Pattern of Antipsychotic Use and its determinants in Razi Psychiatric Hospital

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Objective: The aim of this study was to investigate the prevalence and its determinants of Antipsychotic Use in patients with psychiatric disorders.

Materials and Methods: This study was on patients with psychiatric disorder that have discharged from the hospital. We have assessed all patients with psychiatric interview and evaluation of their psychiatric documentations.

Results: 90.7% of all of patients had taken antipsychotic medications and antipsychotic polypharmacy was in 27.2% of these patients. The most prevalent component of antipsychotic polypharmacy was consisting of Chlorpromazine, Haloperidol and Chlorpromazine, Risperidone and then Chlorpromazine, Olanzapine respectively. There were significant relations between pattern of antipsychotic use and gender, occupation status, type of psychiatric ward, duration of hospitalization and cost of treatment but no relationship with age, educational status and duration of illness.

Conclusion: This study suggests that prevalence of antipsychotic polypharmacy is high in in-patient psychiatric patients.

Keywords: Antipsychotic; monotherapy; Polypharmacy

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Introduction
Nowadays, one of the greatest issues in global health systems is unreasonable drug consumption. The World Health Organization estimates that over half of all prescribed, distributed, or sold drugs are not needed, and half of the patients experience medication failure despite receiving appropriate medication. In addition to high drug consumption, low and unreasonable consumption leads to resource loss and major threats to the health system. Some examples of unreasonable drug consumption are consumption of several drugs or poly pharmacy in one patient without scientific justification, unreasonable consumption of injective form of drugs when the oral form is more appropriate, a prescription that is not in accordance with treatment standards, and self-medication. (1)

In psychology, poly therapy is a code, rather than an exception. Most of the time, when releasing psychic patients from hospitals, there is more than one psychotropic drug in their prescription. (1)

There is no unique description for poly pharmacy in scientific literature. Generally, two descriptions have been proposed. One of them is based on the number of taken drugs at the same time. In this regard, simultaneous consumption of two or more drugs is poly pharmacy. The other description is in accordance to clinical indication and effects of drug prescription. Therefore, unreasonable consumption of drugs that are not clinically required is known as poly pharmacy. (2)

Augmentation therapy is a common method in psychological treatment. Especially, in patients that respond weakly to drugs. According to investigations, old age and being female are factors leading to poly pharmacy. (3) The level of poly pharmacy is increased with increment of sickness period and intensity. (4)

In the past decades, simultaneous drug consumption has increased. In other words, the number of prescribed drugs is three among hospitalized patients. (5)
Simultaneous consumption of psychiatric drugs has increased constantly since the past decade. In some states of the USA, efforts on monitoring and controlling improper consumption of antipsychotics have been successful to some extent. For example, in one state, it has been said that simultaneous consumption of two or more antipsychotic drugs for more than 10 days, should be approved. Simultaneous long-term drug consumption in this state is rare and the most common multi-drug consumption is for one typical drug in combination to an oral atypical antipsychotic drug. In one study conducted to predict mortality in schizophrenic patients from 1983 to 1993, it was stated that the maximum number of antipsychotic drugs that were taken by patients at the same time was considered a factor in predicting mortality. Variables like daily mean consumption dose or overall dose of antipsychotic drugs in life time were not related to mortality statistics; this shows that difference in mortality is not only related to severity of illness. In addition, it was proved that mortality is increased because of cardiovascular effects of typical antipsychotic drugs, and interaction between drugs and other illnesses such as asthma. Generally, many researchers have shown that the combination of two typical antipsychotic drugs is inappropriate; while combination of typical and atypical drugs or two atypical antipsychotic drugs may be appropriate under circumstances. Temporary consumption of several antipsychotic drugs may be useful in drug change stage or acute treatment. When changing a drug, while migrating from one drug to another, one drug’s dose is reduced. In this stage, consumption of the older antipsychotic drug should be continued until appearance of effect of the new drug. In addition, trapping should be prevented, where the patient clinically responds before completion of this stage, and both drugs are prescribed with an accurate amount. In schizophrenia, there is only one treatment guide, which poly pharmacy is considered as a part of its algorithm. The Texas Medication Algorithm Project guideline (TMAP) for schizophrenia constitutes using more than one antipsychotic drug as the sixth stage of the algorithm, after failure of the fifth stage of mono therapy. (7) Sometimes, poly pharmacy is essential, like need to sleep, stress, extreme restlessness and aggression relief, availability of side diagnosis, and generally, severity of illness. However, poly pharmacy can only be considered as a diagnosis when there is a valid certificate for its prescription and interference of pharmacokinetics and pharmaco dynamic are considered. (1, 8-11). In Tapp’s study (2003), from 1749 outpatients, 40% were taking one atypical antipsychotic drug, and 13% had taken antipsychotic drugs as combined medication for duration of at least 30 days. The most important reason for adding antipsychotic drugs in combined medication was treatment of positive and resilient signs, and for atypical antipsychotic drugs, it was change to these drugs. (12) A study carried out in Japan reported the highest rate of poly pharmacy. A combination of Low Potency and High Potency antipsychotic drugs was reported in more than 90% of schizophrenic patients. In the mentioned study, patients that had taken a combination of typical and atypical antipsychotic drugs for more than one month and at least, one of these drugs had been taken for more than six months were considered as subjects. (13) In a study in Austria, 47% of schizophrenic patients were taking two antipsychotic drugs, and for eight percent of them, three antipsychotic drugs were prescribed. (7) Generally, according to psychopharmacology principles in schizophrenics, it is necessary to start medication with one antipsychotic drug and the minimum possible dose. (14) Nevertheless, contradictory records exist on this ground. (15-17) In a study performed by Sim et al. in 2004, poly therapy of antipsychotic drugs was observed in 45.7% of subjects. Poly therapy was observed in male, older subjects, hospitalization condition, and higher doses of equivalent chlorpromazine, longer period of illness, added consumption of anticholinergic and less consumption of atypical antipsychotics. (18) In a similar research in Singapore (2000), antipsychotic poly pharmacy of hospitalized schizophrenics were reported as 73%, while according to previous studies this amount was reported as 59% in the country. (19) In an investigation on the effect of race on prescription of poly pharmacy, it was shown that black people had taken less Serotonin Specific Reuptake Inhibitors (SSRI) and lithium carbonate, and less antipsychotic drugs compared to white people. (20) From one study in the USA, the amount of atypical antipsychotic drug consumption has reached from 3.3% in 1999 to 13.1% in 2004. (21) In another research in Turkey, drug variations were compared from 1999 to 2004, retrospectively. Prescription of typical antipsychotic drugs and atypical antipsychotic drugs had reached from 53.6% and
43.5% to 34.4% and 54.4%, respectively. Overall prescription of psychiatric poly pharmacy had escalated from 11.6% to 20%. (22)

In a descriptive study for prevalence evaluation of poly pharmacy in treatment and educational hospitals (2005), relevance was found to be 39% and 28%, respectively. Simultaneous consumption of two, three, and four antipsychotic drugs in treatment hospitals and educational hospitals was 25%, 13%, and 1%, and 12%, 14%, and 2%, respectively. Consumption of two typical drugs or one typical and one atypical drug were 8.9% and 63.7% in treatment hospitals, and 6.7% and 46% in educational hospitals. However, consumption of two atypical drugs was 27.4% in treatment hospitals, and 47.3% in educational hospitals. (23)

Antipsychotic poly pharmacy has increased dramatically in past decade and this situation is seen in all medication conditions and different countries. (24, 25) In addition, many controlled studies indicate increment of side effects and costs in antipsychotic poly pharmacy without considerable improvement in initial symptoms. (27)

According to available pharmaceutical profiles, combined consumption of one atypical antipsychotic drug with another one or typical antipsychotic drug is considered as rational drug consumption. However, this is a hypothetical concept not verified in medical books. (27, 28) Random controlled studies did not show more effect of poly pharmacy than mono therapy. In two studies (29) poly pharmacy recovery and in one study (27) mono therapy recovery was reported. Poly pharmacy with typical antipsychotic drugs puts patients in danger of extra pyramidal and metabolic effects more than atypical drugs. Consumption of two atypical antipsychotic drugs leads to extra pyramidal effects, which questions consumption atypical antipsychotic drug benefits. (30, 31) Combination of atypical antipsychotic drugs, except Clozapine with typical antipsychotic drugs is the most common antipsychotic poly pharmacy. (27, 32, 33)

In a study conducted in 2005, all the schizophrenic patients who had taken atypical antipsychotic drugs from a point of time were selected. The number of patients who were under medication with one drug and the cumulative number of medication days were specified. During one year, only 30% of patients had mono therapy, while about 57% of patients experienced a long period of poly pharmacy. The mean number of days for mono therapy, poly pharmacy, and without drug was 195.5, 155.7, and 13.9, respectively. It was more probable that patients whose treatment started with Olanzapine stay in mono therapy for a longer period. The mono therapy days for Olanzapine were more than Quetiapine. In addition, Risperidone has the longest mono therapy duration. (34) Poly pharmacy can increase mortality of schizophrenic patients. On the other hand, it can increase their hospitalization period. (35) The reasons for combination of preservative antipsychotics include rational mono therapy failure, inaccurate short-term antipsychotic drug consumption, and combination of drug combinations prior to mono therapy treatment. (36)

While finding proof to support consumption of two drugs in bipolar mode disorder is difficult, many patients benefit from a combination of drugs. Nowadays, many patients take three or more mood stabilizing drugs. (37) Compared to antipsychotic mono therapy, antipsychotic poly pharmacy is accompanied with higher metabolic syndrome levels, higher lipid markers, and higher insulin resistance. (38) In 2005, a study on 31000 schizophrenic patients in the USA revealed that 40% of patients had antipsychotic poly pharmacy. This value for long-term hospitalized patients was 23%. (39) In a study in the USA (2008), it was found that the cost of antipsychotic consumption was the highest for Olanzapine, Risperidone, and Quetiapine, respectively. (40) According to considerable prevalence of psychotic disorders, wide consumption of antipsychotic drugs, possible side effects of these drugs, and high medication cost, we conducted a study to determine the pattern of psychotic drugs consumption and their dependent variables in educational and treatment wards of Razi Psychiatric Hospital. However, it is required to perform further and broader controlled investigations, due to wide usage of poly pharmacy in psychiatric care units.

**Method**

This study was performed on all discharged patients of male and female educational and treatment wards, who had been discharged with at least one antipsychotic drug, at four months from beginning of the study. Sampling was conducted by considering all subjects. Therefore, all the patients who were discharged from hospital during the study and on their discharge prescription contained at least one antipsychotic drug, were studied. After determination of subjects, a meeting was held with
matrons of the wards in order to ask for their cooperation, explaining the implementation stages, eliminating possible obstacles, and asking for suggestions.

Afterward, it was time to take all eligible patients to clinical trial. For all the mentioned patients, a questionnaire for evaluation of variables was completed. In cases that the information was incomplete or in doubt, the case was promptly consulted with their psychologist. If needed, the patient was visited and accurate information was recorded; otherwise, the patient was withdrawn from the study. Eventually, patients were divided into two groups of mono therapy and poly therapy patients, and the effective factors were studied.

In the questionnaire, variables such as diagnosis, gender, age, education, job, illness period, hospitalization period, name and dose of psychiatric drugs were studied. All the data were analyzed using SPSS software. In the descriptive section, statistical indicators such as mean, standard deviation, and absolute and relative frequency distribution were used. In the analytical section, deductive statistical tests and methods, such as correlated t test for analysis of differences and unilateral variance (ANOVA) were employed.

Conscious agreement of patients was the criterion for commencement of the study. In cases that the patients, their family, or their psychologist did not agree, the patient was not selected for the study.

One of the limitations of this investigation was incomplete information forms. To eliminate this limitation, before leaving the hospital, dossiers were checked and special cases were consulted with the psychologist.

**Results**

The number of discharged patients each month was very close to other months; the average number of discharged patients was 200 in each month. 49.6% and 49.4% of patients were hospitalized in educational wards and non-educational wards, respectively. According to demographic characteristics, it can be said that most of the subjects are male (77.5%). The most prevalent age group was 21-30 with 32.5%. Most of the subjects had elementary education (55.1%), and others were unemployed (74.9%).

Some of the subjects (22.4%) suffered from a psychosis disorder for 6-10 years. The maximum hospitalization period of most of the patients, (22.4%) was between 21 and 30 days. Most of the psychiatric diagnosis of patients were 33.42%, 26.71%, and 8.10% for schizophrenia, bipolar mood disorder type 1 (manic phase), and schizoaffective bipolar disorder, respectively.

Table (1) illustrates frequency distribution of the taken amount of psychiatric drugs and polypharmacy in patients, respectively.

As shown in the table, more than 90% of the patients are using anti psychotics but less than 30% of them are under polypharmacy medication treatment.

Among studied patients, there was no foursome antipsychotic poly pharmacy. In 3.35%, three antipsychotic drugs were used and in 23.88%, two antipsychotic drugs were consumed simultaneously. The maximum accompaniment of antipsychotic drugs was for simultaneous consumption of Chlorpromazine and Haloperidol, Chlorpromazine and Risperidone, and Chlorpromazine and Olanzapine.

In ternary antipsychotic poly pharmacy, accompanied consumption of Chlorpromazine, Flopentixol Decaonate, and Risperidone are the most common cases.

Simultaneous consumption of two atypical antipsychotic drugs was observed in seven cases, while in others, simultaneous consumption of one typical and one atypical antipsychotic drug was observed. The only consumed atypical antipsychotic drugs were Risperidone, Olanzapine, and Clozapine.

<table>
<thead>
<tr>
<th>Psychiatric drugs</th>
<th>Polypharmacy of Psychiatric drugs</th>
<th>Antipsychotic drugs</th>
<th>Polypharmacy of Antipsychotics</th>
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<tr>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
<td>Percent</td>
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<tr>
<td>Total</td>
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The relationship between consumption pattern of antipsychotic drugs and variables of age, gender, job, education, illness period, hospitalization period, hospitalization ward, and medication cost of patients have been analyzed respectively.
There was no significant difference between the average of age ($t=0.84$, $P_{value}=0.401$), the education level ($F=0.023$, $P_{value}=0.534$) and the average of illness period ($F=0.003$, $P_{value}=0.998$) of the patients who are under polypharmacy with those who receive monotherapy.

**Chart 1.** The gender difference of two groups of patients

<table>
<thead>
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<th>Polypharmacy</th>
<th>Monotherapy</th>
</tr>
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<tbody>
<tr>
<td>Men</td>
<td>172</td>
<td>23</td>
</tr>
<tr>
<td>Women</td>
<td>395</td>
<td>126</td>
</tr>
</tbody>
</table>

**Chart 2.** The distribution of the education level in two groups of patients

The mean score of gender in chart 1 ($r=0.134$, $P_{value}=0.001$), job ($r=0.126$, $P_{value}=0.001$) chart 2, hospitalization period ($F=4.15$, $P<0.001$) chart 3 and ward ($r=12.9$, $P_{value}=0.001$) chart 4 indicate a considerable difference between these two group of patients.

**Chart 3.** The distribution of the patients in two groups based on the length of hospitalization

Meanwhile the Spearman correlation coefficient between consumption pattern and relative medication cost was -0.195 ($P= 0.001$) that shows the lower medication cost of monotherapy and the correlation coefficient of the ward of hospitalization between two groups was -0.131 that shows the shift of the consumption pattern towards polypharmacy in accordance to the change of the hospitalization ward from educational to non educational.

The dominant psychiatric diagnosis that accompanied polypharmacy consumption pattern was schizophrenia (44.1%).

**Discussion**

According to findings, all the subjects were selected from short-period hospitalization wards. The case study included all the patients whom were discharged from active wards of male and female hospitalization in educational and medical parts of Razi Psychiatric Hospital during the first four months of study.

The average number of discharged patients in each month was 200, which shows high level of activity in reception and discharge of psychiatric patients. The number of patients of educational and non-educational sectors is close to each other. In other words, half of the patients were discharged from educational wards and the other half were discharged from non-educational wards. It should be mentioned that in educational wards, psychiatry faculty and assistants visit patients; while in non-educational wards, psychologists of hospital treatment group visit patients and there is no need for training in these wards.

The higher number of male patients in active wards of the hospital may be due to more reasons for hospitalization in psychiatric hospitals. Indeed,
based on cultural patterns, male patients can show their anger more easily compared to female patients, which is a common reason for psychiatric hospitalization. Therefore, there is more probability for their hospitalization. (41)

Most of our patients were between 21 and 40 years old, which is in accordance with the number of hospitalized and discharged patients of active wards of the psychiatric hospital since in active wards, mostly emergency cases of this age group are hospitalized. (41)

Most of the subjects had elementary education and were unemployed. Lower level of education and inappropriate employment of patients of Razi Psychiatric Hospital can be because most of these people reside in lower social and cultural levels of the society. Many patients and their family who were educated and possessed better employment status, preferred private hospitals for psychiatric rehospitalization.

Most of the studied patients had suffered from a psychiatric disorder between six and ten years. On the other hand, the maximum hospitalization period of most patients was between 21 and 30 days. These findings are in agreement with psychological references. (41)

Most psychiatric diagnosis were Schizophrenia, Bipolar Mood Disorder Type 1 (manic phase), and Bipolar Schizoaffective Disorder, respectively. This outcome is in agreement with psychological references. (5, 41)

The maximum accompaniment for psychiatric diagnosis was Bipolar Mood Disorder Type 1 (manic phase) with mental retardation, and Bipolar Mood Disorder Type 1 (manic phase) with Borderline Personality Disorder, respectively. In fact, accompaniment of Disorder Type 1 with Disorder Type 2 was the most common one. Similarly, this finding is in agreement with psychiatry references. (5, 41)

The amount of psychiatric drug consumption was 98.6%. In addition, poly pharmacy of psychiatric drugs was observed in more than 59% of the cases. Poly pharmacy is a prevalent case in psychiatric medical centers. Nowadays, poly pharmacy contains many complexities. Drugs have improved in their structure and new combinations and simultaneous drug consumption has become more rational and can be supported. For example, in special cases, patients who did not respond to one drug are recommended to take simultaneous drugs. Despite lack of scientific records for poly pharmacy, this issue should be further investigated. (42)

Simultaneous consumption of psychiatric drugs has increased constantly since the past decade. One common clinical justification of poly pharmacy application is that most patients do not recover by mono therapy of available drugs. There also may be another reason and that is when one patient does not respond to one drug, while by addition of other drugs, recovery is obtained (5, 41). In some patients, like patients suffering from bipolar mood disorder, consumption of more than one drug is a principle. (20, 22)

According to our findings, more than 90% of patients consume antipsychotic drugs, while poly pharmacy of antipsychotic drugs was observed in less than 30% of the cases. Among the subjects, there was no foursome antipsychotic poly pharmacy. In 3.35% of the cases, three antipsychotic drugs were used, while in 23.88% of patients, two antipsychotic drugs were taken simultaneously. Different studies resulted in dissimilar outcomes. For instance, only between 8% and 22% of subjects of the Rittmannsberg study (1999) had taken mono therapy, and the average amount of taken antipsychotic drugs was between two and three. Between 5% and 22% of patients took more than five psychotropic drugs (7). In a study in Austria, 47% of schizophrenic patients consumed two antipsychotic drugs, and three antipsychotic drugs were prescribed for 8% of the patients. (7)

The maximum accompaniment of antipsychotic drugs was for simultaneous consumption of Chlorpromazine and Haloperidol, Chlorpromazine and Risperidone, and Chlorpromazine and Olanzapine, respectively. In a study in Japan, the highest level of poly pharmacy has been reported. Combination of antipsychotic drugs of low potency and high potency is reported in more than 90% of schizophrenic patients. In the mentioned study, subjects were patients who had taken a combination of typical and atypical antipsychotic drugs for more than one month, and at least one of these drugs had been consumed for more than six months. (13)

The maximum ternary antipsychotic poly pharmacy is related to simultaneous consumption of Chlorpromazine, Flopentixol Decaonate, and Risperidone. In a descriptive investigation that was conducted, to evaluate poly pharmacy prevalence in treatment and educational hospitals (2005), this prevalence was 39% and 28%, respectively. Consumption of two, three, and four antipsychotic drugs in the treatment hospital was 25%, 13%, and
1%, and 12%, 14% and 2% in the educational hospital, respectively. Consumption of two typical drugs was 8.9% in the treatment hospital and 6.7% in the educational hospital, while this amount for one typical and one atypical drug was 63.7% in the treatment hospital and 46% in the educational hospital. Consumption of two atypical drugs was 27.4% and 47.3% in the treatment and educational hospitals, respectively. Antipsychotic polypharmacy of typical drugs put patients in more danger of extra pyramidal and metabolic effects compared to atypical drugs. (23) Simultaneous consumption of two atypical antipsychotic drugs was observed in seven patients, while in others, one atypical antipsychotic drug was used simultaneously. The only consumed atypical antipsychotic drugs were Risperidone, Olanzapine, and Clozapine. Generally, investigations have shown that combination of two typical antipsychotic drugs is inappropriate, while combination of typical and atypical drugs or two atypical drugs can be appropriate under certain circumstances. (6) The most common form of antipsychotic polypharmacy is combination of typical drugs, except Clozapine, and typical drugs. (27, 32, 33) Medication with more than one antipsychotic drug can be due to prevention of oscillation of each drug’s dose, or the substitute mechanism for cases that partially responded to medication, or did not respond at all. (19) Some of the references show rational polypharmacy. Improvement of mono therapy effectiveness with maximizing the D2 receptor employment in medication-resilient patients and consuming more amounts of receptors, except Dopamine, in patients who have responded to mono therapy, partially or insufficiently, or have not responded at all, can be effective. Antipsychotic medication can result in better recovery with fewer side effects, compared to increment of a single drug dose. (19) The average age of patients with antipsychotic polypharmacy was 34.81 and the average age of patients with antipsychotic mono therapy was 35.64. There was no significant difference between averages (test statistic of 0.84, P=0.401). Gender difference of patients with antipsychotic drugs is significant. Adaptive correlation coefficient with probability value of 0.001 was 0.136. In psychiatry references, mostly, the accompaniment of poly pharmacy with males is stated, which may be due to the expectation that male patients may have a more severe illness, accompanied with aggression and agitation. Physically, they can undergo combined medication more easily. (41) There is significant difference in using antipsychotics versus poly pharmacy in patients. Adaptive correlation coefficient with the P value of 0.001 is 0.126. This difference was due to unemployment in all psychiatry patients in the investigation. The difference between educations of patients with antipsychotic drugs poly pharmacy was not significant. The adaptive correlation coefficient of probability value of 0.534 was 0.023. The average illness period of patients with antipsychotic drugs poly pharmacy and patients with antipsychotic drugs mono therapy was 10.508 and 10.506, respectively. The difference between these averages was not considerable (test statistic was 0.003, P=0.998). The average hospitalization period of patients with poly pharmacy and patients with mono therapy was 36.95 and 31.12, respectively. The difference between these averages was significant (test statistic was 4.15, P<0.001). A relationship between consumption pattern and hospitalization ward was observed (test statistic was 12.09, P=0.001). Meanwhile, the rating correlation coefficient was -0.131. In other words, by changing educational ward to non-educational ward, consumption pattern is directed to poly pharmacy. In educational wards, prescription principles are considered for requirement of observance of scientific principles in drug prescription and supervision on this issue due to presence of psychiatry assistants. In a descriptive study conducted in 2005 to evaluate poly pharmacy prevalence in therapeutic and educational hospitals, this prevalence was found to be 39% and 28%, respectively. Simultaneous consumption amount of two, three, and four antipsychotic drugs in the treatment hospital was 25%, 13%, and 1%, and 12%, 14% and 2% in the educational hospital, respectively. Consumption of two typical drugs was 8.9% in the
The Spearman correlation coefficient between consumption pattern and relative medication cost was -0.195 (P=0.001), which means lower medication cost of mono therapy. Many controlled studies have shown increment in side effects and costs in antipsychotic poly pharmacy, without significant improvement in recovery of initial symptoms. (26)

Conclusion
According to the present study, it was revealed that antipsychotic poly pharmacy has a high prevalence and burdens high costs on patients. In this regard, each physician should consider a number of factors before adding the second drug and during its consumption. On the other hand, the health care system should be capable of controlling patient behavior and interfere when inappropriate poly pharmacy prescriptions occur.

This investigation can be a premise for further studies on changing antipsychotic drugs consumption pattern from poly pharmacy to mono therapy, for psychosis disorders. In addition, it is expected that this investigation be performed for other psychiatric drugs from other groups of psychotropic drugs.

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