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Original article

Prescribing practices in psychiatric hospitals in Eastern Europe

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ABSTRACT

Background: There has been no evidence about the prescribing practices in psychiatric care in Eastern Europe.
Aims: To examine the patterns of psychotropic prescribing in five countries of Eastern Europe.
Method: We conducted a one-day census of psychiatric treatments used in eight psychiatric hospitals in Albania, Croatia, Macedonia, Serbia and Romania. We examined clinical records and medication charts of 1304 patients.
Results: The use of polypharmacy was frequent across all diagnostic groups. Only 6.8% of patients were on monotherapy. The mean number of prescribed drugs was 2.8 (SD 0.97) with 26.5% receiving two drugs, 42.1% receiving three drugs and 22.1% being prescribed four or more psychotropic drugs. Typical antipsychotics were prescribed to 63% and atypical antipsychotics to 40% of patients with psychosis. Older generations of antidepressants were prescribed to 29% of patients with depression. Anxiolitic drugs were prescribed to 20.4% and benzodiazepines to 68.5% of patients. One third of patients received an anticholinergic drug on a regular basis.
Conclusions: Older generation antipsychotics and antidepressants were used more frequently than in the countries of Western Europe. Psychotropic polypharmacy is a common practice. There is a need for adopting more evidence-based practice in psychiatric care in these countries.

1. Introduction

There are great variations in the way psychotropic drugs are prescribed across the world. Despite the emerging evidence of the advantages of psychopharmacological monotherapy, multiple drug prescribing is still common in clinical practice of many countries [10]. A multicentric survey of the prescription of antipsychotic drugs for hospitalised patients in the UK [8] found that nearly 50% were receiving more than one antipsychotic drug. Holloway found that overprescribing of sedatives and anticholinergic drugs was common practice in the UK [9]. A recent survey in Ireland also revealed high prevalence of prescribing of benzodiazepines and hypnotics [7]. An Austrian survey found that a quarter of psychiatric patients received three or more psychotropic agents [20]. A US survey found that antipsychotic polypharmacy was low in the year after the initiation of therapy and that polypharmacy was more common in patients with indicators of more severe mental illness [16].

There is very limited evidence about the prescribing practices in psychiatric care in Eastern Europe. Cross-sectional survey of prescribing habits provides a quick, global estimation of treatment practices. This study was conducted by the Eastern European Psychiatric Scientific Initiative (the EEPSI), a research network of psychiatrists in Eastern Europe that aims to develop evidence-based research in the region [6]. The main objective of the study was to investigate the patterns of prescribing of psychotropic drugs in psychiatric hospitals in five countries in Eastern Europe.

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2. Method

We conducted a one day census in psychiatric hospitals in eight centres: Belgrade in Serbia, Bucharest, Iasi and Targu Mures in Romania, Strumica in Macedonia, Tirana in Albania and Zagreb in Croatia. The census included all patients (aged 18–65 years) that were hospitalised in participating centres at the time of the survey. The study obtained ethical approval before the fieldwork was conducted. A total sample of 1304 patients was examined. The naturalistic design of this study has limitations but is more reflective of the real-world practice.

The data was extracted from clinical records and medication charts for each patient across the centres. We recorded data about sociodemographic characteristics, duration of current hospitalisation and clinical diagnosis using the tenth edition of the International Classification of Diseases (ICD-10) [25]. The data about prescribed psychotropic drugs included the generic and trade names of each drug prescribed in the 24 hour period of the survey. General data about numbers of available beds, staffing levels, clinical, and technical facilities of each centre was collected using the European Service Mapping Schedule (ESMS) version 3 [11].

All psychotropic drugs were included in the survey:

- antipsychotics;
- antidepressive drugs;
- benzodiazepines;
- anxiolytics;
- mood stabilisers;
- anticholinergic drugs.

Diagnostic groups used for comparison were based on ICD-10 categories:

- mental and behavioural disorders due to psychoactive substance use;
- psychosis;
- depression;
- bipolar affective disorder (BAD);
- anxiety;
- personality and eating disorders.

Data was analysed with SPSS version 16 and SATS (SPSS Inc, Chicago, IL, USA).

2.1. Participating centres

The participating psychiatric services share a number of important characteristics. All are representative state institutions and the costs of treatment are covered by national health insurances. The patients in Belgrade were recruited from two different psychiatric hospitals, a large psychiatric hospital that serves Belgrade and its surroundings (Belgrade-1) and a university hospital (Belgrade-2). The patients were recruited from inpatient wards and day centre services. In Bucharest, patients were recruited from five adult inpatient units of the largest psychiatric hospital in Romania. In Iasi, the study was carried out at the university psychiatric hospital; patients were recruited from inpatient wards. In Strumica, the patients were recruited from a psychiatric inpatient unit and an outpatient clinic that provides the only psychiatric service in the region. In Targu Mures, the study was conducted at a university psychiatric hospital; subjects were recruited from the inpatient service. In Tirana, patients were recruited from the inpatient wards at the university psychiatric hospital. In Zagreb, the study was conducted at the University Clinic of Psychiatry; subjects were recruited from the inpatient psychiatric service.

Table 1
Demographic characteristics and duration of hospitalisation at each centre.

Centre	Gender (male)	Age	DoH[a]
	n (%)	mean (95% CI)	Mean (95% CI)
Belgrade-1	260 (51.7)	46.5 (45.3–47.8)	421.3 (288.6–1131.2)
Belgrade-2	43 (51.2)	45.3 (42.9–47.6)	37.3 (32.0–42.6)
Bucharest	112 (33.8)	46.6 (45.1–48.1)	26.1 (22.3–29.8)
Iasi	67 (60.9)	49.2 (46.9–51.4)	9.1 (8.2–10.0)
Strumica	33 (63.5)	38.4 (35.5–41.2)	193.5 (153.0–234.0)
TgMures	34 (48.6)	48.7 (45.4–52.0)	17.0 (15.5–18.5)
Tirana	51 (64.6)	37.1 (34.8–39.3)	18.4 (15.0–21.7)
Zagreb	33 (44)	45.1 (42.1–48.2)	15.1 (12.7–17.6)

TgMures: Targu Mures.
[a] Duration of hospital admission in days.

3. Results

The demographic profile differed between centres (Table 1). The mean age was 45.8 years, with a younger average age in Tirana (37.1 years) and an older average age in Iasi (49.2 years). The duration of hospitalisation varied between centres, with patients in Belgrade-1 having average duration of hospitalisation of 421.3 days. The most frequent diagnosis in all centres combined was psychosis (44.3%), followed by "other" mental disorders (22.4%) and depression (22.1%) (Table 2). The "other" mental disorders category included the ICD-10 diagnoses with low prevalence in our sample (personality disorders, substance misuse and eating disorders). The highest proportion of patients with psychosis was seen in Strumica, Belgrade-1 and Tirana (63.5, 59.2 and 57.0%, respectively). In Iasi, Targu Mures and Zagreb, the most frequent diagnosis was depression. Anxiety disorders were not commonly seen across the centres, apart from Targu Mures and Zagreb (22.9 and 16.0%, respectively).

The mean number of prescribed drugs was similar across centres (Table 3). The mean number of drugs used in all centres combined was 2.8 (SD 0.9). Only 6.8% of patients received monotherapy. Forty-two decimal one percent of patients in all centres combined received three psychotropic drugs, while 23.2 received four or more drugs. None of the patients in Strumica was on monotherapy. Across other centres, monotherapy was used between 4.4 and 8.9%, apart from Iasi were 20.0% of patients received only one drug. Polypharmacy was also present in Iasi, where 25.5% of patients received three psychiatric drugs. None of the patients in Belgrade-2, Strumica, Targu Mures and Tirana was medication-free. The use of polypharmacy was frequent across all diagnostic groups (Table 4). Monotherapy was rarely used for patients whose first diagnosis was depression or anxiety (6.6 and 5.0%, respectively). None of the patients with anxiety was medication-free, while 39.3% received three different psychotropic drugs.

Table 2
ICD-10 diagnosis across centres.

Centre	Depression	Anxiety	Psychosis	BAD[a]	Other
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Belgrade-1	49 (9.7)	3 (0.6)	298 (59.2)	16 (3.2)	137 (27.2)
Belgrade-2	21 (25.0)	2 (3.3)	32 (38.1)	6 (7.1)	22 (26.2)
Bucharest	109 (32.9)	25 (7.6)	116 (35.0)	25 (7.6)	56 (16.9)
Iasi	31 (28.2)	/	23 (20.9)	12 (10.9)	44 (40.0)
Strumica	3 (5.8)	2 (3.3)	33 (63.5)	5 (9.6)	9 (17.3)
TgMures	28 (40.0)	16 (22.9)	10 (14.3)	3 (4.3)	13 (18.6)
Tirana	15 (19.0)	1 (1.3)	45 (57.0)	16 (20.3)	2 (2.5)
Zagreb	32 (42.7)	12 (16.0)	21 (28.0)	1 (1.3)	9 (12.0)
Combined	288 (22.1)	61 (4.7)	578 (44.3)	84 (6.4)	292 (22.4)

TgMures: Targu Mures.
[a] Bipolar affective disorder.

Table 3
Use of polypharmacy across centres.

Number of drugs	0	1	2	3	4 or more	Mean
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	(s.d.)
Belgrade-1	2 (0.4)	22 (4.4)	90 (17.9)	243 (48.3)	146 (29.0)	3.0 (0.8)
Belgrade-2	/	7 (8.3)	25 (29.8)	33 (39.3)	19 (22.6)	2.8 (0.9)
Bucharest	4 (1.2)	19 (5.7)	98 (29.6)	117 (35.4)	76 (28.1)	2.9 (1.1)
Iasi	14 (12.7)	22 (20.0)	43 (39.1)	28 (25.5)	3 (2.7)	1.9 (1.0)
Strumica	/	/	9 (17.3)	31 (59.6)	12 (23.1)	3.1 (0.6)
TgMures	/	6 (8.6)	21 (30.0)	33 (47.1)	10 (14.3)	2.7 (0.8)
Tirana	/	7 (8.9)	39 (49.4)	31 (39.2)	2 (2.5)	2.4 (0.7)
Zagreb	1 (1.3)	5 (6.7)	20 (26.7)	33 (44.0)	16 (21.3)	2.8 (0.9)
Combined	21 (1.6)	88 (6.8)	345 (26.5)	549 (42.1)	301 (23.1)	2.8 (0.9)

TgMures: Targu Mures.

Table 4
Use of polypharmacy across diagnostic groups.

Number of drugs	0	1	2	3	4	>4
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Depression	3 (1.0)	19 (6.6)	91 (31.5)	124 (42.9)	46 (15.9)	6 (2.1)
Anxiety	0 (0.0)	3 (5.0)	23 (37.7)	24 (39.3)	10 (16.4)	1 (1.6)
BAD[a]	1 (1.2)	3 (3.6)	20 (23.8)	36 (42.9)	21 (25)	3 (3.6)
Psychosis	12 (2.1)	16 (2.8)	113 (19.6)	261 (45.2)	165 (28.6)	11(1.9)
Other	5 (1.7)	47 (16.1)	98 (33.6)	104 (35.6)	36 (12.3)	2 (0.7)

[a] Bipolar affective disorder.

Ninety-three decimal one percent of patients with psychosis received antipsychotic treatment. Sixty-nine decimal two percent of patients with psychosis were prescribed one antipsychotic, 22.2% received two and 1.7% received three different antipsychotics concomitantly. In Strumica, 66.7% of patients with psychosis received three psychotropic drugs, while 27.3% were given four different drugs. In Belgrade-1, 50% of psychotic patients received three and 33.6% four different psychotropic drugs. In Belgrade-2, 31.3% of patients with psychosis received three and 34.4% were given four psychotropic drugs. In Tirana, 55.6% of psychotic patients received two, 26.7% three and 4.4% four different drugs. In Bucharest, 44% of psychotic patients received three and 26.7% were given four psychotropic drugs. Typical antipsychotics were given in 63.3% of psychotic patients. Atypical antipsychotics were prescribed to 40% of those with psychosis. Depot antipsychotics were given to 15.4% of psychotic patients.

Among those diagnosed with depression, 83.4% received an antidepressant. The SSRIs were given to 29.4% and other newer antidepressants to 46% of depressed patients. Older generations of antidepressants (tricyclic antidepressants and monoamine oxidase inhibitors) were prescribed to 29.1% of patients. Nineteen percent of patients with depression received two antidepressants concomitantly. In Strumica, Tirana and Targu Mures, depressed patients frequently received three different psychotropic drugs (66.7, 60.0 and 53.6%, respectively). In Bucharest, 19.3% of patients with depression received four different psychotropic drugs.

Among patients with anxiety disorders, 67.2% received an anxiolitic drug. Benzodiazepines were given to 75.1% and antipsychotic drugs to 37.7% of those with anxiety. Antidepressants were prescribed to 82%, but SSRIs were given to 36.1% of patients with anxiety disorders. In Targu Mures, one half of patients with anxiety received three psychotropic drugs. In Zagreb, 41.7% of patients with anxiety received three psychotropic drugs and 25% four different drugs. In Bucharest, 32% of patients with anxiety received three psychiatric drugs, while 24% were given four different drugs.

Mood stabilisers were given to 77.4% of patients with BAD. Antipsychotic drugs were prescribed to 75% and atypical antipsychotics to 34.5% of those with BAD.

One third of patients received anticholinergic treatment on a regular basis. Among patients with psychosis, 48.3% received an anticholinergic drug concomitantly with their antipsychotic treatment. Benzodiazepines were prescribed to 68.5% of all patients. Seventy-five percent of patients with psychosis and 64% of those with BAD received benzodiazepines.

4. Discussion

Our study found high prevalence of polypharmacy across participating centres for all clinical diagnoses. Monotherapy in the treatment of psychiatric disorders is recommended by a number of guidelines [1,17], yet, only small minority of our patients received only one drug. Psychotropic prescribing deviated considerably from the recommendations by these guidelines.

We found high prevalence of concomitant use of two or more antipsychotic drugs in patients with psychosis. This pattern was evident across all study centres. Our findings are in line with the prescribing surveys in Western European countries [8,18]. Taylor et al. found that conventional and atypical antipsychotics are commonly co-prescribed and the combination of a conventional antipsychotic and clozapine is a common practice [22]. There have been reports that conventional antipsychotics are used in around a third of those receiving clozapine in some European countries [19]. Similarly, Divac et al. [4] found that 68% of psychiatric patients in Serbia received two or more antipsychotic drugs concomitantly.

The evidence base shows that the routine use of combined antipsychotics are not more effective than a single antipsychotic and such use may increase the likelihood of additive side-effects. Centorrino et al. showed that patients receiving combined antipsychotics have longer hospital stay and more frequent side-effects [2].

Our study revealed that typical antipsychotics and older generation antidepressants are more commonly prescribed than newer drugs. This is contrary to the trend in developed countries where "second-generation" agents have come to dominate the clinical practice. The recent evidence points that atypical antipsychotics are not more effective than typical drugs [12,15].

However, a recent meta-analysis showed that newer drugs have advantages over the older drugs due to their different profile of side-effects [14].

All hospitals involved in our study are state institutions that have restricted resources. This directly influences the treatment choices in the clinical practice. The availability of medication and prescribing regulations limit the autonomy of the clinicians. However, the appearance of generic new drugs in these countries made the price difference less likely to be the main reason for the use of the older drugs.

We found considerably lower rate of use of depot antipsychotics compared to the evidence from the UK. The national household survey in the UK found that approximately 30% of non-hospitalised individuals with psychotic disorders were receiving depot treatment [5]. This pattern in our centres may arise from the absence of community psychiatric services and the consequent prolonged use of inpatient facilities for those with enduring mental illness where treatment compliance is closely monitored and therefore oral medication commonly used.

Monotherapy was rarely used for those whose first diagnosis was a neurotic disorder. Patients with anxiety disorders were all treated with polypharmacy. None of the patients with anxiety was medication-free. The extensive use of polypharmacy in the management of anxiety may reflect the limited access to psychological interventions in the participating services.

There was very high prevalence of use of benzodiazepines. Previous studies conducted in the general population of Serbia found that the utilization of benzodiazepines has increased over the last decade, indicating a trend to self-medication, particularly in the period of the recent war crisis [3]. Our findings are in line with those from Western European countries. Previous surveys in the UK and Ireland found high prevalence of benzodiazepine use in psychiatric hospitals [24,7], despite the recommendations by a number of guidelines that their use should be restricted to less than four weeks [17,1].

Anticholinergic drugs were commonly prescribed as a regular medication across all centres. This pattern arises due to common treatments with typical antipsychotics with higher propensity to extrapyramidal side-effects compared to atypical antipsychotics.

The sample size for single centres was relatively small to draw definite conclusions, but sufficient to give a representation of prescribing practices. The response rate was almost 100% in all centres, so minimising selection bias.

One of the surprising features of our study is the similarity in the patterns of prescribing among five countries in East Europe. In a series of similar studies [21,10,23], which surveyed the prescription patterns of antipsychotics and antidepressants among six countries in East Asia (China, Hong Kong, Japan, Korea, Singapore, and Taiwan), the pattern of prescription differed greatly country by country. The differences in government policies and service organisation were considered to play a major contribution to the variations in clinical practices in East Asia. Although patterns of prescription might vary country by country, as also shown by another multicentric study (Spain, Estonia and Sweden) [13], polypharmacy with antipsychotic drugs is considered as an international phenomenon. The striking similarity in the patterns of prescribing in our participating centres could be explained by similar economic and educational opportunities, collaboration and bidirectional influences during the past decades, mostly based on government policy. All countries involved in our study share similar organisational characteristics. They are going through a period of transition of psychiatric services and gradual deinstitutalization, but none of them have yet developed community based psychiatric services. Psychiatric care is provided by inpatient facilities, outpatient services and day centres. Another shared characteristic of these countries is the lack of national guidelines for psychotropic prescribing at the time of the survey.

Common prescribing patterns in psychiatric services included in our survey should be improved and action in relation of polypharmacy prescribing is required. This could be achieved with an introduction of clear national guidelines and routine audit of prescribing practices in psychiatric care. There needs to be a shift to a more evidence-based culture. We recommend that consideration be given to the inclusion of a research and quality improvement agenda in the national programmes of mental health.

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