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RESEARCH ARTICLE

The effect of pharmacotherapeutic counseling on readmissions and emergency department visits

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Abstract *Objective* To evaluate the impact of pharmacotherapeutic counseling on the rates and causes of 30-day post-discharge hospital readmissions and emergency department visits. Setting The study was conducted at the Medical Clinic of University Hospital Dubrava, Zagreb, Croatia. *Methods* The study included elderly patients prescribed with two or more medications for the treatment of chronic diseases. The patients randomized into the intervention group received pre-discharge counseling by the clinical pharmacologist about each prescribed medication. The control group received no counseling. *Main outcome measures* The rates and causes of 30-day postdischarge hospital readmissions and emergency department visits. Medication compliance was also evaluated, using the pill count method. *Results* A total of 160 patients were randomly selected for the study. No significant difference was found in the readmission and emergency department visit rates between the intervention and control groups ($p = 0.224$). There were 34.9 % more compliant patients in the intervention group. Significantly more non-compliant patients in the control group were readmitted or visited emergency department because of the disease progression ($p = 0.031$). In the intervention group, significantly more patients were readmitted or visited emergency department because of an adverse drug reaction ($p = 0.022$). *Conclusion* Pharmacotherapeutic counseling can reduce readmission and emergency department visit rates for disease progression. Improved patient knowledge about adverse drug reactions could be the reason for increased rates of readmissions and emergency department visits due to adverse drug reactions in the intervention group.

Keywords Adverse drug reaction · Compliance · Croatia · Emergency department visit · Pharmacotherapeutic counseling · Readmission

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Impact of findings on practice

- Pharmacotherapeutic counseling should be provided to elderly patients as an integral part of the hospital treatment.
- Pharmacotherapeutic counseling improves patient compliance and can reduce readmission and emergency department visit rates due to disease progression.

Introduction

Many hospital admissions and emergency department (ED) visits are drug-related. In the United States, Canada, and European countries, drug-related illnesses account for 2.9–24.1 % of hospital admissions and ED visits [1–3]. An estimated 80.000 drug-related hospitalizations occur in Australia every year [4]. Adverse drug reactions (ADRs) cause 2.5 % of hospital admissions in Croatia [5]. In addition to being a major public health problem, drug-related illnesses pose an increasing economic challenge. The annual cost of drug-related morbidity and mortality in the United States more than doubled in a 5-year period, increasing from $76.6 billion in 1995 to $177.4 billion in 2000 [6].

The risk of drug-related illnesses is the highest in the elderly (aged 65 and older), in whom the likelihood of hospital admission is 2–5-fold higher than the national average [7, 8]. This increased risk is associated with the highest medication use in this population group, with 44–57 % of elderly patients taking at least 5 and 12 % taking at least 10 prescription drugs [9]. The proportion of elderly population in Croatia is estimated to reach 35 % by 2051 [10]. At the same time, the estimated annual increase in drug consumption is about 10 % [11]. Thus, we may expect an increase in drug-related hospital admissions and ED visits.

Many drug-related readmissions and ED visits occur soon after hospital discharge. According to the published data, 38–91 % of high-risk patients are readmitted or visit ED within 1 month after hospital discharge [12, 13]. This can be partially attributed to the shift from inpatient to outpatient treatment, which is a trend in the past decades. Between 1983 and 1993, the number of outpatient visits in the United States increased by 75 %, while the number of inpatient days decreased by 21 % [14]. From 1985 to 2010, the average length of hospital stay in the European Union decreased from 14.7 to 8.1 days [15]. As a result, patients are taking more medications without being properly supervised by healthcare professionals, which contributes to the increased risk of non-compliance and ADRs.

The most commonly identified causes of drug-related readmissions and ED visits are non-compliance and ADRs [1–3, 16]. An estimated 22–57 % of patients are non-compliant, i.e. they do not take medications as prescribed [17, 18]. It has been shown that pharmacotherapeutic counseling can enhance patient compliance [19–21]. Sometimes, blind compliance can lead to harm, if patients are insufficiently informed about the risks of prescribed medicines [22]. Only 20–30 % of patients are informed about possible ADRs [23, 24]. Approximately 19 % of patients experience adverse events within 1 month of hospital discharge, and most of them are adverse drug events [25]. Pharmacotherapeutic counseling can significantly reduce the risk of ADRs. Serious, life-threatening ADRs are more likely to be preventable then non-serious ones [26, 27].

Aim of the study

The aim of our study was to evaluate the effect of hospital pharmacotherapeutic counseling on the rates and causes of 30-day post-discharge hospital readmissions and ED visits.

Methods

The study was designed as a randomized, parallel-group, prospective, interventional study in elderly patients. The protocol was approved by the University of Zagreb School of Medicine Ethics Committee. Before the inclusion in the study, all patients provided a written informed consent.

The study was conducted at the Medical Clinic of University Hospital Dubrava, Zagreb, Croatia. Elderly patients (aged $\geq$ 65 years) admitted to the Medical Clinic between April and June 2011 were considered eligible for the study. Those who were included were followed-up for 30 days. The primary outcome measure was an unplanned post-discharge hospital readmission or ED visit in the follow-up period. Secondary outcome measures were medication compliance and ADRs. The quality of the study was assessed according to the CONSORT 2010 checklist [28].

Patients

To be included in the study, patients had to meet the following criteria: age 65 years or older and hospital discharge to the community with a prescription for two or more medications for the treatment of chronic diseases.

Exclusion criteria were cognitive or perceptual problems, diagnosis of a terminal illness with a life expectancy <1 month, discharge to a long-term care facility or inability to be followed-up.

Randomization

Patients who met the inclusion criteria and signed the informed consent were randomized to either the intervention or the control group. Randomization was carried out using a sealed envelope technique. Before the start of the study, 80 cards with "intervention" and 80 cards with "control" written on them were put in unmarked envelops, which were then sealed and shuffled manually. After the enrollment, each patient was given an envelop, which was then opened and the patient was told to which group he or she was randomized. Although patients and the physician who provided counseling were not blinded to the

intervention, the outcomes were assessed by a research assistant blinded to the treatment assignment.

Interventions

Data on patient age, gender, prescribed medications, and discharge diagnoses were collected. Patients in both groups were discharged from the hospital according to the standard procedure, which includes a discharge letter with discharge diagnoses, interventions, and current medications to be handed to their general practitioner. They received the usual information about prescribed drugs from their physician.

Patients in the intervention group received pre-discharge counseling by a qualified physician, specialist in clinical pharmacology. The counseling was provided within 24 h prior to patient's discharge. During the counseling session, patients received the following information about each prescribed medication:

- indications for drug prescription
- dosage and time of administration
- the importance of compliance
- possible consequences of non-compliance
- possible ADRs
- prevention and early detection of ADRs
- measures to be taken in case of suspected ADR

Each counseling session lasted approximately 30 min. At the end of counseling session, patients in the intervention group additionally received the above-mentioned information in a written form. Patients in the control group received no counseling and no written information.

Follow-up visit

The follow-up visit was scheduled approximately 30 days after discharge (±5 days). If a patient was not able come to the hospital, the visit was arranged at their homes. The data on unplanned hospital readmissions or ED visits were collected by a research assistant blinded to the treatment assignment. The research assistant was a qualified physician, specialist in clinical pharmacology with 14 years of clinical experience. For the patients who visited ED and were admitted to the hospital after the examination, hospitalization was considered the primary outcome. For patients who visited ED and were discharged, ED visit was considered the primary outcome.

In case of hospital admission or ED visit, the research assistant assessed whether the cause was the progression of the disease or an ADR. Disease progression and ADRs were not mutually exclusive. The data were managed in the way that primary cause of hospitalization or ED visit was evaluated. The probability that an ADR was drug-related was estimated using the Naranjo ADR probability scale [29]. ADRs that were fatal, life threatening or required hospital admission were considered serious ADRs [30].

During the follow-up visit, medication compliance was assessed using the pill count method, a valid method for the assessment of drug compliance [18]. Patients were asked to bring with them all the remaining medications and empty packagings to the follow-up visit. They were also asked to bring their medications with them in the case of hospital admission. If they had not had their medications with them at the hospital admission, their relatives were asked to bring the medications from the patient's home. Medication compliance was calculated using the following formula [31]:

$$\text{Compliance } (\%) = \frac{\text{total number of doses taken by the patient since discharge}}{\text{total number of doses to be taken since discharge}} \times 100$$

Patients were categorized by compliance as follows:

- compliant (compliance 80–110 %)
- non-compliant (compliance <80 or >110 %)
- overuse (compliance >110 %)
- underuse (compliance <80 %)

Power calculation

The sample size needed to detect an absolute difference of 20 % in readmissions or ED visits between the intervention and control groups was 62 patients per group. The difference of 20 % was estimated from literature data [12, 13]. The sample size was calculated using a Chi-square test for test of proportion and two-tailed significance level (alpha) of 5 %, with a power of 80 %. The recruitment goal was to include 80 patients in each group.

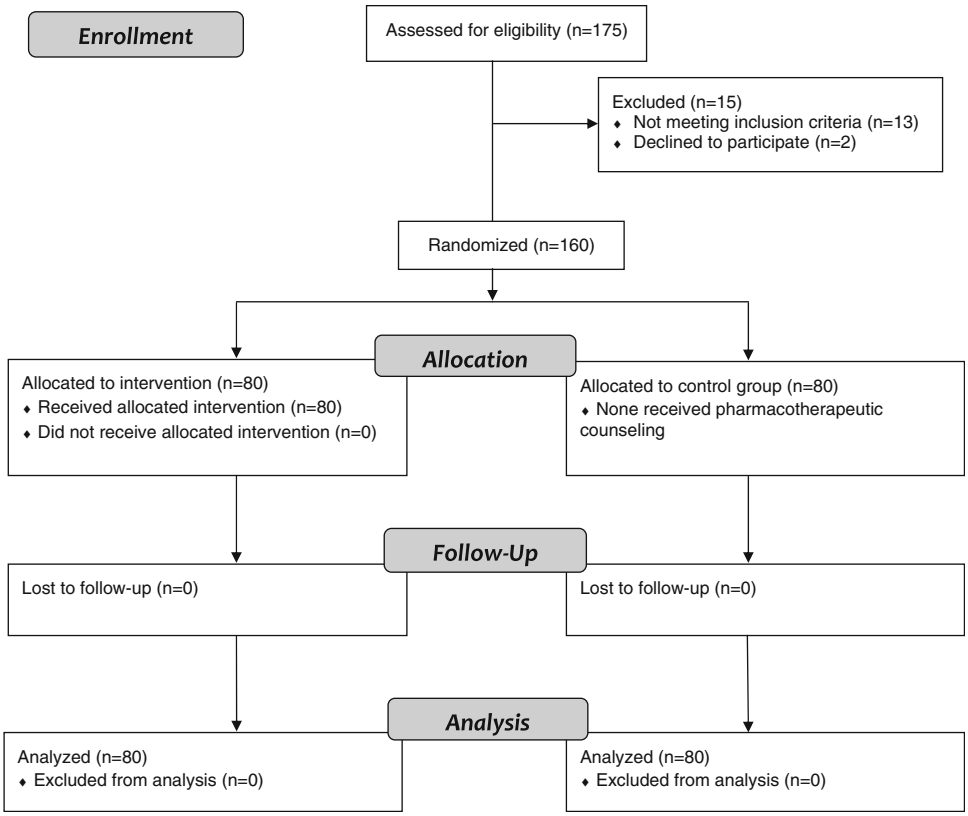

Fig. 1 Flow diagram of patients through the study (according to CONSORT 2010 statement)

Statistical analysis

Differences between the intervention and control groups for continuous variables were assessed using the Mann–Whitney *U* test. Chi-square test and Fisher exact probability test were used to test for differences between categorical variables. $p < 0.05$ was considered statistically significant. Data were analyzed using Statistica version 5.5 for Windows (StatSoft Inc. Tulsa, OK, USA).

Results

Overall, 160 patients were included in the study (80 patients in the intervention group and 80 patients in the control group). Figure 1 illustrates the flow of patients through the study.

No significant differences between the groups were found in age, gender, and number of prescribed drugs (Table 1). The number of discharge diagnoses was significantly higher in the intervention group.

All patients completed the protocol. There was no significant difference in the readmission or ED visit rates between the intervention and control groups 30 days after hospital discharge (Table 2). However, more patients in the intervention group were readmitted, while more patients in the control group visited ED. Nevertheless, the noted differences were not statistically significant.

The causes of readmission and ED visits are shown in Table 3. Significantly more non-compliant patients in the control group were readmitted or visited ED because of the progression of the disease. In the intervention group, significantly more patients were readmitted or visited ED because of an ADR. There was no significant difference between the groups in the number of compliant patients who were readmitted or visited ED because of the disease progression.

At the follow-up visit, medication compliance was significantly higher in the intervention group (Table 4). No significant difference in the number of patients who experienced ADRs was found between the intervention and the control group. One patient in the intervention group and one in the control group developed serious ADRs requiring hospital admission. For patients who were readmitted before the follow-up visit, ADRs and compliance were assessed on the day of readmission. Two patients in the control group were readmitted and subsequently died in the hospital. No patients died in the intervention group.

Discussion

We found that pharmacotherapeutic counseling did not have a significant impact on 30-day post-discharge hospital

Table 1 Characteristics of patients in the intervention group receiving pharmacotherapeutic counseling and in the control group

Patient characteristics	Intervention group (n = 80)	Control group (n = 80)	*p* value
Age, years			
Mean ± SD	74.0 ± 6.7	73.9 ± 5.5	0.959
Range	65–88	65–87	
Gender, n (%)			
Female	43 (53.8)	47 (58.8)	0.523
Male	37 (46.2)	33 (41.2)	
Number of prescribed drugs			
Mean ± SD	6.6 ± 2.4	6.2 ± 2.6	0.219
Range	2–13	2–13	
The most frequent classes of drugs, n (%)			
Diuretics	55 (68.8)	51 (63.8)	0.503
Angiotensin-converting enzyme inhibitors	51 (63.8)	45 (56.3)	0.332
Beta blockers	44 (55.0)	39 (48.8)	0.428
Acetyl salicylic acid	39 (48.8)	36 (45.0)	0.634
Statins	31 (38.8)	38 (47.5)	0.263
Calcium antagonists	31 (38.8)	24 (30.0)	0.243
Number of discharge diagnoses			
Mean ± SD	4.4 ± 1.6	3.9 ± 1.5	**0.022**
Range	1–8	2–8	
The most frequent diagnoses, n (%)			
Arterial hypertension	63 (78.8)	55 (68.8)	0.150
Diabetes mellitus	37 (46.3)	28 (35.0)	0.147
Angina pectoris	19 (23.8)	22 (27.5)	0.586
Atrial fibrillation	20 (25.0)	18 (22.5)	0.710
Hyperlipidemia	22 (27.5)	15 (18.8)	0.189
Heart failure	19 (23.8)	16 (20.0)	0.566

Bold value indicates statistically significant difference ($p < 0.05$)

Table 2 Rates of 30-day post-discharge readmissions or emergency department (ED) visits

	Intervention group (n = 80)	Control group (n = 80)	*p* value
Number of patients with readmission or ED visit, n (%)	20 (25.0)	27 (33.8)	0.224
Readmission	6 (7.5)	5 (6.3)	0.754
ED visit	14 (17.5)	22 (27.5)	0.129

Table 3 Causes of readmissions and emergency department visits

	Intervention group (n = 20)	Control group (n = 27)	*p* value
Progression of the disease, n			
Compliant patients	6	5	0.309
Non-compliant patients	0	6	**0.031**
Adverse drug reaction, n	9	5	**0.022**

Bold values indicate statistically significant difference ($p < 0.05$)

readmission and ED visit rates. This could partially be attributed to the differences in clinical condition of patients in the intervention and control groups. The number of discharge diagnoses per patient was significantly higher in the intervention group. This could have decreased the difference between the groups in the readmission and ED visit rates resulting from the pharmacotherapeutic counseling.

A significant reduction in readmission and ED visit rates due to pharmacotherapeutic counseling was reported in

Table 4 30-day post-discharge medication compliance and adverse drug reactions (ADRs)

	Intervention group (n = 80)	Control group (n = 80)	*p* value
Medication compliance, n (%)			
Compliant	71 (88.7)	43 (53.8)	**<0.001**
Non-compliant			
Overuse	0	2 (2.5)	
Underuse			
Compliance <80 % and ≥50 %	7 (8.8)	29 (36.2)	
Compliance <50 %	2 (2.5)	6 (7.5)	
Patients with ADRs, n (%)	24 (30.0)	30 (37.5)	0.315

Bold value indicates statistically significant difference ($p < 0.05$)

other studies. However, patients included in these studies had a higher risk of drug-related illness in comparison with our patients. In the study by Al-Rashed et al. [12], pharmacotherapeutic counseling significantly reduced the rate of readmissions and ED visits within 30 days after discharge. The patients included in their study were much older than patients in our study. It seems that older patients have a higher risk of drug-related morbidity and pharmacotherapeutic counseling has a stronger impact on the clinical course of the disease [26]. In the study by Koehler et al. [13], medication counseling reduced 30-day post-discharge readmission and ED visit rates by 28.1 %. However, the patients in their study were prescribed almost twice as many drugs as patients in our study. The number of prescribed medications is the major risk factor for non-compliance and ADRs [32]. Thus, pharmacotherapeutic counseling is expected to have a greater influence on drug-related illnesses when patients are prescribed more medications.

Although pharmacotherapeutic counseling did not reduce readmission and ED visit rates in our study, patients in the intervention group experienced benefits as a result of counseling. Pharmacotherapeutic counseling produced a positive effect on compliance; the number of compliant patients in the intervention group was 34.9 % higher in comparison with the control group. Improved compliance could have reduced the disease progression, readmission and ED visit rates. Previous studies have also shown that pharmacotherapeutic counseling can improve the medication compliance by 15–20 % [33, 34]. According to a meta-analysis published by DiMatteo et al., overall difference in medical treatment outcome between high and low compliance is 26 % [17]. Our findings are consistent with the results of these studies.

In the study by Schnipper et al. [27], pharmacotherapeutic counseling reduced the rate of ADRs from 11 to 1 %. In our study, no significant difference was found between the intervention and control groups in the number of patients who experienced ADRs. Pharmacotherapeutic counseling can predominantly prevent ADRs resulting from medication overuse. Since medication overuse in our study was detected in only two patients in the control group, a significant reduction in the ADR rates could not have been expected.

The number of patients who were readmitted or visited ED because of ADRs was significantly higher in the intervention group. This result may imply a favorable influence of pharmacotherapeutic counseling on patient knowledge about ADRs. Patients in the intervention group were informed about possible ADRs, their early signs, and steps to be taken in case of suspected ADR. Thus, they were more able to identify signs of a possible ADR and seek medical attention, if necessary. In this way, serious ADRs could be more effectively prevented [26]. This assumption is supported by the fact that the number of patients with actual ADRs in the intervention group was lower than in the control group, although the difference was not statistically significant. Only two patients, one in the intervention group and one in the control group, developed serious ADRs, which resulted in hospital admission. Thus, it was impossible to evaluate the impact of pharmacotherapeutic counseling on the incidence of serious ADRs in our study.

All patients completed the study protocol as might have been expected given the type of intervention, relatively short follow-up period and the possibility to arrange visits at patients' homes. At the end of pharmacotherapeutic counseling, patients in the intervention group received written information about prescribed medications and possible ADRs. The written information might have been used as a reminder for ADRs. Since patients in the control group received no written information, this may have influenced the outcome on ADRs reporting.

The main limitation of our study was a short follow-up period. Long-term follow-up studies are needed to assess the effect of pharmacotherapeutic counseling on clinical outcomes, such as mortality. Another limitation of this study was the inability to control the level and type of information patients received from their physicians. This could have introduced heterogeneity in patient knowledge. Also, patient compliance could have been influenced by physician communication skills, which could not be assessed and controlled [35]. Another factor that might

have influenced drug compliance and our study results is the tendency of patients to be more compliant because they know they are being observed (Hawthorne effect).

Conclusion

According to our results, pharmacotherapeutic counseling can significantly improve patient compliance and prevent readmissions and ED visits resulting from the disease progression. On the other hand, the increased rate of ED visits due to ADRs in the intervention group could have resulted from increased patient knowledge about ADRs.

Krska et al. [36] suggest that the number of hospital admissions may not be a sufficiently sensitive outcome measure for evaluating the impact of pharmaceutical interventions. When readmission and ED visit rates are used as a criterion for evaluation of pharmacotherapeutic counseling efficacy, each clinical event should be analyzed and its causes should be determined. Thus, the real effect of counseling on the clinical course of the disease can be assessed and sensitivity of readmissions and ED visits as markers of medication management can be increased.

Most hospitals in Croatia do not offer pharmacotherapeutic counseling to patients. In our study, pharmacotherapeutic counseling was provided by a clinical pharmacologist, physician specialized in clinical pharmacology. In addition to clinical pharmacologists, clinical pharmacists could also provide pharmacotherapeutic counseling in their everyday practice.

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Conflicts of interest None of the authors of this manuscript had any conflict of interests related to the study.

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