The clinical pharmacist improves pharmacotherapy in hospital patients

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Chapter 2

Pharmacist-led medication reviews in predialysis and dialysis patients

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Abstract

Background

Pre-dialysis and dialysis patients are at risk for drug related problems (DRPs) due to a high incidence of comorbidities. Pharmacist-led medication reviews might reduce the number of DRPs.

Objectives

The aim of this study was to evaluate pharmacist-led medication reviews in pre-dialysis and dialysis patients by determining the number and type of DRPs, nephrologist acceptance of pharmacist interventions and time investment.

Methods

From September 2017 until December 2018, pharmacist-led medication reviews were performed on pre-dialysis and dialysis patients. DRPs (medication discrepancies, prescribing issues related to drug and dose selection, drug use problems) were identified using the pharmacists' expert opinion and the STOPP/START criteria. Number and type of accepted pharmacist interventions, sustainability of interventions after at least 1 month and time investment were determined. Practical barriers in the process were appraised.

Results

One-hundred twenty five patients were reviewed: 37 pre-dialysis and 88 dialysis patients. In 100 (80%) patients 277 medication discrepancies were identified of which 224 (81%) were accepted by the nephrologist. Pharmacists suggested 422 interventions concerning drug or dose selection for 115 patients; 106 interventions were accepted by the nephrologist, which resulted in 60 patients having medication changed. Ninety percent of those changes remained implemented on follow-up after at least 1 month. In 46 (37%) patients, the clinical pharmacist detected DRPs concerning the drug use process and performed patient counseling. The average time investment was 85 minutes per patient for the clinical pharmacist and 15 minutes for the nephrologist. Besides time investment, unclear responsibility for medication management due to multiple prescribers was an important barrier in the process and the main reason for nephrologists to reject pharmacist interventions.

Conclusion

Pharmacist-led medication reviews in pre-dialysis and dialysis patients led to medication changes in half of the patients. However, efficiency should be improved before adopting pharmacist-led medication reviews into clinical practice.

Introduction

Pre-dialysis and dialysis patients are at risk for drug related problems (DRPs) defined as events or circumstances involving drug therapy that actually or potentially interfere with desired health outcomes.[1,2] These patients have a high incidence of comorbidities like hypertension, cardiovascular diseases, diabetes mellitus and mineral and bone diseases. As a result, they use on average 10-12 different drugs prescribed by multiple physicians.[2] The frequency of hospitalization is high and almost 20% of the hospital admissions might be directly related to DRPs.[2] Different types of DRPs have been found in pre-dialysis and dialysis patients. Medication discrepancies, the use of potentially inappropriate medication and user problems as non-adherence are frequently described DRPs in this patient group.[2-15] A systematic approach of medication reviews might reduce DRPs in (pre)dialysis patients leading to a reduction in hospitalization, length of stay and health care costs.[16-21] Several studies have shown that pharmacist interventions in patients with chronic kidney disease led to a reduction of DRPs, polypharmacy, improved management of anemia, blood pressure, calcium and phosphate parameters, lipid parameters, medication adherence and quality of life.[19-21, 28-31] Two controlled studies investigating pharmacist-led medication reviews on outcomes in hemodialysis patients found that the frequency of hospitalization and drug use were reduced and showed a trend towards a shorter length of hospital stay compared to the usual care group.[32,33] For implementation of this approach, a prominent role for the clinical pharmacist has been proposed.[16-25] Moreover, literature showed that nephrologists and dialysis teams are willing to cooperate with clinical pharmacists.[26,27]

Although there is considerable research showing some evidence for beneficial outcomes of pharmacist-led medication reviews in patients with chronic kidney disease, studies are generally of low methodological quality and included small number of patients.[20] In particular, studies lacked detailed descriptions of the interventions providing the interested readers insufficient information to allow reproduction of the intervention in clinical practice. In the majority of studies, pharmacists seemed to perform only a medication chart review to identify DRPs and did not specify the role of patients in identifying DRPs. In addition, studies did not address the clinical relevance and whether changes in medication were implemented or not. Furthermore, studies did not investigate why pharmacists' recommendations were not followed. Few studies provided data on time spent on specific activities.[19-21] In addition, previous studies have been carried out mostly in North America and Asia and results are not necessarily applicable to countries with other health care systems.[21] In the search for successful health care interventions, which are suitable for wide implementation, extended guidance on development and evaluation has been developed.[34] The importance of testing the interventions' potential

effect and evaluating how interventions work in practice is now widely recognized.[35] Therefore, the aim of this study was to evaluate pharmacist-led medication reviews in pre-dialysis and dialysis patients by determining the number and type of DRPs, nephrologist acceptance of pharmacist interventions and time investment.

Methods

Setting and study population

This study was conducted in the period September 2017 – December 2018 in the Deventer Hospital, a teaching hospital in the Netherlands. Pre-dialysis and dialysis patients, over 18 years of age, who were capable and willing to join this study were included. All dialysis patients and pre-dialysis patients were asked to join the study by the secretary of the dialysis ward. Patients received an appointment letter with information about the medication review procedure when they wanted to join the study. During the study period, there were 110 hemodialysis patients and 92 pre-dialysis patients under treatment in the hospital.

Description of the pharmacist-led medication review procedure

Pharmacist-led medication reviews were conducted in the dialysis ward by one trained clinical pharmacist. Patients were asked to bring all their medication or a medication list to the dialysis ward. In addition, through a safe electronic platform, a complete medication history based on dispensing data of the patients' community pharmacy was obtained by the hospital pharmacy, which is common practice for Dutch hospital pharmacies. The clinical pharmacist interviewed hemodialysis patients during the dialysis session. Pre-dialysis patients were interviewed one week prior their regular visit with the nephrologist. The actual medication use, including non-prescription medicines, was verified with the patient and problems with medication use were addressed using a standardized questionnaire. The clinical pharmacist identified DRPs using her own clinical experience interpreting Dutch standard guidelines, relevant international guidelines, the deprescribing management of McIntyre et al. and the medication safety signals generated by the electronic medication surveillance system.[30, 37-39] We call this "expert opinion" in the following paragraphs. Furthermore, the second revised version of the STOPP/START criteria applicable to the Dutch situation was used to identify potentially inappropriate medication and potentially omitted medication classified as DRPs concerning prescribing issues related to drug selection.[36] The majority of the patients was over 65 years of age (>75%). All recommendations were communicated to the nephrologist. The completion of the pharmacist-led medication review consisted of sending the actual medication list to the patients' general practitioner, to the patients' community pharmacy and directly to the patient. The specific workflow is summarized in figure 1.

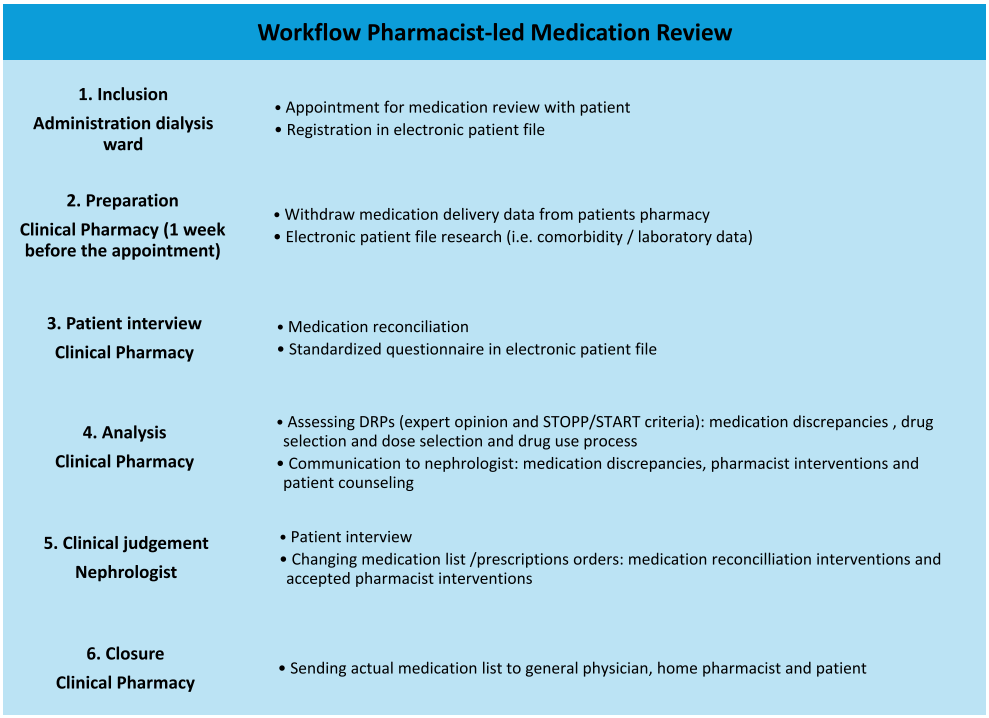

Figure 1 Workflow pharmacist-led medication review

Data collection

Each DRP and the clinical pharmacists' actions were categorized in one of the following three categories:

1. Medication discrepancies, defined as a difference in medication identified when comparing information from the pharmacy record in combination with information from the patient with the hospital medication list.[40]
   The nephrologist decided whether medication had to be changed. In case of change, this was categorized as an accepted medication reconciliation intervention.
2. Prescribing issues related to drug selection and dose selection.
   Drug selection: inappropriate drug due to contraindication, ineffectiveness, regimen or safer alternative available, no indication for drug or indication not treated (missing) therapy.
   Dose selection: drug dose too low, drug dose too high or dosage regimen inadequate according to standard reference sources. The clinical pharmacist recommended changes to the nephrologist which were defined as pharmacist interventions

(stopping a drug, starting a drug or changing a dosage).[41] In case the nephrologist changed the medication, this was categorized as an accepted intervention. For each accepted intervention, the pharmacological category and the type of change (start, stop or dose change) was noted. In addition, it was determined whether the intervention was based on STOPP/START-criteria.

3. Drug use problems by patients were defined as inappropriate timing of administration or drug over- or underused.[1] The clinical pharmacists' actions on these problems were defined as counseling including patient instructions for appropriate timing of administration and education to improve adherence. In general, those actions did not require approval of the nephrologist.

At least one month after the accepted pharmacist interventions, the medical records were reviewed again to check whether changes were persistent, i.e. to establish if the specific medication order remained changed.

The clinical pharmacist actively measured the time investment to perform the whole medication review, during the period January 2018 – July 2018. The time investment per patient for the nephrologist was based on measurements from one nephrologist in 12 patients of time investment for judging and implementing the pharmacists' recommendations.

Furthermore, practical barriers in the process of medication reviews and reasons for rejection of pharmacists' interventions by the nephrologist were documented by the clinical pharmacist.
The pharmacist documented all identified DRPs and associated data. The following data were anonymously collected from medical records, pharmacy records and patient interviews: gender, age, pre-dialysis or dialysis patient, number of drugs used and comorbidity.

Analysis

In order to characterize the patients, the Charlson Comorbidity Index (CCI) was calculated per patient, representing the 10-year survival prediction in patients with comorbidities as an indication for the patients' comorbidity burden.[42] We also calculated the percentage of polypharmacy patients, defined as chronic use of 5 or more drugs from different therapeutic groups or subgroups.[43]

The percentage of patients with the different categories of DRPs and the average number per patient was calculated. Furthermore, the percentage of accepted pharmacist interventions still implemented at least one month after the intervention, the percentage of accepted pharmacist interventions detected with the STOPP/START criteria and the percentage start, stop or dose changes were determined.

The time investment for one accepted pharmacist intervention was calculated by multiplying the total time investment (clinical pharmacist and nephrologist) by the total number of patients included, divided by the total number of accepted pharmacist interventions.

Results

One-hundred-twenty-five patients were included: 88 dialysis and 37 pre-dialysis patients. This was 80% and 40%, respectively, of the total hemodialysis and pre-dialysis patients treated at the Deventer Hospital in the study period. Sixty percent of the approached pre-dialysis patients declined a medication review. The main reasons mentioned were extra time investment (visit to the hospital) and no need according to the patient. The patient characteristics are depicted in table 1. The study sample can be described as older patients with polypharmacy and comorbidity with an average Charlson Comorbidity Index of 7, which is associated with a very low 10-year life expectancy. The results of the pharmacist-led medication reviews are summarized in table 2.

Table 1 Patient characteristics

Patient characteristic	Outcome *n* = 125
Age, years (mean ± sd; range)	72 ± 12 (33-91)
Gender (n (%))	
Male	70 (56)
Female	55 (44)
Dialysis (n (%))	88 (70)
Pre-dialysis (n (%))	37 (30)
Number of medicines used (mean ± sd; range)	14 ± 5 (3-27)
Polypharmacy (n (%))	
yes	114 (91)
no	11 (9)
CCI (mean ± sd; range)	7 ± 2 (2-13)

CCI: Charlson Comorbidity Index

Table 2 Results of pharmacist-led medication reviews

Parameter	Result (n (%))
Medication discrepancies:	
Patients with medication discrepancies	100 (80)
Medication discrepancies	277 (2.8 per patient)
Medication reconciliation interventions	224
Drug and dose selection:	
Patients with pharmacist interventions	115 (92)
Pharmacist interventions	422 (3.7 per patient)
Patients with accepted pharmacist interventions	60 (48)
Accepted pharmacist interventions	106 (1.8 per patient)
Pharmacist interventions still implemented after at least 1 month	95
Accepted pharmacist interventions detected with the STOPP/START criteria	49
Drug use process:	
Patients with patient counseling	46 (37)
Time investment:	
Average time investment (per patient)	
Clinical Pharmacy	85 minutes
Nephrologist	15 minutes
Time investment for one accepted pharmacist intervention	118 minutes

Medication discrepancies

In 100 (80%) patients, 277 medication discrepancies were established (2.8 discrepancies per patient). Two-hundred-twenty-four (81%) of these discrepancies were corrected in the electronic patient file (medication reconciliation interventions) by the nephrologist or by the clinical pharmacist at the request of the nephrologist. These discrepancies mostly concerned medication prescriptions not prescribed by the nephrologist, i.e. prescribed by other physicians, for example dermal products, inhalation medication and psychoactive drugs.

Drug selection and dose selection

In 115 (92%) patients, the clinical pharmacist detected 422 DRPs from the categories drug selection and dose selection with the pharmacists' expert opinion and the STOPP/START criteria. This resulted in 3.7 pharmacist interventions per patient. In 60 (48%) patients, the nephrologist accepted 106 pharmacist interventions (1.8 pharmacist intervention per patient) and changed the medication prescription order accordingly. In total, 106 of 422 (25%) of the pharmacist interventions were accepted by the nephrologist and therefore considered as clinically relevant. Of the accepted pharmacist interventions, 95

of 106 (90%) persisted for at least one month after the identification of the DRP. Forty-nine (46%) of these interventions were detected with the STOPP/START criteria. Of the 106 accepted pharmacist interventions 25 (24%) concerned starting new medication, 48 (45%) stopping medication and in 30 (28%) the dose was changed. In table 3, the accepted pharmacist interventions are stratified per pharmacological category. Most changed medication prescription orders were related to kidney disease treatment.

Table 3 Pharmacological categories of accepted pharmacist interventions

Pharmacological category	Number of accepted pharmacist interventions (n (%))
Vitamin D analoga, calcimimetics and phosphate binding agents	19 (18)
Erytropoeitine stimulating agents and iron suppletion	15 (14)
Antihypertensiva (ACE-inhibitors, betablockers and diuretics)	15 (14)
Proton pump inhibitors	12 (11)
Gout agents	11 (10)
Statins	8 (8)
Antihistaminic agents	3 (<1)
Benzodiazepines	3 (<1)
Urologic spasmolytica	3 (<1)
Other	17 (16)

Drug use problems

In 46 (37%) patients, the clinical pharmacist detected DRPs in the drug use process and performed patient counseling. This concerned advice about changing the time of ingestion, i.e. ingestion of specific drugs after dialysis instead of before dialysis, medicines use not concomitantly due to absorption interactions, food effects or circadian dosing of statins in relation to cholesterol synthesis). Furthermore, medication adherence was stimulated by explaining why and how to take the medicines.

Time investment

The estimated average time investment was 85 minutes per patient for the clinical pharmacist (N=80) and 15 minutes for the nephrologist (N=12). The time for one accepted pharmacist intervention was calculated at 118 minutes.

Reasons for nephrologists not to accept pharmacists' interventions

The most common reason for the nephrologist not to accept the pharmacist intervention and not to change the medication prescription order was that another physician initiated the medication. Other reasons for not accepting the interventions were no valid indication for stopping or starting the drug, the patient did not want to change, the patient had no complaints or was not adherent. Finally, interventions were rejected when laboratory values were acceptable, the nephrologist wanted to wait for further results, the patients' situation had changed during the medication review process, i.e the medication had already been changed, new laboratory results were available or the patient was hospitalized.

Discussion

Pharmacist-led medication reviews in pre-dialysis and dialysis patients identified a large number of different types of DRPs. Overall, 80% of the patients had on average three medication discrepancies per patient and the majority could be resolved. Patient counseling to improve adherence and adequate timing of administration was performed in 37% of patients. In addition, medication reviews resulted in prescription changes in 48% of the patients with nearly two medication changes per patient. These results are in line with literature and show that pharmacist-led medication reviews lead to a high number of accepted medication reconciliation and pharmacist interventions, potentially leading to a significant reduction of DRPs in this patient group.[2-14, 19-21]

The acceptance rate of pharmacist recommendations in this study was 81% for medication discrepancies. Most discrepancies concern non-(pre)-dialysis associated medication that had been prescribed initially by other providers than nephrologists. Nephrologists have to take over these prescriptions to complete the medication list in the electronic patient file. The latter leads to the high number and acceptance rate of medication discrepancies. The acceptance rate was 25% for pharmacist interventions concerning DRPs of drug selection and dose selection. This is in line with the study of Patricia et al. (acceptance rate of medication discrepancies 85% and for DRPs 27%, respectively).[2] The acceptance rate in two systematic reviews about clinical pharmacy practice in the care of chronic kidney disease patients varied from 33% to 95%, but this represented all accepted recommendations including medication reconciliation interventions in the total group of chronic kidney disease patients.[20,21]

Parker et al. found the STOPP criteria to be more suitable for elderly hemodialysis patients than the Beers criteria; because more potentially inappropriate medication use was detected with the STOPP criteria compared to the Beers criteria.[10] We detected

46% of the accepted pharmacist interventions with the STOPP/START criteria, whereas 54% was based on the clinical pharmacists' expert opinion. STOPP/START criteria miss clinically relevant DRPs and some of the criteria are not suitable for this patient group. More specific criteria for medication reviews in this patient population are needed. An example of a limited set of specific criteria already described are the deprescribing tools in hemodialysis patients published by McIntyre et al, which we also used in our expert opinion judgement.[30] Based on the results of this study a more complete set of specific criteria for this patient group can be developed and validated in further research. However, not all DRPs can be captured in a set of standardized criteria and the knowledge and expertise of a pharmacist remains necessary to attribute these criteria.[44]

The main strength of our study is the detailed description of a pharmacist-led medication review workflow in a patient group at risk for DRPs. The medication review was initiated by the clinical pharmacist but is performed multidisciplinary. The clinical pharmacist had access to the electronic patient file and laboratory data. The patient was interviewed and the workflow was implemented in daily clinical practice. The lack of detailed descriptions of pharmacists' interventions is one of the flaws in studies concerning clinical pharmacists' interventions in this patient group.[20] In this study time investment and reasons for rejection of pharmacists' interventions were appraised which were lacking in the reviews of Salgado et al. and Stemer et al.[20,21] DRPs were not only identified but the follow up and persistence of accepted and therefore clinically relevant pharmacist interventions was also established. Limitations of the study were the performance of the medication reviews by a single clinical pharmacist and not measuring patients' satisfaction in this study.

Recommendations

Before adopting pharmacist-led medication reviews in clinical practice, the following barriers have to be dealt with. First, time investment is relatively high, i.e. the time needed to establish one accepted pharmacist intervention is 118 minutes. Second, recommendations were sometimes outdated by the time the nephrologist dealt with them as the patient's clinical situation had changed. Third, about 60% of the approached pre-dialysis patients declined a medication review mostly because they had to invest extra time. In contrast, hemodialysis patients were already at the hospital, so no extra time investment was necessary. Finally, nephrologists sometimes were not willing to alter the medications prescribed by other physicians which shows that it was not always clear who took control (and responsibility) of overall medication management. The efficiency of pharmacist-led medication reviews could be improved by developing specific STOPP/START criteria for hemodialysis patients and pre-dialysis patients based on the clinical important DRPs identified in this study. These criteria can be implemented in

the electronic prescribing system as clinical rules leading to smarter and more efficient medication guidance. For example, coupling laboratory results to starting and stopping of phosphate binders, vitamine D analogues and calcimimetics. Implementing such clinical rules in the electronic prescribing system leads to continuous medication surveillance and -intervention instead of periodical medication reviews 1-2 times a year. This is more effective than periodic review as shown by Tuttle et al.[45] Besides the nephrologist, other prescribers of the patient should be involved in the medication review process. There is a role for the clinical pharmacist in taking control of medication management of this patient group. Outcomes of pharmacists prescribing activities in patients with chronic kidney disease have not been investigated systematically, therefore, we suggest this to be a subject for further research.[20] Responsibilities of the clinical pharmacist in the Netherlands should be expanded to stopping, changing and prescribing of agreed medication and ordering laboratory tests. For specialized nurses this is already regulated by law in the Netherlands. In the United Kingdom, United States of America and New Zealand prescribing and modifying medicines by clinical pharmacists is implemented in practice for several years now.[20] Therefore, this should be pursued for clinical pharmacists in the Netherlands also. Further evaluation of these approaches is necessary.[34,35]

Conclusions

Pharmacist-led medication reviews identified a high number of DRPs in pre-dialysis and dialysis patients and led to medication changes in half of the patients. Before adopting this into clinical practice, efficiency should be improved for example by developing specific STOPP/START criteria to allow continuous electronic medication monitoring and assigning medication management to one designated caretaker, for instance the clinical pharmacist.

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