Evidence Based Practice: Antipsychotic Medications & Inpatient Hospitalizations

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Schizophrenia is life-altering, debilitating mental health diagnosis that is ranked by the World Health Organization as “one of the top 10 illnesses contributing to the global burden of disease” (Fischer & Buchanan, 2022, para. 1). This disease is characterized by chronic or recurrent psychosis affecting social function, occupational impairments, and results in economic catastrophes. Patients with this illness may experience delusions, disorganized speech, paranoia, impairments in cognitions, and altered sense of being. These manifestations are life-long and disabling for both the patient and their families (Fischer & Buchanan, 2022).

Prescription antipsychotic medications can help patients with schizophrenia manage symptoms, achieve a functional lifestyle, and create meaningful relationships. These medications are prescribed either orally on a daily schedule or given as an intramuscular injection once or twice a month (National Institute of Mental Health, 2022). Unfortunately, antipsychotic medications are associated with unpleasant adverse side effects that have contributed to high rates of treatment nonadherence. Kishimoto et al., (2017) reports that 50% of patients with schizophrenia are medication non-adherent limiting pharmacotherapy efficacy. Nonadherence is correlated with increased emergency room visits requiring intervention for psychotic episodes and inpatient hospitalizations. It is reported that hospitalized patients with schizophrenia accrue four times the amount of health care expenses when compared to those who have not relapsed (Lafeuille et al., 2015). Injectable, long-acting antipsychotics were developed as a strategy to combat disease relapse cause by noncompliance (Lauriello & Campbell, 2022).

PICO Question

A PICO question was constructed by the author to integrate best research findings with clinical expertise to aid decision making. The PICO question is as follows: In adults diagnosed with schizophrenia, does the administration of long-acting injectable antipsychotic medications versus oral antipsychotic medications reduce inpatient hospitalizations for acute psychotic episodes related to medication noncompliance? To answer the clinical question, an extensive literature search was conducted, and three applicable, primary research studies were selected. Each article is discussed and appraised for validity and reliability by assessing its level of evidence, applying the CRAAP (currency, relevance, authority, accuracy, and purpose) method, and assessing internal and external validity. After reviewing the literature, a synthesis of findings and applicability to patient care is discussed.

Literature Search

Trustworthy and accurate evidence is needed to answer the clinical question and inform evidence-based practice. A database search was conducted to find reliable information regarding the topic of antipsychotic medications, hospitalizations, and noncompliance. Three databases, Academic Search Premier, The Cumulative Index to Nursing and Allied Health Literature (CINAHL), and MEDLINE, were selected by the author for their high reliability, comprehensive datasets, ease of use, and inclusion of high-quality articles. When searching the databases, it is essential to use major search strategies, such as keyword searching, to ensure all available, relevant data is included (Melnyk & Fineout-Overholt, 2019). The keywords that were selected for this research included schizophrenia, antipsychotic medications, non-adherence, hospitalization, rehospitalization, long-acting injectable antipsychotics, and medication noncompliance. The author used the Boolean operator “AND” while searching the previously stated keywords to focus the search, generate productive results, and eliminate inappropriate findings. The search in all three databases was limited by selecting English language articles, human research studies only, adult age group, and articles that were published within the last ten years.

The CINAHL database yielded 10 results when using the previously stated exclusion criteria and keywords “schizophrenia and antipsychotic medication and hospitalization and non-adherence.” In a similar fashion, the author generated four applicable articles when searching “schizophrenia and long-acting injectable and medication noncompliance” in the MEDLINE database. Finally, Academic Search Premier produced nine research articles when searching “schizophrenia and long-acting injectable antipsychotics and rehospitalization.” This search process generated a moderate number of articles with varying degrees of CRAAP. Through this search process, the author chose articles that were the most specific and applicable to the stated PICO question and received a high CRAAP test score for objective reliability (University of wyoming, 2022).

Annotated Bibliography

Buckley, P. F., Schooler, N. R., Goff, D. C., Hsiao, J., Kopelowicz, A., Lauriello, J., Manschreck, T., Mendelowitz, A. J., Miller, D. D., Severe, J. B., Wilson, D. R., Ames, D., Bustillo, J., Mintz, J., & Kane, J. M. (2014). Comparison of sga oral medications and a long-acting injectable sga: The proactive study. *Schizophrenia Bulletin*, *41*(2), 449–459. https://doi.org/10.1093/schbul/sbu067

A RCT found in the Schizophrenia Bulletin, sought to inform clinical decision making by evaluating the efficacy of oral antipsychotics versus injectable antipsychotics on relapse prevention. This study included 305 patients ages 18-65 years old who were diagnosed with either schizophrenia or schizoaffective disorder based on DMS-IV criteria and had at least one exacerbation in the past 12 months. Prior to participation, all participants provided informed consent and received a baseline assessment. At the start of the research, participants were randomly assigned either long-acting injectable risperidone or a short acting antipsychotic of the physician’s choice. The subjects were seen biweekly over the course of 30 months where they were able to receive their injection/medication supply and trained professionals could assess adherence and/or relapse. Study outcomes were evaluated using predetermined relapse criteria adapted from various rating tools and scales. The hierarchy of evidence developed by Melnyk & Fineout-Overholt (2019) states a RCT is a level two piece of evidence.

The CRAAP method was used to by this author to select the most appropriate evidence (University of Wyoming, 2022). This study is current, as it was published in 2014; however, newer studies have become available since this publication. The research relates to the clinical question in that it compares the utility and efficacy of oral and injectable antipsychotic medications. The reported information is considered advanced; however, can be understood by those with an advanced understanding of the topic. The article has established authority being the authors are listed and have included their contact information. Additionally, organizational affiliations as well as funding is clearly stated. This study is supported by evidence as it includes a reference page; this allows the reader to acknowledge where the information comes from. It is also free from spelling, grammatical, and typographical errors. The conclusions drawn from the research are unbiased and factual or free from emotion. The authors state the purpose of the research is to inform clinical decision making and present the information as fact rather than opinion or propaganda. Although there are institutional affiliations, data is objective and free from partiality.

This author appraised the research findings for validity, reliability, and applicability by questioning several aspects of the study’s methodology. Research participants were randomly assigned to either the experimental or comparison group and no selection bias was given based on age, gender, socioeconomic status, or disease severity. To further ensure validity, participants were not recruited and the reasons why particular subjects failed to complete the study were reported. Additionally, analysis of the intervention occurred over 30 months allowing adequate time to evaluate outcomes. The authors listed tools that were used to measure relapse outcomes; using validated instruments provide a consistent means of data measurement. The size and precision of effect contribute to a research studies reliability. This study identified a large sample of 305 participants; 153 received long-acting injectable risperidone and 152 received oral antipsychotic medication; however, nine participants were excluded after not receiving their assigned medication. After the study concluded, authors provided an in-depth description of the statistical analysis that was completed and then gave a statistically significant P-value of 0.05. Buckley et al. (2014) developed a pragmatic clinical trial to provide greater generalizability rather than enforcing a highly restrictive randomized study. Thus, this study is exceedingly generalizable as it includes a broad representation of the schizophrenic population, allowed physicians to choose oral treatment and flexible dosing, and participants were able to continue the trial after experiencing a relapse. This study had few limitations; however, the biweekly assessments of participants resulting in frequent clinical contact could have limited occurrence of relapse and thus reduce ability to identify difference between the two groups. Additionally, medication non-adherence was not an inclusion criterion which may have impacted the ability to detect difference between the treatment groups.

Through the research findings, authors concluded that oral and long-acting injectable antipsychotics provide no significant difference in relapse or hospitalization. However, researchers did identify a reduction in psychosis severity in the patients treated with long acting injectables over several months. During the 30-month trial, the total occurrence of relapse across the two groups was only 37%; this may be attributed to the frequent, biweekly clinic visits. Biweekly visits are not the current standard of practice and would likely overwhelm the mental health service system; consequently, the applicability of these findings to current practice may not be reliable. This information; however, can be used to inform the need for increased contact with schizophrenic patients via means that do not require in-person contact such as telehealth or phone visits. Thus, authors conclude more research needs to be completed that evaluate the effect of contact and interaction on relapse rates in schizophrenic patients (Buckley et al., 2014).

Kane, J. M., Schooler, N. R., Marcy, P., Correll, C. U., Achtyes, E. D., Gibbons, R. D., & Robinson, D. G. (2020). Effect of long-acting injectable antipsychotics vs usual care on time to first hospitalization in early-phase schizophrenia. *JAMA Psychiatry*, *77*(12), 1217. https://doi.org/10.1001/jamapsychiatry.2020.2076

A research study found in JAMA Psychiatry compares the use of long-acting injectable antipsychotics with oral antipsychotics on the risk for hospitalization in early-phase schizophrenic patients. This RCT included 489 participants across 39 clinics in 19 states. Of the 39 sites, 19 clinics randomly assigned long-acting aripiprazole monohydrate using a computer-generated randomization list and the remaining 20 clinic sites provided typical treatment with oral antipsychotic medications. Inclusion criteria for this study included a schizophrenia diagnosis based on DMS-5 criteria, less than 5 years of antipsychotic medication use, ages 18-35, and the ability to provide consent. Over the course of 2 years, participants were interviewed bimonthly over the phone and asked to complete a ‘service use resource form’ every four months. Use of resources, such as hospitalizations were verified using medical records (Kane et al., 2020). Using the hierarchy level of evidence set fourth my Melnyk Fineout-Overhold (2019) this RCT is a level two piece of evidence.

This article was appraised using the CRAAP method prior to selection (University of wyoming, 2022). Because it was published in 2020, it is considered current and links within the article are functional. A variety of sources were considered; however, this article was selected for its relevancy and ability to help answer the PICO question. Furthermore, the research findings are appropriately reported in easily understood language. Authority is deemed being the authors, their credentials, and affiliations are clearly listed. The authors have provided contact information, contributions, and disclosed conflicts of interest. This article has been peer reviewed and is supported by current evidence. During the appraisal of this article, no spelling or grammatical errors were noted. Finally, the purpose and importance of evidence can be found both in the abstract and body of the article. This research is proposed to further science and improve care deliverance in the schizophrenic population. The objectives are impartial, and the authors disclose no personal biases.

To increase validity, research participants we clustered based on similar location (urban vs. rural) and population factors (first episode vs. current treatment) and then randomized using a computer-generated randomization list. The participants were approached about their willingness to participate but were not incentivized and random assignment was concealed until recruitment was complete. Follow-up assessments occurred over the course of two years allowing sufficient time for the intervention to produce outcomes. Additionally, an independent committee masked to the treatment intervention was tasked with analyzing outcomes to ensure high validity. The study’s large sample of 576 participants increased reliability. However, it is important to note that 83 of the participants were excluded because they refused injectable treatment and 165 declined for unknown reasons leaving 489 participants total. Statistical analysis is explicitly defined and data results including participant characteristics and time to hospitalizations is displayed in easy-to-read tables. Furthermore, the confidence interval is 95% which gives clinicians confidence in research findings. By nature of the study participants and variety in clinical sites, the results are generalizable. However, the study is limited by its population demographics as 75% of the participants were male. Kane et al., (2020) report not all clinic sites were trained in intramuscular injections which limited the success of patient enrollment. Additionally, the author discloses results are limited by only using one long-acting injectable formulation when other second-generation long-acting formulations are available and could also prevent hospitalization.

The research study concludes that long-acting injectable antipsychotics produced a 44% reduction in the first hospitalization in patients with early-phase schizophrenia when compared to patients taking an oral antipsychotic. Strikingly, injectable antipsychotics had a number to treat of 7 in the prevention of hospitalization. The scores of the two scales used to measure outcomes, Brief Psychiatric Rating Scale (BPRS) and Hienrichs-Carpenter Quality of Life Scale (QLS), did not differ between the treatment groups. Authors attribute these results to the long duration between assessments that limited the ability to fully capture disease trajectory. The authors did disclose that some patients, regardless of treatment choice, will require hospitalization for relapse of psychotic symptoms, this phenomenon is not well understood and is an area requiring further research (Kane et al., 2014).

Subotnik, K. L., Casaus, L. R., Ventura, J., Luo, J. S., Hellemann, G. S., Gretchen-Doorly, D., Marder, S., & Nuechterlein, K. H. (2015). Long-acting injectable risperidone for relapse prevention and control of breakthrough symptoms after a recent first episode of schizophrenia. JAMA Psychiatry, 72(8), 822. https://doi.org/10.1001/jamapsychiatry.2015.0270

This research study, obtained from the Journal of the American Medical Association (JAMA) of psychiatry, is a randomized controlled trial (RCT) comparing the efficacy of long-acting injectable risperidone with oral risperidone in schizophrenic patients. The study was conducted throughout Los Angeles inpatient and outpatient psychiatric facilities between the years of 2005 and 2012. The trial consisted of 86 adult patients who had a recent diagnosis of schizophrenia and a major psychotic episode within the past two years. All participants were not recruited or referred and provided written consent. Study participants were randomly assigned treatment with either oral or long-acting injectable risperidone. Over the course of 12 months, these patients received regular psychiatric visits, weekly individual case management by licensed therapists, and either cognitive remediation or healthy-behaviors training (Subotnik et al., 2015). Subotnik et al. (2015) measured outcomes by having the participants complete the Brief Psychiatric Rating Scale (BPRS) every two weeks and monitoring the occurrence of psychiatric hospitalizations. An RCT is considered a level two piece of evidence according to Melnyk & Fineout-Overholt (2019) hierarchy of evidence.

Using the CRAAP method, this article is considered current as it was published in 2015 which is within the last ten years (University of Wyoming, 2022). Information within this study is up-to-date and internal links are functional. Findings from the research, including adults diagnosed with schizophrenia taking antipsychotic medications, can directly be used to help answer the stated PICO question. Several sources were evaluated and explored; however, this article was the most relevant to the clinical question. The authors, their contributions, affiliations, and credentials, are clearly listed on both the title and reference page. Additionally, contact information for the authors is accessible giving the finding of this study authority. Research findings can be deemed reliable and accurate as the article is free from grammatical or spelling errors. Furthermore, findings from other high-level evidence can support these research conclusions and this author can verify information from personal knowledge. The purpose of this research is to inform clinical decision making and contribute to science. The authors clearly state their purpose and disclose any conflicts of interest.

There are several factors that increase this study’s validity. The study spanned over seven years which allowed adequate time for intervention and evaluation outcomes. Additionally, there was no selection bias or inappropriate influences that could have affected the comparison group. Although the participants were randomly assigned an intervention, the validity is limited being the researchers where aware of which participants received which intervention and were not blinded by the treatment condition. Both the experimental and comparison group were equivalent in relevant characteristics such as diagnosis, disease severity, and age.

The reliability of a study can be determined based on total number of participants, number of participants that completed the trial, and event rates in the group. Authors disclosed this study started with 83 participants, 5 participants discontinued treatment prior to the 8-week mark and 21 dropped or changed medications before the end of the study, therefore, 57 patients completed the trial. The authors did include why participants discontinued the trial. Although this is not a large sample, the statistical analysis conducted, data results, and the measure of effect are described giving the findings clinical significance. Because of the study’s exclusion criteria, this study is likely not generalizable to patients who have both schizophrenia and substance abuse. Subotnik et al. (2015) also reports generalizability is limited being all patients in the oral medication group were prescribed risperidone which is molecularly identical to the injectable medication group. This study is limited by its lack of generalizability and failure to blind the individuals tasked with evaluating outcomes.

It is concluded by the authors that long-acting injectable antipsychotic medications increase medication adherence, aid in relapse prevention, and control psychotic symptoms when compared to oral antipsychotic medications. In addition to this, long acting injectables were found to improve cognitive functioning and provide “better maintenance of intracortical myelination” (Subotnik et al., 2015, p. E7). It is postulated through these research findings that using injectable antipsychotic medications early in the disease or with the first psychotic episode can alter disease trajectory and improve long-term outcomes. As stated by authors, injectable medications might be a “game changer” in the field of psychiatric medicine (Subotnik et al., 2015).

Literature Synthesis Summary

Numerous studies have been piloted to assess the efficacy of oral antipsychotic medications compared to long-acting injectable antipsychotic medication in preventing or limiting both relapse and hospitalization for acute psychotic episodes. Three randomized controlled studies, selected by the author, compared the efficacy of oral and injectable antipsychotics with the purpose to inform clinical decision making. Both Kane et al., (2020) and Subotnik et al., (2015) have proven through their research efficacy and superiority in the use of long-acting injectable antipsychotics in preventing relapse and subsequent hospitalization. Conversely, Buckley et al., (2014) did not find a difference in relapse or hospitalizations among the different treatment routes. However, all three studies endorsed injectable, long-acting antipsychotic in limiting psychotic symptoms and improving quality of life. The three studies established that by nature of administration, medication compliance is increased with long-acting injectable antipsychotics. Because of the many limitations of the various studies, researchers agree that additional research and data is needed to conclusively alter the current trajectory of patient care.

Application

Clinicians can use the identified research to aid them in clinical decision making when caring for a patient with a schizophrenia diagnosis. Because of the differences noted, a definitive answer to the posed PICO question cannot be provided; however, these findings alongside clinical judgement can be applied when choosing between oral or injectable antipsychotic medications. Two recommendations, obtained through the literature review, can be provided to mental health professionals. First, non-adherence should be assessed prior to selecting a medication route; this should include an assessment of the patient’s ability to pay for and receive medications. In non-compliant patients or risk for noncompliance, long-acting injectable antipsychotics should remain the drug of choice regardless of early disease progression or chronic, longstanding illness. Secondly, frequent provider-patient engagement is shown to increase treatment compliance and in return decrease relapse/hospitalization. When possible, schizophrenic patients should have frequent follow-up assessment via in-person contact, over the phone, or video conferencing. Schizophrenia is a complex illness with countless variables that need to be evaluated before determining appropriateness of oral or injectable antipsychotics.

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