Düşünen Adam The Journal of Psychiatry and Neurological Sciences 2012;25:43-50
DOI: 10.5350/DAJPN2012250105

Polypharmacy Among Inpatients of a University Psychiatry Clinic: A Retrospective Study

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ABSTRACT

Polypharmacy among inpatients of a university psychiatry clinic: a retrospective study

Objective: It has been reported that polypharmacy was frequent and increased lately. In our study, our purpose was to define the prevalence of polypharmacy and the level of polypharmacy according to the specified diagnostic groups.

Method: The files of 201 inpatients admitted between January 2010 and January 2011 were evaluated retrospectively. For every patient's last admission, prescribed drugs at that admission, time period of that admission, the number of past admissions and demographic data were evaluated and statistical analysis was performed.

Results: In the evaluation of the last admissions of 201 inpatients, it was detected that 145 (72.1%) patients had been given polypharmacy at discharge. Polypharmacy was mostly used in psychotic patients (60%) and number of drugs used per patient was 2.2. Polypharmacy was significantly more frequent in patients living in cities, with a longer hospital stay and in patients with higher number of past admissions.

Conclusion: Our finding of high percentage of polypharmacy shows that treatment algorithms are not followed as much as expected. With the development of the evidence based psychiatry, it is necessary to define ratios of benefits and harms while using polypharmacy. Only by this way, questions about if polypharmacy is a suitable approach or if the treatment algorithms can be changed accordingly may be answered.

Key words: Polypharmacy, inpatients, antipsychotic, antidepressant

ÖZET

Bir üniversite hastanesinde yatarak tedavi gören hastalarda çoklu ilaç kullanımı: Geriye dönük bir çalışma

Amaç: Psikiyatride çoklu ilaç kullanımına (ÇİK) sıkça başvurulduğu ve bunun son dönemlerde giderek arttığı belirtilmektedir. Bu çalışmada, bir üniversitenin psikiyatri kliniğinde yatan hastalarda ÇİK sıklığını ve belirlenen tanı gruplarına göre ÇİK düzeyini saptamayı amaçladık.

Yöntem: Çalışmamızda, Eskişehir Osmangazi Üniversitesi Tıp Fakültesi Psikiyatri Servisinde, Ocak 2010-Ocak 2011 tarihleri arasında yatarak tedavi görmüş 201 hastanın dosyaları geriye dönük olarak incelenmiştir. Her dosyadan, hastaların son yatıştaki tanısı, taburcu edilirken reçete edilen ilaçlar, yatış süresi, daha önce başka yatışlarının olup olmadığı ve demografik verileri kaydedilmiş ve istatistiksel olarak incelenmiştir. Tekrarlayan yatışı olanların son yatışı değerlendirilmiştir.

Bulgular: Dosyaları incelenen 201 hastanın son yatışları değerlendirildiğinde; taburcu edilme sırasında 145 (%72.1) hastada ÇİK saptandı. En çok ÇİK uygulaması (%60) psikotik bozukluklarda iken, hasta başına düşen ilaç sayısı ise 2.2'ydi. ÇİK kentte yaşayanlarda, yatış süresi uzun olanlarda ve daha önceki yatış sayısı fazla olanlarda anlamlı olarak daha yüksekti.

Sonuç: Çalışmamızda oldukça yüksek bulunan ÇİK sıklığı, tedavi protokollerine uyumun beklenilen ölçüde olmadığını göstermektedir. Kanıta dayalı psikiyatrinin gelişmesiyle uygulanan çoklu ilaç kullanımının yarar/zarar oranının belirlenmesi gerekli görünmektedir. Ancak bu şekilde, uygulanan ÇİK'in doğru bir yaklaşım olup olmadığı ve tedavi protokollerinin bu yönde değiştirilip değiştirilmeyeceğiyle ilgili sorular cevaplanabilecektir.

Anahtar kelimeler: Çoklu ilaç, yatan hasta, antipsikotik, antidepresan

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Date of receipt:
March 31, 2011

Date of acceptance:
June 25, 2011

INTRODUCTION

Multiple medication use (MMU) or polypharmacy defines utilization of more than one type of medication. Although single medication use is aimed, MMU is often preferred in psychiatry and MMU has increased 30-40% in the last 20 years (1). MMU is an important problem not only for psychiatry but for other specialties as well (2,3). This situation becomes even more important due to higher prevalence of cardiovascular diseases and dementia in elderly population and reduced working pace of mechanisms responsible for drug metabolism and elimination in the elderly. A Canadian study reported that individuals over 75 years old use an average of six different medications (4). Although there is a pre-specified treatment algorithm for each disease, being treated by more than one physician and expecting more powerful or quicker response from medications cause under–utilization of evidence-based algorithms and overconsumption of medications without adequate evidence. Every medication used has a therapeutic efficacy. Antidepressants, anticoagulants or non-steroid anti-inflammatory drugs may not cause serious problems when used separately. However, when they are used in combination, they may cause serious negative consequences such as drug-drug interactions and gastric bleeding. Moreover, medications may increase or decrease each other's efficacy (5). Multiple medication use leads to confusion of doses of medications and reduced adherence. It was already shown that utilization of smaller number of medications and reducing the complexity of drug regimen increase patients' adherence (6). Adherence to medication may be vital in diseases such as schizophrenia and bipolar disorder. It was reported that 30-60% of patients with schizophrenia have impaired adherence to their medications (7). It is now known that exacerbation of diseases is generally due to withdrawal of medications. Although MMU is not the only reason of withdrawal of medications, effect of MMU is considerable. Moreover, MMU increases treatment costs. Unnecessary utilization of medications causes both biological and economic harm (8).

When all these factors are considered, bringing up the amount of MMU is important for interventions to be implemented. In this study, we aimed to determine the prevalence of MMU and amount of MMU according to diagnostic groups in patients admitted to Psychiatry Inpatient Clinic of Eskişehir Osmangazi University Medical School during the last year.

METHODS

In this study, patient files treated at inpatient clinic of Eskişehir Osmangazi University Medical School, Department of Psychiatry between January 2010 and January 2011 were examined retrospectively. Diagnosis at last admission, medications prescribed when discharged, duration of hospitalization, presence of previous admissions and demographic data were recorded from each file and statistical analysis was performed. Last admission of patients who were repeatedly admitted was taken into consideration. For a healthier statistical evaluation, diagnoses were classified under four categories: psychotic disorders (schizophrenia, schizoaffective disorder, and bipolar disorder), major depression, anxiety disorders and others (somatoform disorder, substance abuse disorder, personality disorder, adjustment disorder etc.). Presence of a difference on MMU between four disease categories was evaluated by chi-square test. Categories with or without MMU were also evaluated by chi-square test for variables of gender, marital status, people who are living with, residence and working status. As gender, duration of education, duration of hospital stay, age of disease onset and number of admissions before index episode did not show normal distribution according to Kolmogorov-Smirnov test, Mann-Whitney U test was used for inter-group comparisons. Statistical significance was accepted as $p<0.05$. Approval was taken from ethical committee of Eskişehir Osmangazi University Medical School for conducting the study.

RESULTS

Files of 201 patients who were admitted to inpatient clinic of Eskişehir Osmangazi University Medical

School, Department of Psychiatry during a one year period were examined in our study. Mean age of patients was 39.11±14.54, mean duration of hospitalization was 25.85±18.86 days and mean duration of education was 8.49±4.16 years. Ninety patients were (44.8%) men and 111 (55.2%) were women. Sixty-three patients (31.3%) were single, 111 (55.2%) were married and 27 (13.4%) were divorced/widows. Fifteen patients (7.5%) reported to live alone, 117 (58.2%) were living with spouses and/or children, 62 (30.8%) were living with parents, 2 (1%) were living in an institution and residence of 5 patients (2.5%) could not be determined. Among patients who were admitted through one year, 48 (23.9%) had bipolar disorder, 35 (17.4%) had schizophrenia, 34 (16.9%) had depression, 7 (3.5%) had somatization/conversion disorder, 22 (10.9%) had anxiety disorder, 6 (3%) had adjustment disorder, 23 (11.4%) had substance abuse disorders, 4 (2%) had schizoaffective disorder and 22 (10.9%) were diagnosed as diseases other than these.

When last admissions in files of 201 patients whose files were evaluated, MMU was detected at 145 patients (72.1%) at discharge. Among patients with MMU, 87 (60%) were diagnosed as psychotic disorder (schizophrenia, bipolar disorder, schizoaffective disorder), 25 (12.44%) were diagnosed as depression, 19 (9.45%) were diagnosed as anxiety disorder and 20 (9.95%) were from other disorders group. Among patients with psychotic disorder and MMU, there was multiple antipsychotic use in 64 patients (73.6%) and use of three or more antipsychotic use in 44 patients (50.6%). Nine patients (4.5%) were using benzodiazepines at discharge. Distribution of with and without MMU patients according to diagnostic groups was shown at Table 1 (Table 1). MMU at discharge was significantly different between patient categories (χ^2=62.62, p<0.001, df=3). Frequency of MMU was

Table 1: MMU according to diagnostic groups

	MMU Present		MMU absent		Total	
	n	%	n	%	n	%
Psychotic disorders	81	93.10	6	6.90	87	100
Major depression	25	73.57	9	26.47	34	100
Anxiety disorders	19	85.72	3	14.28	22	100
Other	20	34.48	38	65.52	58	100

MMU: Multiple Medication Use, χ^2=62.62, p<0.001, df=3

Table 2: Comparison of demographic characteristics according to groups

	Group with MMU (N=145)		Group without MMU (N=56)			
	n	%	n	%	χ^2	p
Gender						
Women	84	57.93	27	48.21	1.543	p >0.05
Men	61	42.07	29	51.79		
Marital status						
Married	78	53.79	33	58.93	0.431	p >0.05
Single/Divorced	67	46.21	23	41.07		
Person living with						
Single	13	8.96	8	42.29	1.222	p >0.05
Spouse/family/children	132	91.04	48	57.71		
Residence						
Urban	106	73.10	51	91.07	7.628	p <0.01
Rural	39	26.90	5	8.93		
Working status						
Working	31	21.38	13	23.21	0.080	p >0.05
Unemployed	114	78.62	43	76.79		

χ^2: Chi-square test

Table 3: Comparison of some demographic and clinical characteristics according to groups

	Group with MMU (n=145)		Group without MMU (n=56)			
	Median	25-75%	Median	25-75%	z	p
Age	36	28-48	36	25.75-53.50	-0.52	p>0.05
Duration of education (year)	8	5-11	8	5-11	-0.36	p>0.05
Duration of hospitalization (day)	24	14-41	15.50	8.25-22	-4.05	p<0.001
Age of disease onset	28	20-38	25.50	19.25- 40.75	-0.42	p>0.05
Number of admissions before index episode	1	0-2	0	0-1	-2.21	p<0.05

MMU: Multiple Medication Use, z: Mann-Whitney U Test

detected highest in patients with psychotic disorder category and lowest at "other disorders" category.

Seventy-four patients (36.8%) with MMU were discharged with three or more medications. It was found that 28 patients (13.8%) were discharged with two or more antidepressants and 74 patients (36.8%) were discharged with two or more antipsychotics. Number of medications per patient was found as 2.2 (min: 1, max: 6). Mostly used antipsychotic in inpatients was quetiapine (n=105, 52.2%) and mostly used antidepressant was trazodone (n=34, 16.9%). Twenty-one inpatients (10.5%) were 60 years old or over, 13 (61.9%) of them had MMU and 8 patients with MMU (38.1%) used 3 medications or more.

When recruited patients were divided into two groups as with and without MMU and compared according to demographic and clinical characteristics, more MMU was found in patients living in urban areas at the time of discharge compared to patients living in rural areas (χ^2=7.628, p=0.006). Moreover, MMU was significantly higher in patients with longer duration of hospitalization (z=-4.05, p<0.001) and higher number of previous hospitalizations (z=-2.21 p<0.05). Comparison of groups with and without MMU according to demographic characteristics was shown in Table 2 and according to clinical characteristics was shown in Table 3.

DISCUSSION

In our study, files of last admissions of inpatients were examined throughout a year retrospectively. It was found that 72.1% of patients were discharged with more than one medication. Mean number of medications per patient was found 2.2. MMU is gradually increasing in recent years due to increasing number of medications developed and complex etiologies of psychiatric diseases. The study of Mojtabai and Olfson (9), showed that prescription of two or more medications in a single prescription increased from 42.6% to 59.8% between 1997 and 2006 in outpatients. In another study done in Netherlands, 323 patients were evaluated and number of medications per patient was found 4.6 (10). In a retrospective study done in our country, Ensari et al. (11) reported frequency of two or more psychotropic medication use as 30.2% at 3 different psychiatry hospitals. Frequency of patients using three or more medications was found 36.8% in our study. In the study of Mojtabai and Olfson, it was reported that prescription of three or more medications increased from 16.9% to 33.2% between 1997 and 2006. In a study in which records of 1304 patients at psychiatry hospitals in Albania, Croatia, Serbia, Romania and Macedonia from Eastern Europe were examined, single medication use was reported only in 6.8% of patients. Mean number of medications per patient was found as 2.8. Among patients whom records were examined, it was found that 64.2% used three or more psychotropic medications (12). When numbers in different studies were analyzed, it can be said that these differences were due to population studied. Frequency of 72.1% MMU in our study is quite high. On the other hand, 2.2 medications per patient is lower than the number in the Flemish study. Location of our study is tertiary care center where patients are also referred from peripheral cities and secondary care centers so it can be said that an important portion of these inpatients are relatively treatment-refractory and severe patients. For this reason, it seems that more medications needed for treatment. It can also

be said that more augmentation treatments in treatment protocols are needed. When the study done at Eastern European countries is taken into consideration, our study figures seem to be lower. In our study, medications prescribed at discharge were evaluated. Higher number of medications during hospital stay can be expected. Difference between 93.2% MMU at that study and 72.1% MMU in our study can be explained by this.

When multiple antidepressant and antipsychotic use in our study is examined, it was found that 13.8% of patients used two or more antidepressants and 36.8% of patients used two or more antipsychotics. In major depression treatment protocol, it was mentioned that treatment can be started by medication, psychotherapy or ECT, replacement, add-on or augmentation treatments can be used when treatment response is lacking or inadequate (13). Although never recommended at any step in this treatment protocol, concomitant use of two or more antidepressants is a frequent condition in practical use. In a study done in Japan, two or more antidepressants are being used in 67.7% of inpatients with depression (14). However, single medication has not been used at adequate doses and duration, and MMU did not contribute to recovery of major depression in patients whom MMU was detected (15). One of the medication groups mentioned frequently due to their adverse effect profiles is antipsychotic medications. Antipsychotics are started being prescribed at increasing number of indications and frequency (16). In a study which 305 patients using antipsychotics, frequency of two or more antipsychotic use was found 23% (17). In another study done in France, prescriptions of 2192 psychiatric patients were examined and 49.3% of them were found to be prescribed more than one antipsychotic (18). Although antipsychotics are not that much frequently used concomitantly, evidence-based data are lacking and antipsychotic combination treatment was not found to be superior to monotherapy (19). Moreover, it was already reported that multiple use of psychotropic medications increases adverse effects (20). The most important adverse effect of antipsychotics attracting attention recently is metabolic syndrome. Metabolic syndrome develops significantly more frequently in patients receiving multiple antipsychotic medications (50%) than patients receiving a single antipsychotic (34.3%). However, multiple antipsychotic use was not found to increase the risk alone when evaluated together with other demographic data in the risk analysis (21). In another study Cerit et al. (22) examined 242 patients with schizophrenia, schizoaffective disorder and bipolar disorder and reported that frequency of metabolic syndrome was found higher in patients using multiple antipsychotics. Extrapyramidal adverse effects which are one of the most frequent adverse effects seen with antipsychotics were also reported to increase by increasing number of medications used and this increase was related to higher cumulative dose in patients using multiple medications (23). No clear finding was concluded in two studies examining effect of multiple antipsychotic use on cognitive functions and negative effects of conventional antipsychotics were reported rather than multiple antipsychotic use (24,25). No difference between monotherapy and multiple antipsychotic use was reported in another study investigating natural causes of death in patients with schizophrenia (26). However, Weinmann et al. (27) reviewed mortality studies done at schizophrenia patients and reported that results of 2 of 4 studies on multiple medication use were negative. According to this study, much the same as metabolic syndrome, there are no exact data on mortality.

Medication use in elderly population is being increasingly important in recent years due to prolonged life-span. Frequency of psychiatric diseases concomitant with cardiac and other somatic diseases increases in this period. MMU is a particularly important issue in this population which is more sensitive to medication doses. In a study done in France, mean number of medications per inpatient 75 years old or older was reported to be 5.7 (28). Such a high number of psychotropic medication use is particularly important for drug-drug interactions due to reduced hepatic and renal functions in the elderly. In our study, 10.5% of inpatients were over 60 years old and two or more psychiatric medications were used in 64.8% of these patients. Adverse effects and interactions were not evaluated in our study and for this reason, possible drug-drug interactions could not be determined

in the elderly population. However, in a study done in two geriatric psychiatry clinics in Britain, number of medications per patient was 8.3 and combinations which may cause potential drug-drug interactions were reported in 96% of them (29). It was also reported that multiple antipsychotic use causes falls which is one of the most important reasons causing reduced quality of life and disability in elderly population and is an important risk factor from this point of view as well (30).

MMU was significantly variable between disease categories in our study. In the psychotic patient group (schizophrenia, schizoaffective disorder and bipolar disorder), two or more psychiatric medication use was found in 81 patients out of 87. In the study of Santone et al. (31), while frequency of unipolar depression and anxiety disorder was higher in patients using antipsychotic monotherapy, schizophrenia was reported more frequently in the group using multiple antipsychotics. In the same study, it was reported that multiple antipsychotic use is more frequent in patients who have difficulty in cooperation and having worse insight of their diseases. Among patients using antipsychotics, multiple medication use was reported more frequently in schizophrenia patients and the ones having less insight.

In our study, longer duration of hospital stay and higher number of previous hospitalizations were found to be correlated with MMU. This may be due to more severe and/or refractory disease course and recurrences and MMU may be one of the methods tried to control the disease. Böke et al.(32) found duration of hospitalization of patients taking multiple antipsychotics longer than patients taking a single antipsychotic and stated that this can both be interpreted as diseases of patients taking multiple antipsychotics are more difficult to be treated and multiple antipsychotic use does not reduce duration of stay as well. Similarly, in the study of Hatıloğlu et al. (33) done with psychotic patients, MMU frequency was found higher in groups who were unemployed, had higher number of admissions and, longer duration of hospital stay and medication use. They reported that this finding may indicate decreased response of the disease to treatment and treatment-refractoriness. Besides, higher number of hospitalizations in the group with multiple medication use in our study is consistent with findings of the study of Özalmete et al. (34). This condition has been related to inadherence to multiple medications. In a study comparing clozapine and MMU done with treatment-refractory schizophrenia patients, it was reported that MMU increased treatment costs and efficacy on symptoms is minimal (35). In the same study, it was stated that single clozapine therapy is generally initiated late in most patients due to multiple antipsychotic use.

The most important limitation of our study is its retrospective nature and difficulties in access to required information. Other limitations were lack of an investigation towards relationship between drug adverse events and MMU with drug adverse events, doing the study at a tertiary institution, not knowing reasons of MMU preference of clinicians and not stating duration of MMU.

In this study we aimed to determine frequency of MMU of psychiatric medications. We found that increasing number of MMU practice all over the world is not different from findings of our study. Frequency of MMU at time of discharge (72.1%) and other high numbers of MMU in other studies indicate that adherence to treatment protocols is not at an expected level. By evidence-based psychiatry evolving, it seems that benefit/harm ratios of MMU should be determined. Questions whether MMU is a valid approach and whether treatment protocols will be changed according to this can be answered only by this way.

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