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REVIEW OPEN ACCESS

The Integration of Olanzapine and Cognitive Behavioural Therapy for the Treatment of Schizophrenia: A Literature Review

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Abstract

Introduction: Schizophrenia is a serious psychiatric disorder that significantly impacts a person's quality of life. This condition is characterized by three groups of symptoms: positive, negative and cognitive. There have been developments of new therapeutic methods for treating schizophrenia, both pharmacological and psychotherapeutic. Antipsychotic drugs such as the second generation antipsychotic olanzapine are often the first course of treatment, for the purpose of controlling symptoms. However, research has determined that using antipsychotics alone may limit its long-term effectiveness and produce adverse effects. Psychosocial interventions like cognitive behavioural therapy (CBT) aim to reduce psychotic symptoms and prevent relapse when used in conjunction with medication. This review aims to discuss the effectiveness of the integration of olanzapine and CBT, and how these treatments improve symptom reduction, reduce relapse and reduce the occurrence of adverse effects.

Methods: A literature search between the years of 2010 to 2020 was conducted using PubMed and PsycInfo. Keywords included variations of "schizophrenia", "treatment", "olanzapine", and "cognitive behavioural therapy".

Results: Olanzapine by itself was found to improve symptom reduction, yet showed adverse effects such as weight gain and extrapyramidal symptoms. CBT used as a lone treatment of schizophrenia showed less adverse effects than antipsychotics, yet was significantly less effective than both antipsychotics alone and the combinatorial treatment of CBT and olanzapine. The integration of olanzapine and CBT demonstrated an overall improvement in a schizophrenic patient's health.

Discussion: The integration of olanzapine and CBT show promise for symptom reduction, relapse prevention, reduced occurrence of adverse side effects, and the overall improvement of one's health.

Conclusion: Individuals diagnosed with schizophrenia experience emotional, physical and social hardships, thus it is imperative that physicians are aware of current treatments that can be tailored to best treat their patients.

Keywords: schizophrenia; treatment; olanzapine; cognitive behavioural therapy

Introduction

Schizophrenia is a serious psychiatric disorder, affecting approximately 1% of the world's population and significantly impacting a person's quality of life [1]. This disabling condition is commonly characterized by three groups of symptoms: positive, negative and cognitive. Positive symptoms include the presence of superimposed behaviours, such as hallucinations and delusions [2]. Negative symptoms represent the inability or absence of a normal function, such as poverty of speech and a lack of pleasure [2]. Cognitive symptoms fall under a new category, including disorganized thoughts and difficulties with memory [2]. Schizophrenia is commonly diagnosed in patients who are in their late teens or early adulthood; however, diagnosis is not uncommon for patients in their middle ages [3]. There is an increasing amount of evidence that suggests that men are more likely to have early-onset schizophrenia than women, particularly in young adulthood [3]. Despite the extensive studies done in the field of schizophrenia and countless treatment options discovered, a cure has yet to be found [4]. There have been vast developments over the years outlining new therapeutic methods for treating schizophrenia, both pharmacological and psychotherapeutic. Together, these methods of treatment aim to not only relieve the symptoms of schizophrenia, but to also increase the patient's quality of life [3].

There have been various pharmacological interventions that have been prescribed for the treatment of schizophrenia including antipsychotics, antidepressants, and tranquillizers [5]. The most commonly prescribed medication between the years of 2000-2015 among pharmacological treatments was antipsychotics, which was administered to 94.8% of patients

in an observational study conducted by Toto et al. in 2019 [5]. Antipsychotic drugs are often the first course of treatment, as patients usually experience positive symptoms first, which need to be controlled [6]. Thus, during early onset of the disease, treatment with antipsychotic drugs results in significant symptom reduction of hallucinations and delusions [6].

A class of antipsychotic drugs that have been most commonly used are second-generation antipsychotics (SGA). This class of medication has been succeeded by first-generation antipsychotics (FGA), and are found to be more effective in terms of improving cognitive function [7] and their association with fewer extrapyramidal symptoms [8] when treating schizophrenia. These extrapyramidal symptoms are characterized as drug-induced movement disorders, which can include motor restlessness [9]. The American Psychiatric Association (APA) also notes that SGAs, with the exception of clozapine, are the first-line of treatments for schizophrenia [8].

FGAs are D2 antagonists, which means they work by blocking only the dopamine D2 neuroreceptor [10]. This is in contrast to SGAs, which typically function by blocking both the dopamine and serotonin receptors, specifically the D2 dopamine and 5HT2A receptors, respectively [10]. A blockage caused by these SGAs would impact serotonin's roles in behaviour and motor activity, as well as dopamine's involvement in motor function, emotion and cognition [10]. The inhibition of downstream signaling pathways by both classes of medications results in the reduction or prevention of psychotic symptoms.

The use of SGAs significantly increased from 2005 (62.5%) to 2010 (88.9%), due to various studies that showed they were more effective than FGAs [5]. The most common SGAs according to their prescription rates found in 2015 were clozapine (21.3%), olanzapine (20.7%), risperidone (17.7%) [5]. All three oral medications display antipsychotic efficacy; however, adverse effects and neurophysiological activities vary between each medication.

Clozapine was one of the first SGAs to be approved by the FDA in 1990 [11]. The drug was developed as an alternative option to then-current treatments for schizophrenia such as chlorpromazine, due to their involvement in causing movement disorders [12]. Recent research has described clozapine to be a third-line treatment or to be used for treatment-resistant patients, due to the serious adverse effects associated with it [13]. These adverse effects include but are not limited to: agranulocytosis, seizures, myocarditis, and respiratory and cardiac arrest [12,14]. Due to its status as a third-line treatment and its abundant amount of adverse effects, clozapine as a method of treating schizophrenia will not be a focus in this review.

Olanzapine and risperidone are considered to be first-line medications for schizophrenia [15]. Both drugs were found to have similar beneficial effects in terms of improvement of symptoms; however, minor variations of adverse effects were found to be associated with these two drugs [16]. Studies comparing these two antipsychotics found that olanzapine is more effective at treating negative symptoms and decreasing the overall clinical severity of schizophrenia [16,17,18,19]. Adverse effects including weight gain, hyperlipidemia and hyperglycemia were comparable with both groups and did not show significant variation [16]. Further studies show the superior efficacy of olanzapine compared to other antipsychotics, based on its high adherence and improvement of the Positive and Negative Syndrome Scale (PANSS) and Brief Psychiatric Rating Scale (BPRS) [20]. The PANSS is a 30-item scale used to measure the severity of symptoms for individuals diagnosed with schizophrenia [21], while the BPRS is a 24-item scale used to measure psychiatric symptoms, including depression, anxiety and hallucinations [22].

Previous research has determined that using antipsychotics as a treatment alone may limit their long-term effectiveness and produce further adverse effects [4]. In an empirical study conducted in 2013 by Valenica et al., patients who received antipsychotic treatment combined with psychosocial interventions, specifically social skills training, showed a higher symptom reduction rate compared to those prescribed antipsychotics alone [23]. Psychosocial interventions are interpersonal activities that involve educating the patient on their disorder, and the importance of medication adherence, family involvement and counselling, social skills training, and cognitive behavioural therapy (CBT) [24]. Like antipsychotics, the particular psychosocial interventions used in a patient's treatment plan should be tailored to the patient's needs and preferences. Of these methods of psychotherapy, CBT has received much attention due to having a strong evidence base for treating schizophrenia [25]. CBT is a highly effective psychotherapeutic treatment for psychological disorders, dating back to the early 1950s where it was used to treat depression and anxiety [26]. CBT as a method of treating schizophrenia has been proven to ameliorate both positive and negative symptoms of the disorder, and reduce the chance of patient relapse [26]. When CBT is used as an adjunct to pharmacotherapy, this course of treatment aims to reduce symptom relapse and increase antipsychotic adherence [25]. A review conducted by Rector and Beck in 2012 determined that patients undergoing CBT in conjunction with pharmacotherapy demonstrated a greater reduction of negative symptoms and patient relapse, compared to those who underwent pharmacotherapy alone [26]. CBT involves various self-help and coping strategies with the patient's illness, cognitive restructuring, and reality testing, with the overall goal being to develop healthier ways to manage their diagnosis [26]. CBT encourages social integration with a community, partaking in regular exercise, and helps reduce suicidal ideation and other violent thoughts and behaviours [24,27].

This review aims to discuss current therapies that have been shown to improve the overall treatment response

outcome for schizophrenia, in the context of symptom reduction, reduced relapse and reduced occurrence of adverse effects. The effectiveness of using either CBT or olanzapine as a method of treating schizophrenia, compared to their combined use will be explored. Lastly, this review will explore the advancements and limitations of these two types of interventions that have been made throughout the last decade.

Methods

A qualitative literature search was conducted using databases, PubMed and PsycInfo. Reports between the years of 2010 to 2020, with language restricted to English, were included and examined. Further criteria for inclusion were as follows: i) patients between the ages of 16-64 diagnosed with early-onset schizophrenia characterized by non-severe symptoms, ii) intervention includes cognitive behavioural therapy, second-generation antipsychotics, specifically olanzapine or a combination of both, and iii) has the outcomes of symptom reduction, relapse prevention, reduced occurrence of adverse side effects and overall improvement of one's quality of life.

Keywords included variations of "schizophrenia", "treatment", "olanzapine", and "cognitive behavioural therapy". The process of data extraction was performed by the authors and was managed through a spreadsheet that outlined the articles and corresponding data.

Results

Through the database search, 145 articles were identified through the given inclusion criteria. After removing duplicates and reviewing the titles, 90 articles remained. After reviewing the abstracts with the application of the exclusion criteria, 18 articles remained. Following screening the full-text articles, 10 studies were included and utilized for data collection and analysis.

Olanzapine

Olanzapine demonstrated a vast improvement in symptom reduction as described by the PANSS and BPRS scales [28,29,30,31]. However, common adverse effects that were mentioned were significant weight gain [29,30,31] and extrapyramidal symptoms [31]. In addition, the study by Jones et al. in 2015 found that olanzapine resulted in reduced relapse and hospitalization, which was demonstrated before and after follow-up (8.3% vs 32.6%, respectively) [32].

CBT

It was determined that CBT showed less adverse effects than those who took antipsychotics, or a combination of antipsychotics and CBT [33]. Two adverse events occurred in the CBT group; one attempted overdose, and one patient posed as a risk to others [33]. No other adverse effects were observed [33]. The PANSS scores were consistently lower in the CBT group, compared to those who had not received antipsychotics in 6 months, but were still receiving usual care [33]. It was also noted that CBT alone was significantly less effective than the combinatorial treatment of CBT and antipsychotics [33].

Integration of Olanzapine and CBT

The combined treatment of antipsychotics and CBT demonstrated a reduced amount of adverse effects, a reduction in relapse rate, a greater symptom reduction, treatment adherence, and an overall greater quality of life [34,35,36,37]. One study found a significant 7% lower patient relapse rate in the combined intervention group, in comparison to the medication-only group [35]. This improvement in symptom reduction was demonstrated within the improvement in the PANSS score [34,35,37].

Discussion

Information on the treatment for schizophrenia, both pharmacological and psychosocial, is vast and extensive. This can be seen as overwhelming for both care providers and patients, where it may be difficult to establish a treatment plan. SGAs are considered by the APA as the first-line of treatment for schizophrenia; however, the list of SGAs is widespread [8]. This literature review aims to provide a reference and basis for a combination of psychosocial and pharmacological interventions, and its associated data which describes its effectiveness. The combination of olanzapine and CBT as a treatment for schizophrenic patients was found to demonstrate a reduction in symptoms, adverse effects, and rate of relapse [34]. Additional psychiatric comorbidities are prevalent in schizophrenic patients. The majority of studies took depression and anxiety into account [30,31,33,34,36], while other studies specified other comorbidities as part of their exclusion criteria [29,35,37]. Two studies had no indication of any psychiatric comorbidity [28,32]. These comorbidities serve as an external factor that may influence the overall treatment outcome. It is understood and demonstrated that every patient is different, and the treatment plan in which they are assigned will be unique according to their needs. Thus, creating a specific treatment plan for each patient is vital for optimal treatment outcomes. It is important for care providers to have a reference base of the limitations and efficacy of the current medications and/or interventions in tailoring a treatment plan for their patients.

A search of available treatments for schizophrenia showed that olanzapine and CBT were ranked as one of the best antipsychotic medications [5] and psychosocial interventions [25], respectively. As these two treatment methods are individually successful, this review focuses on the possible outcomes of the integration of these two treatment options. As previously mentioned, olanzapine provides a significant reduction of negative symptoms and decreases the overall severity of schizophrenia [16,17,18,19]. Recent literature investigating olanzapine's recommended dosage of 10 mg/day has determined that a lower dose, a

reduction of 50%, has a higher response rate and improvement of negative symptoms in schizophrenic individuals [38]. In addition, there has been an increased amount of research and trials conducted on this drug, with studies investigating and comparing its efficacy and amount of adverse effects with other antipsychotic medications [28,29,30]. Overall, olanzapine has remained quite consistent over the past decade, with additions in terms of evidence and research, such as the impact of dose reduction [38].

Similarly, CBT has proven to improve both negative and positive symptoms of the disorder and reduce patient relapse [26]. CBT has not varied in relation to practice and method, as it is already such an adaptive form of treatment with set guidelines [39,40]. Through the data and preliminary evidence described by Morrison et al. in 2018, it has been suggested that CBT may be advantageous for individuals experiencing psychosis who choose to not take antipsychotic medication [34]. In addition, there have been recent explorations in terms of the integration of both olanzapine and CBT. Based on the data extracted and analyzed from the literature review, it was found that the integration of olanzapine and CBT effectively reduced the positive, negative and cognitive symptoms of schizophrenia [34,35,36,37]. Morrison compared the effectiveness of CBT to various antipsychotics, such as olanzapine, for the treatment of schizophrenia [33,34]. Morrison's main findings were that CBT alone had less adverse effects than antipsychotics or the combinatorial group; however, antipsychotics integrated with CBT was significantly more efficacious than CBT alone [33,34]. Current literature describes that a combination of psychosocial interventions and pharmacological treatments are best when treating schizophrenia [41]. The integration of olanzapine and CBT further emphasizes this claim, as the combination has shown a greater reduction in symptoms, adverse effects, and rate of relapse when compared to one treatment alone [34].

Although olanzapine is associated with a limited number of adverse effects in the treatment of schizophrenia, these antipsychotics are associated with an increased risk of weight gain, obesity and cardiovascular diseases [37]. The Superwellness Program conducted in 2017 assessed the effect of a CBT-based intervention on the weight gain of patients who were prescribed antipsychotics, namely olanzapine, compared to those receiving treatment as usual [37]. The results of this study revealed that the integration of CBT had decreased the individuals' body mass index (BMI) by 0.6 kg/m [2], whereas those who did not undergo CBT had shown an increase in their BMI levels [37]. This study determined that the longer the patient had been diagnosed with schizophrenia, the less of an impact CBT had on reducing BMI levels [37]. Thus, the decrease in BMI levels due to the integration of CBT with regular antipsychotic treatment may reduce the risk of obesity, as well as cardiovascular disease, particularly when integrated into treatment at the early stages of diagnosis [37]. In a study by Birur et al. in 2016, schizophrenic patients being treated with olanzapine observed a mean weight gain of 2 kg and incurred a significant number of extrapyramidal symptoms [31]. It's also important to note that using CBT in conjunction to antipsychotic treatment has been determined to be less effective when the patient does not view themselves as having a mental health problem [42].

As there are countless antipsychotic medications with various efficacies and side effects to treat schizophrenia, care providers must create a comprehensive treatment plan that is tailored to the individual's condition and needs. When creating a treatment plan, it's necessary for the clinician to take into consideration the patient's potential to incur adverse effects, as well as non-adherence [8]. Shared decision making (SDM) is a treatment approach which allows patients to have a more active role in the decision of their treatment, whilst collaborating with their clinician [43]. Both the clinician and the patient must be committed to the SDM approach, with the patient being open and honest during consultations, and the clinician willingly sharing the responsibility of creating the treatment plan [43]. The patient's preferences can be accounted for by using stated-preference methods, such as surveys and discrete-choice experiments (DCE) [44]. These DCEs provide patients with a list of hypothetical treatment options, from which they can select their preferences [44]. In a statistical analysis conducted by Levtain et al. in 2015, 301 schizophrenic patients who completed a DCE indicated that a reduction in positive symptoms is the most important outcome of their treatment [44]. This importance in the reduction of positive symptoms provides insight into the surveyor's preferences, and it allows their physician to take this into consideration when collaboratively creating the patient's treatment plan.

Due to the nature of the data and the overall concept of this review, there are some limitations that are important to consider. A limited number of articles were yielded during the literature search and selection process. This can be due to the 10-year restriction that was imposed during the selection process. However, based on this finding, it can be argued that there has not been much research on this topic within the past decade. Due to this lack of data, additional research and examination are needed for the combinatorial treatment of olanzapine and CBT, in order to better understand its effectiveness and interaction with one another. Another limitation that was identified during the literature review was the use of strictly CBT-only treatment for schizophrenia; as it's uncommon for antipsychotics to not be prescribed to a schizophrenic patient, there was a low yield of articles for CBT-only treatment [8]. CBT-only treatment is mainly associated with psychiatric conditions, such as depression and anxiety [26]. When used in conjunction with antipsychotics to treat schizophrenia, CBT primarily aids in the reduction and management of symptoms [25,26]. In the review by Pontillo et al. in 2016,

CBT reduces the perceived power of voices due to schizophrenia, but not the actual experience of voices [45]. Additionally, there is no standardized treatment plan for schizophrenia in terms of which medication or psychosocial intervention a patient should be prescribed. Treatment programs are ever-changing, emphasizing the existence of second- and third-line medications as patients can become treatment-resistant [46]. Psychiatrists can either add, modify or switch medications if they see the efficacy of the drug declining, or if no response is evident [47]. This further emphasizes the fact that schizophrenia is a multi-faceted and complex disease, where treatment plans are tailored to the patient's needs.

Conclusion

Individuals diagnosed with schizophrenia experience emotional, physical and social hardships. Thus, it is imperative that care providers are aware of the therapeutic effects and limitations of current interventions, equipping them with the most recent information which can be used to create the best treatment plan for their patients. The information presented in this literature review is vital, as it further emphasizes previous findings of the effectiveness of the integration of olanzapine and CBT in the treatment of schizophrenia. Furthermore, recent data was used to compile information on these two treatments, both used individually and in conjunction. The integration of these treatments shows promise for symptom reduction, relapse prevention, reduced occurrence of adverse side effects, and the overall improvement of one's health. As previously mentioned, one limitation of this review was the fact that there was a limited amount of research conducted within the past decade on the integration of olanzapine and CBT. As the research in this review demonstrated the promising outcomes of this integrated treatment, it is imperative that more research is conducted to further support this claim.

List of Abbreviations Used

CBT: cognitive behavioural therapy
SGA: second-generation antipsychotics
FGA: first-generation antipsychotics
APA: American Psychiatric Association
PANSS: Positive and Negative Syndrome Scale
BPRS: Brief Psychiatric Rating Scale
BMI: body mass index
SDM: shared decision making
DCE: discrete-choice experiments

Conflicts of Interest

The authors, Raymond Tolentino and Aoife McMahon, declare that they have no conflicts of interest.

Ethics Approval and/or Participant Consent

This literature review did not require ethics approval and/or participation consent.

Authors' Contributions

RT: made substantial contributions to the design of the study, collected and analysed data, drafted the manuscript, and gave final approval of the version to be published.
AM: made substantial contributions to the design of the study, collected and analysed data, drafted the manuscript, and gave final approval of the version to be published.

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