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Original Article

Prevalence of medication transfer errors in nephrology patients and potential risk factors

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ABSTRACT

Background: Medication reconciliation in transitions of care can prevent medication transfer errors (MTE). MTE can cause patient harm. Since performing medication reconciliation for every patient is not always feasible, identification of potential risk factors of MTE could aid in targeting this intervention to the right patients.
Objective: To establish the proportion of patients with one or more MTE in the outpatient nephrology setting. Secondary patient characteristics associated with MTE, type and potential harm, and medication groups were investigated.
Methods: This retrospective observational cohort study was conducted in the Leiden University Medical Center, the Netherlands, between November 2017 and April 2018. The cohort involved patients in whom medication reconciliation was performed by a medical attendant using the electronic tool 'Medical Dashboard' prior to visiting the nephrologist. MTE were defined as unintended discrepancies between the medication in the hospital system and the result of the medication reconciliation. The proportion of patients with one or more MTE was calculated and the association of patient characteristics (age, sex, number of medications and kidney function (CKD-EPI)) with MTE was analyzed using multivariate logistic regression.
Results: Of 380 patients, 235 patients (61.8%) had at least one MTE. On average patients used 10.3 medications. The number of medications per patient was significantly associated with MTE; OR 1.11 (95%CI 1.05–1.16). No association was found for age, sex, and kidney function.
Conclusion: In ambulatory nephrology patients 61.8% had at least one MTE. Nephrology patients using a higher number of drugs are more prone to MTE.

1. Introduction

Incomplete medication overviews may increase the risk of patient harm both in and outside the hospital. Approximately two thirds of all patients have at least one discrepancy in their medication overview at hospital admission compared to their home medication. [1,2] Medication reconciliation in transitions of care is known to prevent medication errors. [3,4] The Dutch guideline 'Medication accuracy at transition in care' states that an accurate medication overview is required at each transition point of care. [5] In daily practice medication reconciliation for outpatient visits is not yet implemented in every hospital in the Netherlands, since this is very time consuming. Van der Gaag et al. [6] showed that medication reconciliation in an outpatient internal medicine clinic decreased unintentional discrepancies between medication use and the medication reported in the hospital record. Wilson et al. [7] provided evidence that ambulatory medication reconciliation increased patient safety and potentially prevented adverse events. In addition, implementation of ambulatory medication reconciliation resulted in improved safety by resolving medication discrepancies in advanced chronic kidney disease patients. [8] Nephrology patients are of special interest, since they often have polypharmacy and medication is frequently adjusted.

Although different studies have shown that medication reconciliation in ambulatory nephrology patients can increase patient safety [6–8], medication reconciliation is a time consuming process. It would be more efficient if this process could be focused on patients at risk of

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medication transfer errors. This would require knowledge of potential risk factors. A number of studies have been performed with the aim to determine risk factors of medication errors at admission. The most prevalent risk factors are higher age and number of medications. [4,9] A review of Hias et al. [2] has identified sixteen significant variables, of which higher age and polypharmacy were the most frequently found risk factors for medication errors at admission. In ambulatory primary care patients the number of medications in use was significantly associated with the occurrence of medication discrepancies. [10] However, nephrology patients use, on average, much more medication than the average primary care patient. Furthermore, nephrology patients usually have other comorbidities and visit different health care professionals. [7,8] Due to many different health care providers more Medication transfer errors (MTE) could occur, because at each contact medication reconciliation may fail. On the other hand, because nephrology patients are used to taking a lot of medications they could be more involved in their medication use and therefore less MTE could occur. Furthermore in nephrology patients the stage of the kidney disease varies over time and therefore a lot of medication adjustments are frequently necessary.

Due to these reasons, the risk factors found in primary care might not be applicable to the nephrology outpatient population. To our knowledge, in ambulatory nephrology patients no studies have been performed to identify risk factors of medication errors. A few studies have been performed to determine the prevalence of MTE in nephrology outpatients, however the percentage of errors differs between 48 and 80%. [6–8] Therefore, the primary aim of this study was to establish the proportion of patients with one or more medication transfer errors. The secondary aim was to identify characteristics associated with medication transfer errors in the outpatient nephrology setting, as well as to study the type and potential harm of the medication transfer errors and the medication groups involved.

2. Methods

2.1. Study design

This retrospective observational cohort study was conducted in the Leiden University Medical Center (LUMC), the Netherlands. According to the Dutch Medical Research in Humans Act, medical ethical approval was not required and patients did not need to provide informed consent, since their data were handled anonymously by the researcher. All patient data were coded according to Dutch Privacy Law. Only the treating physician had access to the code key and thus the patient data.

2.2. Study population

All patients using medication visiting the outpatient transplant nephrology clinic between November 13th 2017 and April 24th 2018, were included in the study. If a patient visited the nephrologist multiple times during the research period only the first visit was included.

2.3. Data collection

Medication reconciliation was performed by a medical attendant who is familiar with the medication of these nephrology patients and received specific training to use the tool ‘Medical Dashboard’ to perform medication reconciliation. The ‘Medical Dashboard’ combines information about medication use from the electronic patient record of the hospital with medication dispensing information from the community pharmacy obtained through the ‘Landelijk Schakelpunt’ (LSP). The medication is than shown in the Medical Dashboard grouped by medication class. Doublings between LSP and the electronic patient record are therefore comprehensively shown in lines below each other. The medication overview of the electronic hospital patient record is a combination of outpatient and inpatient medication prescribed at the hospital. The LSP is an electronic connection tool from which drug dispensing information of the community pharmacy can be obtained by a health care provider, if the patient has given consent to the community pharmacy (or several community pharmacies, should they visit more than one). The generated medication list in the ‘Medical Dashboard’ was discussed with the patient during an interview with the medical attendant. For each drug on the list the medical attendant could select one of the following options: correct, adjust, remove, ‘add from LSP’, or ‘patient does not know’. If the medical attendant did not select any of these options it was scored as unknown. After screening the known medication from the two sources, medication that was in use but not available in one of the two sources could be added. The following patient characteristics were derived from the hospital electronic patient record: age, gender, number of prescription medications at the outpatient visit and kidney function (most recent glomerular filtration rate, as calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)) .

2.4. Medication transfer errors

Medication discrepancies were defined as any difference in medications, dose, frequency or route between the medication in the hospital electronic patient record and the result of the medication reconciliation recorded in the ‘Medical Dashboard’. All identified medication discrepancies were considered unintended, because medication reconciliation took place before the medical specialist could prescribe any new medication that could be considered as an intended discrepancy. For this reason, the medication discrepancies were defined as medication transfer errors (MTE). The MTE were classified into three categories: omission (observed to be in use but not recorded in the electronic patient record); commission (not observed to be in use, but documented in the electronic patient record) and change in dose, frequency, or route. Potential harm of the MTE was assessed using the National Coordinating Council on Medical Reporting and Prevention (NCC-MERP) classification system. [11] Categories A and B of the NCC-MERP were not included in this study because these are categories that do not reach the patient. Therefore, MTE were classified in category C to I (Table 1). Two authors (ME and HE) scored individually. When there was no agreement a third author (KG) was consulted to make the final decision.

2.5. Outcome

The primary outcome was the proportion of patients with one or more medication transfer errors (MTE). The secondary outcome was the association of potential risk factors with these MTE and the type and potential harm of the MTE, and the medication groups involved in the MTE were investigated.

2.6. Data analysis

The sample size calculation was based on the incidence of medication transfer errors in the intervention group of Van der Gaag et al. [6] of 38%, an alpha of 0.05 and the assumption that not more than four independent variables (age, gender, number of medications and kidney function) would be included. Using these data a minimum of 105 patients was required.

The dataset was extracted from usual care data. To validate these data unusual values and duplicates were checked. Since different ways to record a change in dose in the ‘Medical Dashboard’ system were possible, all dose changes were checked and recoded.

Data were collected in Microsoft Excel 2010 (Microsoft Cooperation, Redmond, Washington, USA). Data analysis was performed in IBM SPSS Statistics version 24 (IBM Corporation, Armonk, New York, USA). Using descriptive statistics, mean and standard deviations or total number and percentages were reported.

The association of patient characteristics (age, sex, number of

Table 1
Potential harm of the medication transfer errors.

Category	Occurrence (%)	Definition	Example
A	0	Circumstances or events that have the capacity to cause error	NA[a]
B	0	An error occurred but the error did not reach the patient (An "error of omission" does reach the patient)	NA[a]
C	172 (29%)	An error occurred that reached the patient but did not cause patient harm	*Example:* Frequency change of alfacalcidol 0.25 μg daily to 0.25 μg three times per week.
D	321 (54%)	An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm	*Example:* Frequency change of metformin 500 mg twice daily to 500 mg three times daily.
E	74 (13%)	An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention	*Example:* Omission of fenprocoumon 3 mg daily.
F	7 (1%)	An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization	*Example:* Omission of prednisolone 5 mg daily.
G	15 (3%)	An error occurred that may have contributed to or resulted in permanent patient harm	*Example:* Omission of tacrolimus 4 mg daily.
H	0	An error occurred that required intervention necessary to sustain life	NA[b]
I	0	An error occurred that may have contributed to or resulted in the patient's death	NA[b]

Potential harm classification according to the National Coordinating Council on Medical Error Reporting and Prevention (NCC-MERP) classification system. [11].
[a] Categories A and B were not applicable in the current study, because in this retrospective study all errors reached the patient.
[b] In the current study no MTE were classified into categories H and I.

medications and kidney function) with MTE was analyzed using univariate and multivariate logistic regression. Only parameters with a p-value < .20 in the univariate analysis were included in the multivariate model. The results of the logistic regression analysis were reported as odds ratios (OR) and 95%-confidence intervals (95% CI). The number of medications was analyzed as a continuous variable and in four groups to be able to select patient groups.

Interrater reliability of the classification of the potential harm of MTE was analyzed and Cohen's kappa was reported.

3. Results

During the study period medication reconciliation was performed for 380 patients. Fig. 1 shows that after removing duplicates 3615 medications in 380 patients remained for analysis. For 290 medications it remained unclear what the exact use of the medication was after medication reconciliation with the medical assistant. These medications were presented to the nephrologist and discussed during the outpatient visit, and were excluded from the analysis. Characteristics of the included patients are shown in Table 2.

A total of 589 medication transfer errors (MTE) was identified in 235 of the 380 patients (61.8%). An average of 1.55 (± 2.28) MTE per patient was found. The number of medications was significantly associated with the occurrence of MTE. Age, sex and kidney function were not significantly associated with MTE (Table 3), but kidney function and age showed an association with a *p*-value < 0,2. In the multivariate

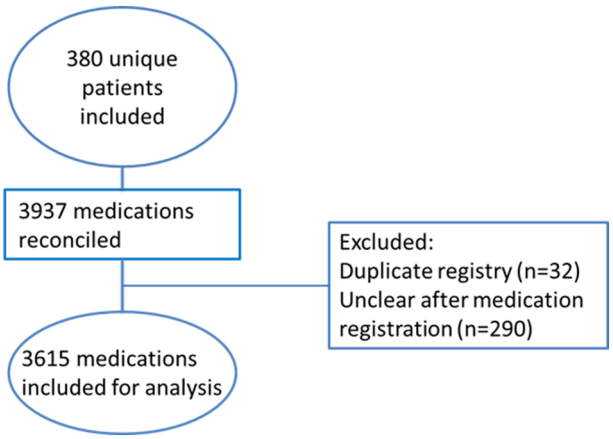

Fig. 1. Study flow. The medications that remained unclear were presented to the nephrologist and discussed during the outpatient visit.

Table 2
Patient characteristics (n = 380).

Characteristics	Mean ± SD/n (%)
Age (years), mean ± SD (range)	53.9 ± 15.7 (20–93)
Male, n (%)	206 (54.2%)
Number of medications, mean ± SD (range)	10.3 ± 4.6 (1 – 31)
Number of medications in groups, n (%)	
0–4	38 (10%)
5–9	127 (33.4%)
10–14	148 (38.9%)
>14	67 (17.6%)
eGFR (ml/min/1.73 m^2) mean ± SD (range)	53.3 ± 23.0 (7–90)

logistic regression model adjusting for age and kidney function only the number of medications remained significant OR 1.10 (95%-CI 1.04–1.16). When analyzing the number of medication in groups, it was shown that using >10 medications significantly increases the risk of MTE (Table 3).

Of the 589 MTE, 244 (41%) were omissions, followed by 208 (35%) commissions, and 137 (23%) changes in frequency, dose or route. In Table 1 the potential harm and examples per category of the MTE are shown. Cohen's kappa for the interrater variability was 0.68 which represents a substantial agreement between the two researchers. Medications from the ATC group Alimentary tract and metabolism (20.4%), Cardiovascular system (15.4%) and Nervous system (12.2%) were most often involved in MTE.

4. Discussion

This study shows that almost two third of nephrology transplant outpatients encounter MTE. This corresponds with literature for outpatient medication reconciliation where 47.6% [7] to approximately 80% [6,8] of patients were reported to have encountered MTE. The high percentages of MTE in this study can be explained by the high average number of (10.3 ± 4.6) medications that is used by this patient population. This is in accordance with the systematic review of Hias et al. [2] in which the number of medications was found to be the most frequently identified predictor for medication errors.

Age, gender and kidney function were not associated with the occurrence of MTE in this study. However, Hias et al. [2] reported that higher age and gender are found to be associated with MTE at admission in some studies, albeit within a different population. Stewart et al. [10] studied the association between patient characteristics and MTE in an outpatient primary care clinic. Our results are In accordance with the results of Stewart et al. [10]. Stewart et al. reported patients using

Table 3
Association of patient characteristics with medication transfer errors.

Parameter	Patients without medication transfer errors (n = 145)	Patients with medication transfer errors (n = 235)	Univariate Odds Ratio (95% CI)	Multivariate Odds Ratio[c] (95% CI)
Age	52.4 ± 15.5	54.9 ± 15.7	1.010 (0.10–1.02)[a]	1.00 (0.99–1.02)
Sex	81 (55.9%)	125 (53.2%)	0.90 (0.59–1.36)	–
Number of medications	9.0 ± 4.3	11.0 ± 4.7	1.11 (1.06–1.17)[b]	1.10 (1.04–1.16)[b]
0-4	22 (15.2%)	16 (6.8%)	N.A. reference group	
5–9	57 (39.3%)	70 (29.8%)	1.69 (0.81–3.51)[a]	1.57 (0.74–3.32)
10–14	50 (34.5%)	98 (41.7%)	2.70 (1.30–5.58)[b]	2.37 (1.10–5.07)[b]
>14	16 (11.0%)	51 (21.7%)	4.38 (1.87–10.3)[b]	3.80 (1.56–9.24)[b]
Kidney function	55.2 ± 22.7	52.1 ± 23.2	0.99 (0.99–1.00)[a]	1.00 (0.99–1.02)

[a] *p*-value <.20.
[b] *p*-value <.05.
[c] In the multivariate model age, number of medications and kidney function were included.

three or more medications to be associated with the presence of at least one discrepancy, as compared to patients using one or two medications, while age and gender were not found to be associated with the occurrence of discrepancies. [10] The high number of medications used by and relatively young age of our outpatient population is probably the reason that only the number of medications is associated with MTE.

In the literature renal and cardiovascular medications are most often found to be associated with medication discrepancies in accordance with the findings of this study. [7,8] The potential harm of the MTE in this study was found to be different when compared to earlier studies. In this study 71% of the MTE was assessed as having the ability to cause potential harm or to need intervention to prevent harm. In earlier studies [7,8] this percentage was only 30%. This difference could be explained by the different inclusion criteria used. In this study only the first medication reconciliation results were included for a patient, while the cited studies included multiple results per patient. After the first medication reconciliation the MTE that are found in a later stage are likely to be less harmful.

To our knowledge this is the first study that explores the association of risk factors for MTE in nephrology transplant outpatients. Another strength of this study is the use of data gathered in usual care. No specific patients were excluded, as all patients used medications. However, several limitations need to be mentioned as well. For 290 medications the actual medication use remained unclear even after medication reconciliation. Therefore, the number of MTE identified may be an underestimation. This could be due to the fact that medication reconciliation was performed by a medical attendant, instead of a pharmacist or a pharmacy technician. In earlier studies it has been shown that pharmacy professionals perform medication reconciliation more effectively. [12] However, due to the use of the 'Medical Dashboard' the crucial step of combining medication information from two sources has become automated, making it easier to perform medication reconciliation. Furthermore, the results of this study cannot be extrapolated to all outpatient clinics because the average number of medications in use by this outpatient nephrology transplant population is very high. Therefore, the risk of MTE for this population is high as well. Finally, due to the monocenter design our results may not be applicable to other outpatient nephrology clinics.

Medication reconciliation in ambulatory nephrology transplant patients is clinically relevant. A higher number of medications used is associated with more MTE. Therefore, medication reconciliation is especially important for patients with extensive medication lists. However, medication reconciliation becomes more time consuming when more medications need to be reconciled. Therefore, the potential use of a time saving electronic tool like the 'Medical Dashboard' warrants further study. In current practice it is not feasible to perform medication reconciliation for every outpatient visit with a structured interview, so it would be interesting to investigate if a tool like the 'Medical Dashboard' would empower patients to perform their own medication reconciliation. If patients are able to perform their own medication reconciliation this could result in less MTE in a time efficient way.

5. Conclusion

Medication transfer errors (MTE) were found in 61.8% of the nephrology transplant outpatients. The number of medications used is significantly associated with the occurrence of MTE. Omissions are the most common (41%) type of MTE. Lastly 71% of the MTE were assessed to cause potential harm or to need intervention to prevent harm.

Declaration of Competing Interest

The authors have no competing interests to declare.

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