



Pharmacist-Led Medication Review: Supports for New Role of Pharmacists

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ARTICLE INFO

Article type:
Review article

Keywords:
Pharmacist
Drug Therapy
Patient Care
Pharmaceutical Services

ABSTRACT

In recent decades, by increasing complexity of drug therapy, pharmacists considered as health-care members who can help optimizing drug therapy. We know that medicines do not have the anticipated effects all the times and a vast variability may exist in their behaviors in the body. So, it is very crucial to individualize treatment for every single patient. Nowadays, optimizing drug therapy in patients needs a collaborative interdisciplinary approach to patients care and treatment. Specifically when drug therapy is considered for a condition, pharmacists can enroll as a valuable professional to help for modification of therapy along with other clinicians. Abundant number of studies and reports exist in the literatures which address usefulness of pharmacist engagement in patient care. In this review we have presented some valuable evidences supporting pharmacist role in different clinical settings.

J Pharm Care 2013; 1(4): 153-160.

► Please cite this paper as:

Sadeghi K, Mohammadi M, Najmeddin F, Mashayekhi M, Mojtahedzadeh M, Javadi MR, Gholami K. Pharmacist-Led Medication Review: Supports for New Role of Pharmacists. J Pharm Care 2013; 1(4): 153-160.

Introduction

After describing “Pharmaceutical care” - a new horizon of pharmacy profession- by Helper and Strand in 1990 (1), a rapid movement occurred to engage pharmacists in patients’ care process, in a more responsible manner. For the first time, some distinct categories about problems with drug therapy described and *pharmacists’* role as a health care professional in decreasing these problems, emphasized.

“A *drug therapy problem* is any undesirable event experienced by a patient which involves, or is suspected to involve drug therapy, and that interferes with achieving the desired goals of therapy”, Strand et al., described in 1990 (2). For the first time, they took place drug therapy

problems in the eight categories. Other classification systems developed for identifying drug therapy problems in recent years (3). Some other terms that may be used alternatively, are: “*drug related problems (DRPs)*” and “*Medication related problems*”. In recent years there is a growing attention to identifying, prevention and management of DRPs. One study has shown that up to 80% of hospitalized patients experience some forms of DRPs in general hospitals (4) and some studies have reported the incidence rate of 63-93% for DRPs in patients when discharging from hospitals (5, 6).

In recent years, pharmacist role has evolved from a pure drug consultant to a more accompanying member of a multidisciplinary team engaged in patient care (7). A large systematic review and meta-analysis concluded that pharmacist-provided patient care can lead to a better patients’ outcome in various health care settings and disease conditions (8). Likewise in the outpatient setting, it has been shown that pharmacist-led medication review

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can positively decrease DRPs in geriatric patients (9).

Need for a medication review program

Medication review has been defined as assessment of an individual patient's drug therapy to evaluate the regimen appropriateness. This can be accomplished either by recommendations or through direct interventions that result in changes in drug therapy (10). Not all medication errors can harm patients, but some of them may lead to dangerous or annoying events and because of widespread use of drugs, it is logical to set a systematic approach to prevent errors (11).

Numerous studies illustrating the role of pharmacist as a medication reviewer have been published and the body. The body of literature generally supports this.

Pharmacist role in emergency department

Medication error is common in patients admitted to Emergency Department (ED) due to its time limited nature and the presence of discrepancies. (12).

Patanwala et al., examined the role of pharmacist in preventing medication errors in a prospective multi-center study (13). Pharmacists recorded their interventions at each of four included centers for 250 hours of continuous presence in the ED (1000 hours collectively). Recorded items comprised efforts for preventing a medication error, type of intervention and error. Throughout the study 16,446 patients received medical services and 364 confirmed medication errors occurred; a majority of them happened during prescribing step (n=300; 82.4%), followed by administering (n=27; 7.4%), dispensing (n=15; 4.1%), transcribing (n=12; 3.3%), and monitoring steps (n=10; 2.8%). Also, wrong dose was the most common corrected error (n=161; 44.2%). A remarkable point of this study was that about two-third of medication error interventions occurred when a pharmacist was engaged in consultation during first drug therapy decision making, suggesting greater benefit of implementing pharmacists' knowledge while patient-specific factors are considered. Of course this should not account to ignore the value of medical order review to find errors. The potential capability of pharmacists to detect and prevent harmful errors in ED has also been verified in other studies (14, 15).

Pharmacists may also contribute to safe discharge of ED patients. In a study aiming pharmacists' role in optimizing discharge prescriptions, interventions consisted of both error prevention and drug therapy optimization were recorded (16). At the end of the study, pharmacists intervened on 68 of 674 discharge orders (10.1% of orders, 95% CI = 8.0%-12.7%). Beside the point, 95% of ED staff believed that pharmacist supervision in ED can significantly improve patient safety and satisfaction and optimize medication regimens.

These results illustrate the areas of pharmacist activity in ED and underline the need for incorporation of

pharmacists in ED care team.

Pharmacist role in hypertension management and cardiovascular disease

With the expanding population of hypertensive patients during recent decades, team-based practice is gaining popularity for better control of an array of less-than-optimal controlled chronic health issues specially hypertension, hyperlipidemia, diabetes, heart failure and chronic kidney disease (17-19).

Determining utility of a pharmacist-based hypertension clinic, Erhun et al., enrolled 51 outpatient hypertensive participants in a 1-year prospective randomized cohort study (20). All patients were diagnosed with hypertension by a physician and were receiving medications consisted of methyldopa and/or combination diuretic (amiloride + hydrochlorothiazide) prior to enrollment in clinic. Pharmacists participating in the study, measured patients' blood pressure, set individualized goals of lifestyle changes, educated patients regarding hypertension, adjusted drug therapy regimen and followed patients for a 6-months period to evaluate outcomes. The study group was compared to a historical group of control patients that were treated in a physician-managed hypertension clinic under a similar setting. A significant decrease was noted in both systolic and diastolic blood pressures compared to baseline values at the time of enrollment [mean SBP = 167.90 ± 30.32 mmHg at enrollment and 126.20 ± 6.20 mmHg at last visit (p<0.01); mean DBP = 103.09 ± 32.09 mmHg at enrollment and 80.60 ± 4.66 mmHg at last visit (p<0.05)]. Also comparing with control group a marked reduction in treatment failure rate and more satisfaction and compliance of patients were observed. Encouraging results of such studies have prompted pharmacists to experience independent practice through self-prescribing of antihypertensive medications (21, 22). Pharmacist-managed programs also have been associated with reduced overall cost to health system. Houle et al., developed an economic model to assess cost-saving potential of a pharmacist-based management program for hypertensive patients. They found that the program was cost saving. Their calculations showed an average of \$131 for the annual net total cost savings/patient for a program lasting 6 months or \$115 for a program lasting 1 year (23).

Trials have also been conducted in different populations of patients with cardiovascular disease. Based on previous encouraging small trials suggesting improved outcome with pharmacist intervention in heart failure patients, Lowrie et al., randomly assigned 2164 primary care heart failure patients to either non-specialist pharmacist-led collaborative drug review (1090 patients) or usual care by physician (1074 patients) (24). After a median follow-up of 4.7 years, there was not any significant difference in primary outcomes of death or hospital re-admission

between groups [35.8% for intervention vs. 35.4% for control group; Hazard Ratio = 0.97; 95% CI = 0.83-1.14; $p = 0.72$]. Similar results were also noted in another trial which incorporated post-discharge chronic heart failure patients (25). Although pharmacist intervention in these trials led in modest improvement in use of disease-modifying agents such as angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, it seems that targeting improved outcomes of death or hospitalization rate requires specialized clinical pharmacy service and more stringent collaborative practice.

In addition, other trials have shown that pharmaceutical services may contribute to decrease in door-to-balloon time in ST-Segment elevation myocardial infarction (26), improve detection and prevention of adverse effects of anti-arrhythmic agents (27) and enhance efficacy and safety of anticoagulation (28).

Pharmacist role in diabetes care

Successful Pharmacists' efforts to optimize glycemic control in various diabetic subpopulations have been reported consistently in many controlled trials. A majority of these trials have suggested the development of pharmacist-led diabetes clinics as a way to improve patient adherence, glycemic control, prevent adverse drug reactions and disease complications (29-35). Enhanced patient satisfaction and reduced cost to health-care system have also been reported in patients with type 2 diabetes which received pharmacist services as a part of multidisciplinary team (36).

Collins et al., conducted a meta-analysis on randomized controlled trials in type 1 and 2 diabetic population in which the effect of pharmacist intervention on hemoglobin A1C was evaluated (37). Fourteen trials ($n=2073$) were identified and included in the analysis. Pharmacist intervention led to a significant reduction in hemoglobin A1C concentration [Weighted mean differences (WMDs) = -0.76%; 95% CI = -1.06 to -0.47]. Fasting blood glucose was measured in 4 trials which also showed a significant reduction [WMD = -29.32 mg/dl; 95% CI = -39.54 to -19.10].

Although may not be applicable to diabetic population, pharmacist team intervention has been associated with better glycemic control and reduction in hypoglycemic episodes in peri-operative hyperglycemic patients (38).

No single intervention may eventuate in the consistent results of these trials. Instead, better outcome is the result of a series of activities including appropriate communication, review of expected adverse effects of drug therapy prior to treatment initiation and strategies to manage them, regular follow-up visits and timely collaboration with other health-care providers.

Pharmacist role in chronic kidney disease care

Considering the wide range of medical co-morbidities, linked to chronic kidney disease, poly-pharmacy is a

common finding in this population. By increasing the number of drugs used by a patient, the likelihood of drug related problems may also be increased. Pharmacists can assist by promoting patient adherence to medication use and reducing the cost and health-related issues through minimizing poly-pharmacy (39). There are numerous studies in chronic kidney disease or hemodialysis patients, predicating positive impacts of clinical pharmacist's participation on patient or disease outcomes such as higher percentage of patients attaining hemoglobin (40) or blood pressure goals (41), improved patients' knowledge of disease (42), decreased hospitalization (43) and improved quality of life (44).

A systematic review appraising clinical pharmacy activities in chronic kidney disease and end-stage renal disease (ESRD) population revealed promising results (45). Twenty-one studies were included among them four were controlled trials. The most common complication targeted by clinical pharmacists was anemia that trended favorably toward predefined target levels. In general, pharmacists' intervention in these trials improved the quality of life, increased patient knowledge and reduced hospitalizations. Physicians accepted clinical pharmacy suggestions at a median rate of 79%.

Regarding cost issues, it has been proposed that \$3.98 is saved per every \$1 spent on pharmaceutical care in end stage renal disease population (46). Collectively, such positive results have been translated into establishment of clinics that specifically provide ESRD patients with pharmaceutical care (47).

Pharmacist role in antibiotic therapy and infectious disease care

Playing role in the area of infection control and antibiotic therapy represents a potential opportunity for pharmacists please delete "either" to be accepted as a member of patient care team (48).

To explore the benefits associated with multidisciplinary approach to infectious diseases, Gums et al., enrolled 252 consecutive inpatients in a prospective randomized trial (49). All patients were receiving suboptimal intravenous antibiotic therapy confirmed by a clinical pharmacist. Patients were randomized to intervention ($n=127$) and control ($n=125$) groups and physicians received relevant recommendations by clinical pharmacist for optimal drug choices and dosages. Although both groups had a similar disease severity, infection type and time from admission to randomization, median hospital stay after randomization was 9.0 vs. 5.7 days for control and intervention group respectively ($p=0.0001$). Median hospital cost also was substantially reduced in intervention group (\$2642/ intervention). Overall, implementing multidisciplinary approach to manage intravenous antibiotic therapy resulted in shorter duration of hospital stay and significant cost saving.

Hand K., highlighted important roles of pharmacists in the infectious disease ward and antibiotic therapy and discussed some typical responsibilities of pharmacists in UK hospitals. He named these pharmacists as “antibiotic pharmacists” (50). Some potential roles of antibiotic pharmacist summarized in table 1.

Pharmacist role in critical care

Medication-related errors alone results in about 80% of medical errors in patients admitted to an intensive care unit. Each individual patient endures an average of 1.7 medication errors per day and nearly all patients experience at least one life-threatening error during ICU stay (51, 52). One study reported that antibiotics, electrolytes and cardiovascular agents are among the most error-susceptible categories (53).

A prospective 10-week study evaluated the efficacy of a critical care pharmacist participation in medical rounds to prevent drug interactions (54). The clinical pharmacist reviewed patients drug profiles daily and made recommendations to prevent significant drug interactions. This was compared to a baseline period when clinical pharmacist was not present. Pharmacist interventions led to a significant decrease in drug interactions that needed drug therapy modification (Poisson regression $B = -1.036$; 95% confidence interval, -1.318 to -0.753 ; $P < 0.01$). Although the lower rate of drug interaction did not translate into decreased mortality ($p=0.45$ for single regression; $p=0.09$ for multiple regression analysis), and t -test did not show significant differences in length of stay (8.29 vs. 6.91 days, $P=0.915$), but multiple linear regression analysis showed that it was associated with shorter length of hospital stay ($p < 0.01$).

Role of critical care pharmacist also has been appreciated in other sub-populations of critical care patients. In a study conducted by MacLaren et al., ICUs without clinical pharmacist had higher mortality rate, longer hospital stay and greater Medicare billings for patients affected by nosocomial-acquired infections, community-acquired infections and sepsis compared to ICUs that had clinical pharmacist (55). Same authors also reported that implicating clinical pharmacists in care of patients with thromboembolic or infarction-related events resulted in reduction in mortality and cost of care (56).

The great knowledge and skills required to approach treatment of patients facing complicated states, necessitates pharmacist incorporation as a member of decision-making team (57). In general, broad spectrum of health problems encountered by critical care practitioners and complicated drug-therapy in critically ill patients, provides pharmacists with a unique opportunity to apply their knowledge of pharmaceutical care to clinical states.

Pharmacist role in cancer management

Treatment of cancer usually needs a combination

therapy with highly toxic drugs. Along with anti-neoplastic agents, patients need frequent supportive therapies by multiple medications. This in turn enhances the risk of medication-related problems such as drug-drug interactions and medication errors that either may cause excessive toxicity or treatment failure (58-60).

Yeoh et al., conducted a study in 118 elderly cancer patients (61). In this study the effect of a medication therapy management service on reducing drug-related problems (DRPs) was assessed. A total of 361 DRPs were found. Of 44 interventions made by pharmacists, 40 were accepted (91% acceptance rate) and two thirds were graded as ‘highly significant’ by three independent judges.

Furthermore, hematopoietic stem cell transplantation (HSCT), as a gold-standard strategy to various types of hematologic malignancies, is followed by poly-pharmacy. Medication safety in such patients calls for a team-care approach. To determine the effect of pharmacist implication in patient care after allogeneic HSCT, Ho et al., organized a prospective clinic-based study (62). Thirty-five post-transplant patients who referred to clinic were separately visited by a pharmacist and medication related interventions were applied, recorded and then analyzed by a panel of physicians. At the end of study, pharmacists identified 50 medication discrepancies and 70 drug therapy problems; 27 of them were recognized as clinically significant errors by the panel. Pharmacist in this study helped safe medication use in post-HSCT patients.

Pharmacist role in geriatric medicine

Compared to general population, elderly people are more prone to adverse drug reactions and the consequences are more pronounced (26). Controlled trials evaluating drug use specifically in this population are lacking. Altered pharmacologic actions of drugs and frequent co-morbid conditions also add to the complexity of drug therapy in the elderly (63). In addition, medication error is common in elderly so that in some studies more than half of subjects were exposed to a potentially dangerous error during study period (64, 65).

A randomized multi-center study performed in a Swedish elderly population confirmed efficacy of pharmacist-conducted medication review in detecting potentially inappropriate medications (PIMs) (66). Three hundred sixty nine elderly patients (age ≥ 75 years) residing nursing homes or community were assigned to intervention ($n=182$) and control ($n=187$) groups. All patients were receiving ≥ 10 drugs and ≥ 3 psychotropics. PIMs were present in one-third of patients at each group. A pharmacist reviewed medications of intervention group and recommended physicians for appropriate changes. At the end of a two months period, the number of patients with at least one PIM was significantly lower in

Table 1. Potential roles of pharmacist in the area of antibiotic therapy (Updated From reference 50).

Potential roles of pharmacist in the area of antibiotic therapy	
–	Expert advice: To provide expert recommendations about optimum antibiotic therapy in individual cases
–	Education and training: Education and training of all health care providers about different aspects of antibiotic therapy and to aware them about hospital policies and guidelines
–	Liaison role: As a link between microbiology and pharmacy departments (antibiotic formulary, new antibiotics, antibiotic susceptibility testing and TDM of antibiotics)
–	Formulary enforcement Monitoring of prescribers' compliance with hospital antibiotic formulary
–	Antibiotic guidelines To establish and maintain antibiotic guidelines in hospital
–	Antibiotic policy Special policies about antibiotic administration e.g. considering alternative drugs, automatic stop orders, switching from IV to oral drugs and etc.
–	Antibiotic serum level monitoring and dosing Pharmacists have a major role in TDM of certain antibiotics such as aminoglycosides and vancomycin
–	Monitoring and feedback Regular feedbacks to physicians by analyzing related data and development of controlling systems
–	Research and development Coordinating with other health care providers in designing and performing research projects about antibiotic therapy and patient care

intervention group compared to control group ($p = 0.007$). The number of patients that were receiving 10 or more drugs also was reduced in intervention group ($p = 0.001$). There were drug related problems in 93% of 182 patients of intervention group. Although the number of patients taking at least three psychotropic agents did not differ during study but doses were lowered in intervention group. Hanlon et al. in a literature review found 14 randomized controlled trials about DRPs in elderly patients (≥ 65 years) and related health outcome (67). They concluded that there are convincing evidences that clinical pharmacy services and interventions can reduce DRPs significantly but supportive evidences about positive effects of such interventions on morbidity, mortality and cost are lacking.

Elderly usually suffer from multiple chronic health problems. Exacerbation of disease also may occur several times. Medication errors may arise during transition from home/long-term care facility to acute care setting and vice versa. Medication reconciliation is often a neglected step in this transition. In a review of studies evaluating controlled transition, clinical pharmacist medication review proved to be efficient in prevention of medication errors (68).

Pharmacists as a member of multidisciplinary team

With the evolving viewpoint of patient care, multidisciplinary approach has gained popularity as the standard of care. The interplay needed to fulfill this goal, recalls different specialties under a same identity to improve patient care. Pharmacists, as well, are experiencing new horizons and opportunities in this revolutionized patient-centered view. Clinical pharmacists have appreciably incorporated the science of drug therapy in various specialties (69, 70). While this has been linked to creation of new professional opportunities in pharmacy practice, new challenges have emerged as well. Now pharmacists are going away from time-consuming tasks such as dispensing or commercial activities and seek "private space" to visit patients. They need to get access to patients' medical records. Direct contact with other health care professionals that has been lost mostly in community pharmacy practice is now growing progressively (71). Not surprisingly, more close inter-professional work increases implementation rate of recommendations (72).

In a study performed in primary care setting, two

different views prevailed in contributing pharmacists (73). A group tended “physician-oriented” practice favored to act as drug-consultants and provide physicians with drug information. The other appreciated more engaged practice, from direct care of patients to interventions at system levels that guarantees rational drug use. Although this diversity may be regarded as a challenge for new era of inter-professional practice, it may indicate different roles that pharmacists can perform.

Outcome measurement

Expected outcomes of pharmacist intervention can generally be categorized as disease-related outcomes, patient-related outcomes and cost saving.

Disease-related outcome are specific to each illness and has been reviewed extensively in previous sections of this article. Patient-related outcomes can be explained as patient knowledge of disease, readmission rate and quality of life. Although a few studies failed to demonstrate reduced medication-related hospital readmissions with implementing medication reconciliation (10, 74, 75), numerous studies have verified the efficacy of pharmacist intervention to achieve these outcomes (76, 77). Unfortunately the majority of studies performed in this area have not incorporated cost analysis in outcome measurement, but few studies that did so, consistently validated cost saving (46, 78).

In general, there is no evidence of worse outcome after initiation of medication review by pharmacist in any of mentioned subcategories and the majority of studies authenticate better outcomes after participation of pharmacists (79).

Practical issues

Collaborative working of pharmacists within a medical team requires predefined agreements on responsibilities, site of care, patient groups and etc. Areas of activity may include but not limited to drug interactions, laboratory monitoring, adverse effect management, therapeutic alternatives and also non-pharmacologic therapies. Patient referral should take place as needed. Instituting educational programs for other health care members comprises another task that can be undertaken by pharmacists. Patient visit at the same time and same place may develop mutual respect and trust between pharmacist and physician (80).

Future of medication review

Going away from long-established dispensing roles, pharmacists are facing new demands to care patients in a more directed manner. As previously stated, two models are prevailing; drug consultant model and team-based model. There are no large-scale comparative studies to ascertain which model comes better, but a prospective study conducted in an oncology ward reported more

successful drug-related problem detection when pharmacists acted in a collaborative patient visit (81).

Another issue facing the future of medication review arises when the running setting is considered. There is a scarcity of studies performed in private setting. In fact, most of positive results reported yet have been gained in educational and university-affiliated hospitals or clinics.

It seems that seeking better models of intervention and extending activity to private setting are among future challenges of pharmacists engaged in medication review.

Conclusion

Tasks allocated to pharmacists have changed dramatically over last decade. New opportunities have produced new challenges that were not encountered previously. Generally, outcome of pharmacist-led medication review is promising and needs more consideration by health-care systems.

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