The role of the pharmacist in the care of patients with cardiovascular diseases

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INTRODUCTION

The inclusion of a pharmacist into the multidisciplinary team caring for the patient and the integration of modern pharmaceutical services with medical care and nursing is one of the most important challenges facing the health care system in Poland. Currently, both public and hospital pharmacies remain primarily the places to dispense medicines and ensure the quality of medicinal products stored and distributed. The development of clinical pharmacy remains fragmented and limited to a few centres. The modern community pharmacy practice, especially in Anglo-Saxon countries such as the United Kingdom, proves that modern pharmaceutical services contribute to improving health and increasing the quality of patients’ lives, improve the cooperation between physicians and pharmacists, and finally lead to the rationalisation of human and financial resources. The latter point is especially important, particularly when common problems are the availability of financial resources and human resources deficits. Currently, the number of pharmacies in Poland allows for the efficient dissemination of advanced pharmaceutical services. Moreover, Polish pharmaceutical law defines a pharmacy as a base to protect public health, setting a significant role for the pharmacist in the health care system. In practice, however, the legislature has not given sufficient tools for the pharmacist to be able to execute advanced pharmaceutical services; for example, the lack of exchange of medical information between the doctor and the pharmacist to a sufficient extent to complete the tasks defined by law remains an unsolved problem. Another obstacle involves the matters related to the refund of advanced pharmaceutical services with public funds, which seems to be an important prerequisite for the popularisation of the new role of the pharmacist in groups of elderly patients with high-risk of multiple diseases and thus polypharmacy [1]. It seems that equally important is the problem of the lack of in-depth communication between the pharmacist and the doctor, and without bilateral collaboration it is difficult to talk about the evolution of the competency of the pharmacist in the health care system.

A patient with a diagnosis of cardiovascular disease (CVD) requires, as part of the optimal secondary prevention, medication for life. Despite the enormous role of non-pharmacological methods of secondary prevention, such as proper diet [2] or smoking cessation, properly conducted drug therapy and a high degree of treatment adherence are the most effective known ways to prevent cardiovascular events [3, 4]. This relation is particularly well studied for adherence to antiplatelet therapy, where a properly applied drug protects against the risk of stent thrombosis and recurrent myocardial infarction [5, 6].

The purpose of this article is to discuss advanced pharmaceutical services regarding their usefulness in the process of optimising pharmacotherapy of patients with CVDs. The analysis was made for common diseases such as hypertension, type 2 diabetes, patients with heart failure (HF), and patients diagnosed with acute coronary syndrome. In all of these areas, the work is intended to articulate the relationship between the implementation of advanced pharmaceutical services and increased levels of adherence and hence improved outcomes of the treatment (Fig. 1) [7].

THE ROLE OF THE PHARMACIST IN THE PROCESS OF OPTIMISING PHARMACOTHERAPY

As mentioned earlier, in the Polish health care system the main role of the pharmacist is the dispensation of medicinal products and the provision of medicines of appropriate quality to the public. Scientific reports in recent decades, however, have proven that the essential task of the pharmacist is to optimise pharmacotherapy, leading to reduction of adverse drug–drug interactions and iatrogenic complications, and reduce the intensification of adverse events. In addition, community pharmacies remain the point of supply for pharmaceutical services and health services to which the patient has almost unlimited access — thus he/she always has the ability to dis-
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Information on all drugs that a patient uses, both prescription and over-the-counter (Rx) and over-the-counter (OTC) drugs or even dietary supplements. Additionally, after consultation with the doctor, issues related to compliance with treatment recommendations should be discussed with the patient. Dutch experience shows that the service carried out this way reduces the occurrence of drug problems in half of the patients, which is indeed closely associated with the phenomenon of polypharmacy. In the context of health policy, it is worth reflecting which patient group will get the most significant clinical benefit from the drug overview [9].

Currently, the research is moving away from the application of the term ‘pharmaceutical care’ towards pharmacist intervention. It seems, however, problematic as the concept of ‘intervention’ is more associated with a single and unitary contact with the patient, which basically negates the concept of pharmaceutical care as a process of continuous and constant collaboration with the patient. It should be emphasised that only constant contact of a pharmacist with the patient with harmonious cooperation with doctors and representatives of other health professions (e.g. nurses and nutritionists) leads to a significant improvement in health condition, health-related quality of life, and beneficial modification of the patient’s lifestyle. Such conclusions also result from the observation of patients with renal infarction, as indicated by Davis et al. [10], where interrupted pharmaceutical care leads to a rapid loss of its positive effect on the health and quality of a patient’s life. A few voices suggest that, in itself, even the best-designed, advanced pharmaceutical service, e.g. a drug overview, will not optimise the treatment process to achieve more satisfactory outcomes. In the global debate about the effectiveness of pharmaceutical care, these suggestions should be considered, however marginal [11, 12].

LOOKING FOR A COMMON DENOMINATOR
— HEALTH-RELATED QUALITY OF LIFE

In this context, the difficult task is to find a common denominator for advanced pharmaceutical services. The key, therefore, seems to emphasise the relationship between taking care of the patient and improving the quality of life. One of the recent studies, a meta-analysis of Mohammed et al. [13] showed that pharmaceutical care significantly improves social and physical functioning as well as overall health of patients covered by this process. It is also worth noting that the authors of this publication clearly emphasise that one of the current challenges of social pharmacy is the search for perfect instruments for assessing the quality of life useful in the context of pharmaceutical care. Of note, the study by Tumkur et al. [14] using, among others, a commonly adopted questionnaire assessing the quality of life — EQ 5D 5L — showed a significant impact of pharmaceutical care on the quality of life of patients with coronary artery disease. Compared with controls, coronary artery disease patients had a particular improvement in the realms of psychological, and
emotional and social well-being during the 12-month study. One of the few randomised clinical trials in the area of social pharmacy carried out among patients with Chagas’ disease complicated by HF showed a significant improvement of life of patients under pharmaceutical care as a result of reducing the number of drug problems and improved adherence [15]. Similar conclusions can be drawn from another study, which included patients with type 2 diabetes [16]. The search for further scientific evidence on the relationship between pharmaceutical care and improving health-related quality of life remains one of the most important challenges of the current scientific discourse. Finally, in 2013, a new definition of pharmaceutical care was proposed, one reflecting the development of pharmacy and social pharmacy, which proposed to emphasise respect of pharmaceutical care with achieving more satisfactory outcomes — ‘Pharmaceutical Care is the pharmacist’s contribution to the care of individuals in order to optimise medicine use and improve health outcomes’ [17]. In essence, therefore, the optimisation of pharmacotherapy should bring improvement in outcomes, especially those that are the most cost-intensive for the healthcare system, i.e. premature mortality, disability, and associated loss of productivity. Consequently, this minimises the most cost-intensive component of patient care: hospitalisation, which could be avoided by conducting optimised outpatient treatment. Traditionally, it has been adopted that advanced pharmaceutical services performed in public pharmacies qualify in the strict sense as pharmaceutical services, while the contribution of the pharmacist in patient care in hospitals has been treated as a matter of clinical pharmacy. This division, however, should be regarded as purely methodological and having no practical implications.

THE ROLE OF THE PHARMACIST IN THE TREATMENT OF CVD

The intervention of a pharmacist leading to optimisation of pharmacotherapy is a clinically effective solution of improving the quality of care for patients diagnosed with CVD. Pharmaceutical care seems particularly useful in the context of the assessment of factors of cardiovascular risk and the patient’s impact on dependent therapeutic effects such as the level of health literacy [18], the degree of treatment compliance, and subjective assessment of the quality of life. A systematic review from 2013 identified 59 studies, 45 of which were randomised, whose aim was to evaluate the clinical efficacy of pharmaceutical intervention in the secondary prevention of CVDs. The effectiveness of these interventions was considered high, reaching almost 70% [19]. Moreover, the interventions proposed by the pharmacists in the area of optimising pharmacotherapy achieve a high level of cardiologists’ acceptability — during one of the tests 1416 (92%) of the 1541 pharmacists’ clinical recommendations were accepted by the surgeons taking care of the patients [20]. Another study showed that in the case of 964 patients admitted to the hospital, in 29.8% of them drug-related problems were identified with the particular risk factor for this case being polypragmasy, commonly found in patients with even one CVD [21]. Eventually, pharmaceutical intervention can effectively increase the level of compliance of pharmacotherapy with current guidelines — which by definition means optimising pharmacotherapy in accordance with the principles of evidence-based medicine [22]. Interesting in this context is the study conducted by Lowrie et al. [23] in the setting of patients using drugs recommended by current guidelines. Despite this, the intervention of a pharmacist has brought improvement in compliance of pharmacotherapy. However, no difference in composite endpoint comprising death or hospitalisation due to worsening of HF symptoms was observed between the study and control groups despite covering large groups of patients, i.e. more than 1000 per group, and long follow-up of 4.7 years [23]. It is worth asking the question about the cost-effectiveness of pharmaceutical care. The estimates of Houle et al. [24] are interesting: they estimated the profit per patient at $131 Canadian for a six-month programme, and $115 for the annual programme of pharmaceutical care. Financial benefits were also evident when, after six months of cessation of further pharmaceutical care and over time, the impact of pharmaceutical services on the value of the blood pressure should be considered doubtful (Fig. 2) [24].

PHARMACEUTICAL CARE OF CARDIOLOGY PATIENTS

A retrospective study published in mid-2016 showed that pharmaceutical care is a clinically effective way for patients diagnosed with CVD to have more satisfactory outcomes. In the period before taking pharmaceutical care 54.4%, 79.0%, and 27.3% of patients presented satisfactory levels of systolic (SBP), diastolic (DBP) blood pressure, and lipid profile, respectively. During the two-year observation period (2010-
–2012) after the pharmaceutical intervention, the percentages were 93.0% for SBP and DBP (p < 0.001) and 60.6% for total-cholesterol (p < 0.001) [25]. Similar conclusions can be derived from another, recently published, randomised clinical trial. The Albert vascular Risk Reduction Project Community Pharmacy (The RxEACH) proved beyond doubt that taking pharmaceutical care of the patient leads to a significant decrease in the risk of cardiovascular events. Said study involved 723 Canadian patients. The main objective of the intervention was the patient’s medication therapy management, within the framework of complex and multidisciplinary interventions based, among others, on the measurement of blood pressure, making laboratory tests (including lipids), an individual assessment of cardiovascular risk based on the patient’s medical history and the Framingham risk score, and finally re-prescription of drugs. The absolute cardiovascular risk in the group covered by the pharmaceutical care was 21% lower than in the control group. In addition, a statistically and clinically significant reduction in SBP was obtained, as well as improvement in glycaemic control and improvement of the lipid profile. An important limitation of the study is the three-month follow-up period; this prevented assessment the impact of interventions on smoking cessation, and it makes one cautious about approaching with optimism the resulting reduction in cardiovascular risk [26]. These results are in part consistent with the observations made by Lee et al. [27] wherein the pharmaceutical intervention among the geriatric patients significantly improved their lipid profiles (low-density lipoprotein [LDL] –0.86 ± 0.56 mmol/L, p = 0.038, triglyceride –1.15 ± 1.09 mmol/L, p < 0.001). In contrast to the Canadian study, there was no significant improvement in blood pressure and glycaemia [27]. Improvement in blood glucose was observed, however, in another study conducted in China, where the haemoglobin A1c (HbA1c) levels were significantly reduced in the intervention group compared with the control group (-1.57 ± 1.50% vs. -0.40 ± 1.19%, p < 0.001) after intervention based on a medicine use review obtained during hospitalisation of patients with type 2 diabetes [28]. Similar conclusions can be drawn from a randomised study conducted by Chen et al. [29] in which the group covered by the pharmaceutical intervention had significantly better glycaemic control. In this study the mean HbA1c level significantly decreased (0.83%) after six months in the intervention group compared with an increase of 0.43% in the control group (p ≤ 0.001) [29]. The Diabetes in ADolescence Engagement and Monitoring by pharmacists (DIADEMA) study, conducted simultaneously in Bosnia and Herzegovina and Germany, also lead to similar conclusions — the improvement in HbA1c levels was significantly greater in the intervention group vs. the control group at six months (change from baseline –0.54 vs. +0.32%, p = 0.0075) [30]. The extraordinary usefulness of pharmaceutical care in the geriatric population diagnosed with type 2 diabetes and hypertension was shown in the study performed by Brazilian Neto et al. [31], where the length of follow-up was 36-months. In the group of patients under pharmaceutical care the significant difference in clinical characteristics of patients at baseline and after 36 months observed was as follows: decrease in SBP (156.7 mmHg vs. 133.7 mmHg; p < 0.001) reduction in the DBP (106.6 mmHg vs. 91.6 mmHg; p < 0.001), glycaemic control by determining HbA1c (7.7% vs. 7.0%; p < 0.001), improvement in the lipid profile of patients manifested by lowering levels of LDL (–112.4 mg/dL vs. 102.0 mg/dL, p < 0.001), and total cholesterol (202.5 mg/dL vs. 185.9 mg/dL, p < 0.001). It should be emphasised that the study took place in a country where pharmaceutical care has not yet been established and the role of the pharmacist is limited to dispensing medicine, and the health system is not highly developed [31]. In another Brazilian study, the positive impact of pharmaceutical intervention on the level of treatment compliance by patients was demonstrated. Assessment of the level of adherence was made using the most widely encountered tool, the Morisky Green-test, whereby it was shown that 50.5% of patients at baseline were adherent vs. 83.5% of adherent patients after 36 months; p < 0.001 [32]. An increase in adherence was also observed in other studies in which other diagnostic tools, such as the Malaysian Medication Adherence Scale, were used [33], it was also confirmed that pharmaceutical care reduces the risk of premature discontinuation of medication [34]. It is also evident that public pharmacies can play an important role in the optimisation of pharmacotherapy. An Australian study showed that pharmaceutical intervention lowers cholesterol levels as a result of any improvement in non-pharmacological treatments, i.e. eating habits and physical activity, and not due to the increase in the level of adherence [35].

EXPANDING PHARMACY SERVICES — THE NEED FOR A MULTIDIMENSIONAL APPROACH

A Norwegian study showed only partial effectiveness of clinical pharmaceutical intervention. The study included 102 patients, aged 18–32 years, with coronary heart disease. Pharmacist intervention was focused on medicine-use review, patient education, and therapeutic conversation, the purpose of which was to increase the degree of adherence. The protocol used three-time intervention, i.e. at the end of hospitalisation, and three and 12 months after leaving the hospital. Despite the study design and repeated intervention, improvement was only seen in the area of patients’ lifestyle, and there was no improvement in laboratory values such as LDL cholesterol or HbA1c [36]. Also, a study conducted on a population of patients with a diagnosed hypertension confirmed that multifaceted pharmacist intervention during hospitalisation leads to increased levels of adherence. Based on data from pharmacy records, it was estimated that 20.3% of the subset under pharmaceutical care met the criteria of...
a non-adherent, with 30.2% in the control group. The key elements on which pharmaceutical intervention was based were medicine-use review and a motivational conversation with the patient about treatment compliance, explaining the doubts and fears of the patient in relation to the pharmacotherapy and the development of the disease. Despite these efforts, there was no significant difference in blood pressure between the two groups or differences between the combined clinical endpoint of cardiovascular death, stroke, or acute myocardial infarction among patients in the control group [37]. In turn, the results of the Alberta Clinical Trial in Optimising Hypertension (RxACTION) indicate that additional expansion of pharmaceutical services to standalone Rx prescription drugs may have an impact on the effectiveness of clinical pharmaceutical care. Pharmaceutical care provided to patients in this case also had a multidimensional character; it was based on individual assessment of cardiovascular risk, patient’s education, prescribed antihypertensive medications, and monthly consultation with the pharmacist during the study. In the group covered by the intervention a reduction in SBP of 18.3 mm Hg was obtained, compared to 11.8 mm Hg in the control group (p = 0.00060). It should be mentioned that patients in the control group received standard medical and pharmaceutical care that was characteristic of Canadian clinical practice [38]. It should be emphasised that for both the scientific community as well as the practitioners, the clinical effectiveness of pharmaceutical care is not contested. One meta-analysis has shown that the effectiveness of studies performed so far in the context of the impact of pharmaceutical intervention at the height of blood pressure is very diverse, and an attempt to find the determinants that may make it easier to predict the effectiveness so far has not succeeded [39]. It seems beneficial to combine advanced pharmaceutical care with cardiac rehabilitation, which may result in increased adherence [40–42]. The search for ways of increasing the efficiency level of advanced pharmaceutical services has led researchers to integrate devices in the process of pharmaceutical care. An example of such a solution is the study by Verret et al. [43], in which CoaguChek XS device and a self-management dosing algorithm were included in the process of optimisation of anticoagulant therapy, achieving satisfactory intervention results. In addition, various alternatives and support for advanced pharmaceutical services have been sought, including primarily supporting the process through Internet applications and specialised software dedicated to this [44].

**OPTIMISATION OF PHARMACOTHERAPY — SEARCHING FOR DRUG-RELATED PROBLEMS**

In addition to the impact of the degree of therapeutic compliance, the most important element of almost any pharmaceutical intervention is the search for drug-related problems. First and foremost is the identification of adverse events and adverse drug–drug interactions because it seems important to find clinical situations in which the patient receives the wrong therapy (presence of contraindications) or incorrect dose (sub-therapeutic or toxic). One recent study showed that the preparation of a special notification system for doctors on clinically relevant drug interactions leads to an improved safety profile of the patients. Despite the reduction of adverse drug reactions at the end of hospitalisation, Roblek et al. [45] did not observe the impact of this phenomenon on the endpoint of the research, i.e. re-hospitalisation or death in the six-month follow-up. To optimise pharmacotherapy by pharmacists, Dempsey et al. [46] have identified a number drug therapy-related problems in patients diagnosed with HF, such as sub-optimal pharmacotherapy, the choice of unfavourable treatment (due to drug interactions or contraindications) and the use of sub-optimal therapeutic doses (Fig. 3).

**QUO VADIS POLAND?**

One of the most important issues determining the difficulty of making a thorough assessment of the effectiveness of clinical pharmaceutical care is the issue of the length of observations in the framework of scientific research. Even in countries with a well-established role of the pharmacist in the health care system, getting a long follow-up, not to mention long-term observations and providing the basis for registration studies, seems to be the hardest thing that clinical and social pharmacy have faced. The conclusions of the study clearly show that pharmaceutical care should be a continuous process of patient care and that a single short intervention will not lead to more satisfactory patient outcomes. This raises the question about the need to develop a long-term financing strategy for this type of service and clarified model of health care system with an established position of the pharmacist. It is necessary to
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References


