

Pharmaceutical care in a long-stay psychiatric hospital

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ABSTRACT

Objectives The aim of this study was to evaluate implementation of services provided by a clinical pharmacist for long-term-hospitalised patients with schizophrenia in a pharmaceutical-care-naive developing country.

Method This was a prospective, healthcare-system, interventional, 'before-and-after' study. Long-term (≥ 6 months) inpatients with schizophrenia were included. A clinical pharmacist reviewed the full patient notes, identified drug-related problems (DRPs), and proposed interventions using a DRP Registration Form (PCNE classification V6.2). Acceptance rate and outcomes of interventions were assessed.

Results For 49 patients, 71 DRPs were identified, ranging from one to four problems/patient (1.43 ± 0.68), predominantly related to tolerability and treatment effectiveness. The DRPs were mostly caused ($N=184$) by inappropriate drug selection (64%) or dose (23.4%): too many drugs for indication ($N=33$); a non-cost-effective choice ($N=29$); inappropriate combination ($N=27$); an inappropriate drug ($N=23$); lack of therapeutic drug monitoring ($N=14$); subtherapeutic ($N=13$) or supratherapeutic ($N=11$) dosing. Excessive treatment duration was observed for 14 DRPs. The clinical pharmacist proposed 182 interventions (70% at the drug level): discontinuation of medication ($N=58$); dosage change ($N=35$); other interventions (monitoring) ($N=35$); a change of drug ($N=18$) or instructions for use ($N=9$); and/or introduction of a new drug ($N=7$). Physicians accepted 91 interventions and refused 36. Finally, 38 DRPs were solved (25 completely and 13 partially), for 25 a solution was either not needed or not possible, and, for eight, the outcome was not known.

Conclusions The study underlines the high potential for pharmaceutical care to improve prescribing practices in developing countries without shared pharmacist–physician decision-making.

INTRODUCTION

The success of the launch of chlorpromazine (in the 1950s) fundamentally shifted the model of care of schizophrenia from controlling to treating the ill.¹ Subsequently, antipsychotics (APs) became the mainstream treatment for schizophrenia, rendering outcomes and associated costs mainly dependent on the appropriate use of medications.²

To optimise prescribing, numerous evidence-based guidelines for schizophrenia were published,^{3–5} and much was done to develop methods for improving adherence.^{2–5, 6} However, real-life contexts still raise questions with no straightforward answers.^{2, 7}

The role of pharmacists in psychiatric hospitals has been noted since the 1970s⁸ with increasingly documented effectiveness.^{9–12} Studies reviewed by

Finley *et al*⁹ reported improvements in treatment outcomes, prescribing, resource use and patient satisfaction. Recent reviews^{11, 12} have acknowledged the competence of pharmacists in detecting, preventing or resolving drug-related problems (DRPs), enhancing the appropriateness of prescribing, providing comprehensive drug information,¹¹ and improving¹² clinical, economic and humanistic outcomes in inpatient mental health settings.

Pharmacists in Canada,¹³ the UK, the USA, Australia and New Zealand are now held accountable for therapeutic decisions and remunerated for providing collaborative, non-dispensing, pharmaceutical care services (PCSs).¹³ In some of these countries,^{14–16} psychiatric pharmacy has also been established as a specialty.

The clinical and economic benefits of pharmaceutical care (PC) have been well documented.^{17–19} A decrease in adverse events, adverse drug reactions (ADRs), medication errors, inappropriate prescribing, length of stay, and mortality rates is well established for PC in inpatient settings.^{9–13, 17–19} Methodological issues, contextual factors, insufficient details on PCSs and/or usual care, different intermediate and distant final outcomes might be reasons why findings for outpatient PCSs have not been so conclusive.^{17, 20} The benefits of medication reconciliation are the most consistently documented and are essential for medicine optimisation,²⁰ and, for people with a high risk of errors, such as those with chronic conditions (eg, severe mental illness), on polypharmacy or drugs requiring special monitoring (eg, lithium or warfarin), medication review should be considered.²⁰ The last of the series of economic evaluations¹⁷ found that PCSs are cost-effective or have a good benefit–cost ratio (ranging from 1.05:1 to 25.95:1), with the exception that three UK studies demonstrated no or minimal benefits in clinical outcomes and an added cost with community-based PCSs. A lack of PCSs in hospitals was associated with an increase in the number of ADRs per 100 admissions (from 4% in hospitals without pharmacist-provided pharmacokinetic consultations to about 86% in hospitals without pharmacist-provided admission drug histories).²¹ It was calculated that hospitals without pharmacist-provided ADR management had a 34.9% higher number of ADRs per 100 occupied beds, a 53.64% higher fatality rate, 13.64% higher total medical care charges, and 8.16% higher drug charges.²¹

Identified barriers for implementation of PC are: poor motivation; inadequate communication; poor access to medical information; a lack of time and self-confidence regarding medication review skills;²² a lack of appropriate regulation; an unfavourable environment; and a poor collaborative culture.²³ All these barriers are much



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more pronounced in less developed countries. Besides this, in developing countries with an emerging evidence-based healthcare paradigm,^{23–24} pharmacists are inherently perceived as stock-keepers, dispensers and medicine compounders.²³ The need for more research in the field of psychiatric pharmacy services in inpatient settings is recognised globally,¹² and the under-representation of developing countries has been underlined in the literature.^{23–24}

Recognising that 30–50% of medicines are not taken in the way intended, which coincides with an overall increase in the patient's age, multimorbidity and polypharmacy,²⁰ and taking into account that 5–8% of unplanned hospital admissions are due to medication issues, PC becomes 'indispensable' and is recommended by the Council of Europe as a pivotal strategy for healthcare policy makers.¹⁸

Since PC is not recognised or regulated in Montenegro, a randomised interventional design was needed to investigate its implementation here. The aim was to perform and document medication review by a clinical pharmacist, reveal DRPs, develop PC interventions, communicate them to the relevant physicians, and assess their acceptance and outcomes.

METHODS

This prospective, healthcare-system, interventional 'before-and-after' study was conducted between August and December 2014 at the Dobrota Psychiatric Hospital in Kotor, the only long-stay mental institution in Montenegro. It is a 241-bed, non-research facility for patients with severe mental illnesses, with 141 beds for long-term patients. No pharmacists are employed by this hospital.

Patients with a diagnosis of schizophrenia (as defined under the F20.0–F20.9 codes of the WHO tenth edition of the International Classification of Diseases, Diagnostic Criteria for Research (ICD-10)²⁵) who had been hospitalised for more than 6 months were included in the study, and every second one of the total 99 eligible patients was enrolled in the study—that is, 49 patients in total.

An independent clinical pharmacist (with an MSc in clinical pharmacy (3-year postgraduate course) from Robert Gordon University, Scotland, UK) with no previous practical experience in direct PC provision was engaged for the purpose of this study. She performed a level-2 medication review²⁶—a treatment review using patients' full records. The extended version of the DRP Registration Form (PCNE Classification V6.2)²⁷ was used as a validating tool in documenting PC and communication.

The populated forms were validated by the clinical pharmacologist (no changes were suggested) and disseminated to physicians. The pharmacist visited the physicians to resolve any issues before they decided whether to accept the recommendations.

Ethics approval for the study was obtained before the start of the study from the ethics committee of the Clinical Centre of Montenegro (Podgorica, Montenegro) and from the ethics committee of Dobrota Hospital.

Study variables

In the 'Description & Comments' section of the form,²⁷ a comprehensive narrative was presented.

Medications were listed, underlining: AP(s) generation(s) prescribed, AP combinations, total daily dose (in chlorpromazine equivalents); benzodiazepine(s) prescribed, total daily dose (in diazepam equivalents); antiparkinson agents, anticonvulsants, lithium, and/or antidepressants.

DRPs and pharmacist interventions were elaborated with reference to the relevant evidence (evidence-based guidelines,^{4–5}

locally adapted national guideline for schizophrenia,⁵ British National Formulary (BNF), Summaries of Product Characteristics, etc).

As required by the instructions for completing the DRP registration form,²⁷ for each DRP detected, we indicated up to three causes and proposed not more than three interventions. The outcome of the interventions was also recorded.

Statistical analysis

The data were analysed using descriptive statistics. Means and SDs were used to describe continuous variables, and frequencies of categorical variables were expressed in percentages.

RESULTS

The demographic characteristics of the patients included in the study are presented in table 1.

For the 49 patients, 71 DRPs were identified, ranging from one to four (mean±SD 1.43±0.68) per participant. DRPs were recorded as potential for 27 participants, manifest for 13, and nine patients had both potential and manifest DRPs. Safety (P2) and effectiveness (P1) were the most common problem types (table 2).

Most of the 184 causes revealed comprised inappropriate selection of drug (C1) or dose (C3): antipsychotic polypharmacy (APP) (C1.6); (inappropriate) combinations (C1.3) (eg, two first-generation antipsychotics, digoxin with furosemide, or long-acting haloperidol injections with clozapine) prescribing thioridazine, benzodiazepines or haloperidol for patients with significant cardiac disorders (C1.1); no plasma monitoring for clozapine or lithium (C3.5); a clozapine dose of 75 mg daily (C3.1); benzodiazepines prescribed long term (C4.2); or excessive daily dose in diazepam equivalents (C 3.2) (table 3).

The clinical pharmacist proposed 182 interventions, and 70% (127) of them were related to the drug. Discontinuation of medication (I3.5) was the most commonly (58) proposed, with a comprehensive explanation and a tapering scheme provided, if applicable.

Changes to the dosage (I3.2), drug (I3.1) or instructions for use (I3.4) and/or starting a new drug (I3.6) were proposed 35, 18, nine and seven times, respectively. Monitoring (I 4.1) (extrapyramidal symptoms, differential white cell count and bowel movements) or information provided or asked for from the prescriber were recorded 35, two and 18 times, respectively.

Physicians accepted and implemented 91 interventions, but 36 interventions were not implemented at the physicians' recommendation (eg, 'clozapine dosage cannot be increased because of adverse effects', or 'diazepam cannot be stopped since it is not possible to control anxiety with other therapeutic methods' or 'SGAs (second-generation antipsychotics) cannot be introduced because of the occurrence of diabetes mellitus').

The outcomes of interventions were not known for seven DRPs, 25 were completely solved, 13 were partially solved, and, for 25, there was no need or possibility to solve the problem.

The total number of prescribed drugs per patient was significantly reduced (table 1), while the total daily dose of APs was not changed significantly (daily chlorpromazine equivalents before and after the intervention were 603.9±460.1 and 618.0±395.7, respectively; $T_{\text{paired}}=-0.407$, $p=0.686$).

DISCUSSION

First, this study is important locally in the pioneering implementation of PC in Montenegro. Moreover, a recent Cochrane review²³ of pharmacists' non-dispensing services in

Table 1 Demographic characteristics

Characteristic		Patients exposed to intervention (N= 49)	Control group (N=50)	Difference between exposed and control groups
Gender	Female	12	12	$\chi^2=0.003$, $p=0.955$
	Male	37	38	
Age (years), mean \pm SD (range)		54.9 \pm 9.5 (33–88)	54.8 \pm 11.9 (32–88)	T=0.010, $p=0.992$
Age categories (years)	30–40	3	5	$\chi^2=7.708$, $p=0.103$
	41–50	8	16	
	51–60	24	12	
	61–70	13	13	
	71–90	1	4	
Diagnosis	F20	46	45	$\chi^2=6.002$, $p=0.423$
	F22	1	1	
	F29	1	1	
	F23, F25 F33	1	3	
Duration of disease (years), mean \pm SD (range)		21.5 \pm 10.9 (1.0–44.0)	18.4 \pm 10.2 (1.0–45.0)	T=-1.466, $p=0.146$
Duration of hospitalisation (years), mean \pm SD (range)		12.1 \pm 9.0 (1.0–42.0)	10.9 \pm 9.7 (1.0–45.0)	T=-0.617, $p=0.539$
Hospitalisation (number of patients)	Dismissed at weekends	11	13	$\chi^2=0.170$, $p=0.680$
	Continuous	38	37	
Number of prescribed drugs per patient, mean \pm SD (range)	Before the intervention	4.2 \pm 1.5 (2–8)	4.0 \pm 0.9 (2–8)	T=-0.828, $p=0.410$
	After the intervention	3.4 \pm 1.6 (0–7)	3.9 \pm 0.9 (2–8)	T=-1.017, $p=0.312$
	Difference before/after	T _{paired} =-3.263, $p=0.002^*$	T _{paired} =-1.003, $p=0.320$	

*Significant difference.

non-high-income countries identified only one study in which the intervention targeted healthcare professionals.

Overall, the findings affirm the value of the contribution of pharmacists to prescribing decisions for long-term inpatients with schizophrenia and add a perspective in a pharmaceutical-care-naïve developing country. Acceptance and implementation of the majority of the pharmacists' interventions demonstrate that PC is recognised by prescribers, even though it is not part of the official healthcare system.

The contextual distinction should be considered when the acceptance rate of 50% is interpreted. Also, the 19% refusal rate, at the recommendation of physicians, further potentiates features of the settings (extensive permanent hospitalisation, severity of disease, comorbidities, etc) and shows that findings from randomised controlled trials are not workable in daily practice.^{6,7}

Pharmacists' interventions (PIs) are generally highly accepted.²⁸ Graabæk and Kjeldsen²⁸ systematically reviewed the impact of pharmacists' medication reviews in hospitals. High acceptance rates (>69%) were reported in 16 out of the 31

included publications (ranging from 39% to 100%). However, when only implementation of the intervention was regarded as acceptance, lower rates were recorded. Psychiatric settings with long-established, advanced clinical pharmacy services record consistently higher acceptance rates of pharmacists' recommendations.²⁸

Although contextually different, the acceptance rates recorded were comparable to acceptance rates of PIs involving psychotropic drugs recorded in French hospitals²⁹ (57% accepted, 19% refused, 24% non-assessable).

Table 2 Types of problems

P, Problem type	Sum
P1 Drug effect	30
P1.2 Effect of drug treatment not optimal	25
P1.3 Wrong effect of drug treatment	4
P1.4 Untreated indication	1
P2 Adverse reactions	40
P2.1 Adverse drug event (non-allergic)	36
P2.3 Toxic adverse drug event	4
P3 Treatment costs	1
P3.1 Unnecessary drug treatment	1
Total P1+P2+P3	71

Table 3 Causes of drug-related problems

C, Cause	Sum
C1 Drug selection (total)	118
C1.6 Too many drugs for indication	33
C1.7 Not cost-effective choice	29
C1.3 Inappropriate combination	27
C1.1 Inappropriate drug	23
C1.2 No indication for drug	5
C1.4 Inappropriate duplication	1
C2 Drug form (total)	2
C2.1 Inappropriate drug form	2
C3 Dose selection (total)	43
C3.5 No therapeutic drug monitoring	14
C3.1 Drug dose too low	13
C3.2 Drug dose too high	11
C3.6 Pharmacokinetic problem	4
C3.7 Deterioration/improvement of disease	1
C4 Treatment duration	14
C4.2 Treatment duration too long	14
C5 Drug use process	7
C5.1 Patient gets/takes drug at the wrong times	5
C5.2 Drug under-used/under-administered	1
C5.6 Drug abused (unregulated overuse)	1

In the literature,²⁸ PIs in psychiatric settings have included dose and medication changes as well as laboratory and drug-level monitoring. In our study, the most frequently proposed intervention was discontinuation of medication, mainly as a consequence of the prevailing practice of APP and inappropriate prescribing of benzodiazepines.

Not evidence-based, APP is prevalent globally and prescribers' explanations have already been listed: illness severity, complexity, chronicity, or refractoriness.^{3 4 6} Also, benzodiazepines have their place in schizophrenia-prescribing patterns,⁴ but are limited to the desired ultra-short-term sedation of acute agitation.⁴ The provision of clear instructions and tapering schemes was appreciated by physicians in the study. Nevertheless, in some cases, specific patient clinical features, disease and medication history were justifiable reasons for not implementing evidence-based recommendations.

The major weakness of the study is its lack of generalisability potential, because of its single focus, single PC provider, and a health system with no inherent concept of clinical pharmacy. Since we used only written communication with physicians, this was associated with lower acceptance rates of the pharmacists' recommendations; the lack of a collaborative culture in developing countries makes multifaceted communication even more warranted.

The non-expectance of physician–pharmacist collaborative decision-making observed in our study has already been identified as a barrier to PC implementation.²³ The importance of standardised and documented PC has been shown previously in developed countries.³⁰ The PCNE DRP extended form facilitated consistent and comprehensive explanations of the findings and evidence-based proposals of interventions.

What this paper adds

What is already known on this subject

- ▶ As pharmacotherapy experts, pharmacists are competent to detect, prevent or resolve drug-related problems, enhance appropriateness of prescribing, and provide comprehensive drug information.
- ▶ Pharmaceutical care provision can have a positive impact on clinical, economic and humanistic outcomes in inpatient mental health settings.
- ▶ In developing countries, pharmacists are traditionally perceived as stock-keepers, dispensers and medicine-compounders.
- ▶ The need for more research on psychiatric pharmacy services in inpatient settings is recognised globally, and the under-representation of developing countries in the literature is generally highlighted.

What this study adds

- ▶ The findings further support the contribution a clinical pharmacist can make to prescribing decisions for long-term inpatients with schizophrenia.
- ▶ The study adds a perspective to the clinical pharmacy profession from a pharmaceutical-care-naïve developing country.
- ▶ Acceptance and implementation of the majority of the pharmacist's interventions demonstrated that pharmaceutical care was recognised by prescribers even though it was not part of the official healthcare system.

CONCLUSION

The treatment review performed by the clinical pharmacist revealed the significant burden of DRPs. The demonstrated acceptance rate of the PC interventions underlines the potential for improvement of prescribing practices in developing countries without shared pharmacist–physician decision-making. Efforts should be made to implement PC in order to realise the positive effects obtained in more favourable settings.

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