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ORIGINAL PAPER

Evaluation of Risk Factors for Antipsychotic Polypharmacy in Inpatient Psychiatry Units of a Community Hospital: A Retrospective Analysis

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Abstract
Antipsychotic polypharmacy (APP) is a common practice while treating severe mental illness but the benefits of APP over antipsychotic monotherapy is controversial. This is a retrospective analysis comparing risk factors for people on APP and those on non-APP in inpatient psychiatry units. Two years data with 72 people in non-APP group and 82 people in APP group were analyzed quantitatively. The diagnoses of schizoaffective disorder (OR 11.5), schizophrenia (OR 4.65) and depression (OR 0.31), and history of > 2 psychiatric admissions (OR 3.2) and > 2 psychiatric emergency visits (OR 2.87) in 2 years were studied as potential risk factors for APP. Similarly, history of violence (OR 1.7) and history of substance abuse (OR 0.51) were also studied. Schizophrenia spectrum disorder, higher number of psychiatric hospitalizations, and psychiatric emergency visits were positively associated while depression and substance abuse were negatively associated with APP in our study.

Introduction

Antipsychotic medications are the mainstay of treatment for psychosis. Antipsychotic polypharmacy (APP) refers to the concurrent use of two or more antipsychotic medications. Most current guidelines recommend APP to be used as the last resort (Hasan et al. 2012; Lieberman et al. 2005; Moore et al. 2007; NICE guideline 2014; Rush et al. 1999). A recent randomized controlled trial (Constantine 2015) highlighted the advantage of APP by finding that study participants who switched to antipsychotic monotherapy had more symptoms and they discontinued the medication earlier than those who were continued on 2 antipsychotics. Similarly, a meta-analysis (Correll 2009) found better clinical efficacy and longer duration of adherence on APP. However, the findings have not been consistent in other studies (Freudenreich 2007; Josiassen 2005). A Cochrane review (Cipriani et al. 2009) showed some therapeutic advantages but data lacked for adverse effects and outcome. Potential strategies for practicing APP might be utilization of different mechanisms of action, better tolerance of adverse effects, or augmentation of antipsychotic effects among others. The disadvantages of APP have been highlighted by different studies (Fleischhacker and Uchida 2014; Gallego et al. 2012a, b; Lochmann et al. 2013; Velligan et al. 2015) which include adverse outcomes, medication non-adherence and high treatment cost. Some of the adverse outcomes associated with APP are increased global side effect burden, rates of Parkinsonian side effects, anticholinergic use, hyperprolactinemia, sexual dysfunction, hypersalivation, sedation/somnolence, cognitive impairment and diabetes. Despite limited indications and increasing evidence of disadvantages, APP continues to be a common practice in the United States and in the world (Gallego et al. 2012b; Velligan et al. 2015). Various factors are implicated in the pattern of polypharmacy including treatment setting, prescriber characteristics, nature of illness, and characteristics of study participants (Kadra et al. 2016). Many studies have shown that chronic psychosis with severe symptoms and having comorbid psychiatric illnesses are potential risk factors for receiving treatment with APP (Correll and Gallego 2012). There are limited studies which looked for psychiatric rehospitalization and APP, while there are inconsistent reports on the potential role of substance abuse as a risk factor for APP (Kreyenbuhl et al. 2007; Weinmann et al. 2004). Even though metabolic side effects of antipsychotic medications are well known there are few studies evaluating association of those conditions with APP. In that context, our study evaluated the potential risk factors for being on antipsychotic polypharmacy, as well as

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the association of antipsychotic polypharmacy with metabolic parameters in short-term inpatient psychiatry units of a community hospital setting.

Methods

This is a retrospective analysis comparing risk factors for study participants on APP and those on antipsychotic monotherapy in the inpatient psychiatry units of Berkshire Medical Center (BMC), Pittsfield, MA. Anyone receiving antipsychotic medications at the time of admission, or who received an antipsychotic prescription at the time of discharge from the adult psychiatry units of BMC were eligible for the study. The Quality Control division of the hospital provided the discharge record of the people on antipsychotic medications from the BMC adult psychiatry units. From October 2012 to December 2014, a total of 1563 cases were admitted to the psychiatry units. Among them, there were 1047 cases that were prescribed at least one antipsychotic medication. Out of 1047 cases only 82 were actually on APP at the time of admission, and this group was identified as the APP group. Similarly, total number of cases discharged on only one antipsychotic medication was 877 during the study period. To match the number of APP group, every 10th case was randomly selected for the non-APP group. Out of randomly selected 87 cases 15 cases were duplicate cases due to rehospitalizations, and only 72 patients were included in the final non-APP group. There was mismatch between number of cases and number of patients in the provided list as the list contained all the cases discharged in the study period including rehospitalization cases. Study participants in the non-APP group were either on one antipsychotic medication or were not on any antipsychotics at the time of admission. They were, however, prescribed only one antipsychotic medication at the time of discharge. Since our focus was the retrospective evaluation of potential risk factors for receiving APP we emphasized the use of antipsychotic medication during the time of admission. We reviewed the electronic medical record of the selected study participants retrospectively for 2 years prior to the index admission date. We focused on demographic features, metabolic disorder, diagnosis, history of violence, substance abuse, number of psychiatric ED visits and the number of psychiatric admissions within the 2 year period. The clinical diagnoses were based on the discharge summary. The findings were analyzed quantitatively using standard statistical tools and analysis of variance was used to compare risk factors between the APP and the non-APP groups. The study was part of a quality improvement project of the Berkshire Medical Center, Pittsfield, MA.

Results

Demographic Features

Majority of the study population were male in both the APP and the non-APP groups. There was no significant difference in gender in terms of receiving APP but males in the age group 31–40 and females in the age group 51–60 were receiving treatment with APP with significantly higher proportion (Table 1).

Psychiatric Diagnosis as a Risk Factor for APP

Chronic psychosis including schizoaffective disorder and schizophrenia was the most common psychiatric diagnosis. Out of 82 study participants only 56 (68.3%) of them had diagnosis of schizophrenia or schizoaffective disorder in APP group (Table 2). About one-third (31.7%) of the study participants in the APP group had other than primary psychosis diagnoses. The diagnosis of schizoaffective disorder ($OR = 11.5$, $p < 0.0001$) and schizophrenia ($OR = 4.65$, $p = 0.001$) were the risk factors for receiving treatment with APP. Interestingly, all the study participants ($n = 7$) with the diagnosis of paranoid schizophrenia were on APP ($OR = 14.4$, $p = 0.06$). The diagnosis of major depressive

Table 1 Illustrating gender and age distribution between APP and non-APP group

Age group (years)	No of female: APP	No of female: non-APP	No of male: APP	No of male: non-APP	Total: APP	Total: non-APP	Total
11–20	0	1	1	1	1	2	3
21–30	6	6	8	11	14	17	31
31–40	9	6	14	8	23	14	37
41–50	4	10	8	10	12	20	32
51–60	14	2	7	7	21	9	30
61–70	2	2	6	4	8	6	14
> 70	2	1	1	4	3	5	7
Total	37	28	45	37	82	72	154

Table 2 Distribution of psychiatric diagnoses among study groups

Psychiatric diagnoses	No of study participants in APP group	No of study participants in non-APP group
Schizophrenia	16	4
Schizoaffective	40	9
Psychosis NOS	0	4
Bipolar disorder[a]	15	18
Mood disorder NOS	5	10
Major depressive disorder[b]	5	15
PTSD	7	11
Generalized anxiety disorder	1	4
Others	0	3
Total[c]	89	78

[a]5 patients in APP and 2 patients in non-APP group with psychotic features

[b]1 patient in APP and 0 in non-APP group with psychotic features

[c]Total number of diagnoses is different than the total number of patients on APP or non-APP group because of multiple admitting diagnoses

disorder (OR = 0.31, p = 0.006) was negatively correlated with receiving treatment with APP. No other psychiatric diagnosis examined in our study was found to have significant association with APP.

Substance Abuse and History of Violence as Risk Factors for APP

Study participants with history of violence (OR 1.7, p 0.22) were more likely to receive treatment with APP but this finding was not statistically significant. There were 25 study participants with a history of violence; 10 in the non-APP group and 15 in the APP group. Out of 116 people with no history of violence, 62 were in the non-APP group and 54 were in the APP group. Interestingly, people with a history of substance abuse (OR 0.51, p 0.03) were negatively associated with receiving treatment with APP in our study population. Out of 74 study participants with a history of substance abuse, 33 were in the APP group. Similarly, out of 80 study participants with a negative history of substance abuse, 49 were in the APP group.

Psychiatric Hospital Visits as Risk Factors for APP

About one-fourth of people who were receiving treatment with APP did not have any psychiatric hospitalizations during the last 2 years. Another one-fourth of the people in that group had only 1–2 psychiatric hospitalizations within the same period (Table 3). Having more than 2 psychiatric hospitalizations within the last 2 years was strongly associated with receiving APP (OR = 3.2, p < 0.001). Similarly, more than 2 psychiatric emergency visits within a 2 year period (Fig. 1) was significantly associated with receiving treatment with APP (OR = 2.87, p < 0.001). Number of psychiatric admissions and psychiatric emergency visits evaluated in this study excludes the index hospitalization.

Table 3 Illustrating number of psychiatric hospitalizations during last 2 years as risk factor for APP

Number of psychiatric hospitalizations in last 2 years period	Number of study participants on APP group	Number of study participants on non-APP group	Total
0	20	25	45
1–2	21	30	51
3–6	30	16	46
> 6	11	1	12
Total	82	72	154

Metabolic Diseases Associated with APP

Our study did not find a significant association of APP with diabetes (OR 0.57, p 0.29). Out of 17 study participants with diabetes only 7 of them were on APP while 75 out of 137 study participants without diabetes were in the APP group. Similarly, high BMI was not associated with APP (OR 1.3, p 0.45). Out of 43 study participants with high BMI, 25 were in the APP group. We found a negative association of APP with abnormal lipid profile (OR = 0.25, p = 0.02). Out of 22 study participants with high cholesterol levels, only 4 of them were in the APP group while 26 out of 49 study participants with normal cholesterol level were in the APP group.

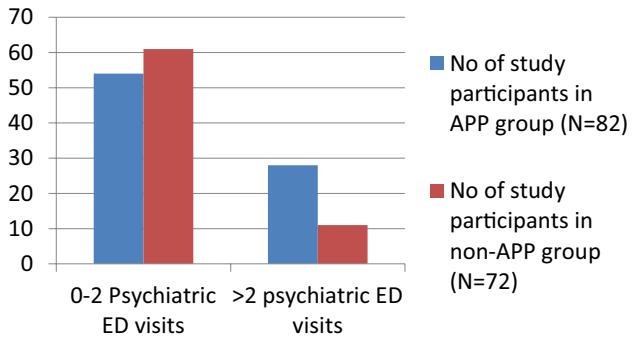

Fig. 1 Illustrating number of psychiatry emergency visits as risk factor for APP

Discussion and Conclusion

Our study found higher prevalence of APP among 31–40 age group males and 51–60 age group females. Unlike our findings, a recent study (Kadra et al. 2016) found association of APP with young age. People with schizoaffective disorder and schizophrenia were associated with a very high risk of receiving treatment with APP in our study (Table 4). Previous studies (Kadra et al. 2016; Weinmann et al. 2004) have shown that severity of psychosis might be associated with APP but our study did not have information on the severity of the symptoms. Another notable finding was the prevalence of APP in people with paranoid schizophrenia. Although, it is no longer a separate entity in DSM-5, all study participants with paranoid schizophrenia in our study had multiple antipsychotics (OR 14.4, p = 0.06). Psychopharmacologic interventions are more effective at treating the positive symptoms. Therefore, it is likely that paranoid symptoms were targeted more.

Violent history and incarceration usually means erring on the side of caution and calls for aggressive management of symptoms. But our study revealed that the association between history of violence and receiving treatment with APP was statistically non-significant (Table 4). It is likely that our study did not have enough power to describe this phenomenon. Homelessness was found to be a risk factor for APP in a recent study (Kadra et al. 2016) but our study did not look at homelessness rather we looked at a history of violence and incarceration, which has close association.

People with substance abuse were negatively associated with APP in our study (Table 4). Many studies have suggested substance abuse as a risk factor for APP but the finding is not consistent (Kreyenbuhl et al. 2007; Weinmann et al. 2004). Most cases of substance induced psychoses are self-limiting and can present as an acute exacerbation of a psychotic episode. They typically last a few days and do not require continuous use of antipsychotic medication, hence might present to hospital without history of current use of antipsychotics.

Hospitalization patterns varied among people on APP but those on APP were more likely to be hospitalized than people who were not (OR = 2.32, p = 0.0009). People with more severe mental illness tend to be on multiple antipsychotic medications and therefore are likely to be frequently admitted. Even though few studies (Cipriani et al. 2009; Constantine et al. 2015; Correll et al. 2009) have suggested APP to be effective to manage severe psychotic symptoms, our study suggested that despite being on APP, people had more re-hospitalizations. Our finding of association of APP with more than 2 psychiatric emergency visits within 2 years period (OR = 2.87, p = 0.0086) suggests either people receiving APP had more severe symptoms or APP was not effective to address the symptoms. Our study also looked for potential association between APP and metabolic disorders. People with abnormal lipid profiles were less likely to receive treatment with APP (Table 4). This could be because the providers were influenced against APP among people who were already at high risk, which indicated good practice. However, there was no significant association of APP for high basal metabolic index (BMI) and diabetes. Metabolic side effects are the hallmark of atypical antipsychotics but our retrospective study could not evaluate that finding.

Our study has a few limitations. This is a retrospective study which can reveal the association, and a prospective study might be better to determine the risk factors of APP. Our study could not include many social factors which might have influenced the risk of APP. We did not have data on the severity of symptoms among patients with schizophrenia and schizoaffective disorder, which might be able to differentiate whether people with severe symptoms are associated with APP. The higher rate of psychiatric hospital visits is strongly associated with APP in our study but we could not verify whether those patients with increased rehospitalizations were also the sickest people. As this study is not a controlled one, we do not have any evidence if the study participants who were prescribed APP were adherent to the medications. As there is potential for antipsychotic withdrawal the non-adherence can lead to decompensation requiring high rate of rehospitalizations. Besides some shortcomings, our study had a good sample size and found some interesting findings, notably the association of APP with chronic psychosis, paranoid schizophrenia and higher rate of psychiatric hospital visits.

In summary, our study in inpatient setting found strong and statistically significant association of APP with schizoaffective disorder (OR = 11.5), schizophrenia (OR = 4.6), more than 2 psychiatric hospitalizations (OR = 3.2) and more than 2 psychiatric emergency visits (OR = 2.8) within a 2 year period. The diagnosis of major depressive disorder (OR

Table 4 Displaying the association of APP with the studied major potential risk factors

Potential risk factors	Odds ratio (OR)	p value
Diagnoses/metabolic conditions		
Schizoaffective disorder	11.5	< 0.0001
Schizophrenia	4.65	0.001
Paranoid schizophrenia	14.4	0.06
Major depressive disorder	0.31	0.006
History of substance abuse	0.51	0.03
History of violence	1.7	0.22
High BMI	1.3	0.45
Diabetes	0.57	0.29
Abnormal lipid profile	0.25	0.02

0.31), history of substance abuse (OR = 0.51) and having abnormal lipid profile (OR = 0.25) were negatively associated with APP. The association of APP with bipolar disorder, diabetes, obesity, and history of violence were not statistically significant. Prospective studies and randomized controlled trials will be necessary to confirm our findings.

Compliance with Ethical Standards

Conflict of interest None of the author has any financial disclosures to be reported and there is no conflict of interest among the authors.

Informed Consent No human interaction was involved in the study as we reviewed charts of the patients included in the quality improvement project. All the study participants were deidentified before analyzing the data, and we have not included any identification parameters of any study participants in the manuscript. Because of the nature of the study, the informed consent was waived.

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