

*“Risperidone Long-acting Injection in Schizophrenia Spectrum Illnesses Compared to First Generation Depot Antipsychotic in an Outpatient Setting in Canada,”* (Lammers et al., 2013) provides another effective course of treatment for patients on the schizophrenia spectrum. RLAI proved to have a lower incidence of TD and EPS compared to FGAI. Similar to the study by Percinel et al (2014), low patient numbers compromised the analysis. There was also no significant difference between treatments in terms of treatment discontinuation or hospitalization, but the significant difference found in the decreased likelihood of EPS, shows the necessity for further research into RLAI treatment.

While the evidence from the study done by Kokurcan (2019) is promising for future research, it had several limitations. Being a cross-sectional study, it is impossible to draw conclusive causal associations between the factors observed. In addition to this, the patients studied had a wide variety of clinical characteristics due to the nature of the disease and this was not or possibly could not, be accounted for. Comparing two popular forms of medications is vital for our understanding of the psychopathology of schizophrenia. More long term studies need to be done to further analyze the implications of singular versus combined medication treatment options.

In sum, people suffering from schizophrenia have a choice when it comes to pharmacotherapy, and combining CBT is proven to reduce overall and positive symptoms. Experiments are currently being done that examine side effects of past, current, and future medications and the scientific community is aware that more research is required. Treatments for schizophrenia has many undiscovered features and limitations that future research aims to uncover.

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