Potential role of a pharmacist to enhance medication-related aspects of clinical trials conducted in a dedicated clinical research unit

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A B S T R A C T

Purpose: Pharmacist involvement in medication reconciliation has been shown to have a positive impact on patient care in a number of settings [1–6], but there have been no evaluations of the effect of this pharmacist role on patient care during the conduct of clinical trials. Pharmacist involvement in the medication reconciliation process for clinical trials may provide improved protocol compliance.
Methods: This was a retrospective pilot study conducted in a dedicated research unit that assessed completeness of the medication reconciliation process by clinical trial teams for patients participating in a clinical trial involving investigational medication(s). Patients' medication lists in the EHR were reviewed after their study visit. Pharmacy staff evaluated the medication list for accurate inclusion of IDs and any prohibited or restricted concomitant medication(s) per the study protocol.
Results: Ninety-five patient visits over two months were evaluated and showed only 20.6% of IDs were listed in the EHR after study visits. Of those included, only 40% had the correct dose and 50% had the correct frequency listed. There were 20 potential protocol prohibited medications identified. There were four medications listed in a fashion that may have compromised maintenance of blinding status in the EHR.
Conclusions: This pilot study showed potential roles for pharmacy personnel involvement in medication reconciliation in the clinical research setting. Pharmacists have the opportunity to ensure that IDs are accurately included in patient medication lists and to identify the use of potential protocol prohibited concomitant medications.

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1. Introduction

The protocol is the backbone of a clinical research trial involving investigational drugs (IDs). It outlines the selection of subjects, intervention(s), and procedures. Protocols also include information regarding management of interventional and concomitant medications. A protocol deviation is considered any change, divergence, or departure from the study design or procedure that can be controlled by the investigator [7]. Drug-related deviations (DRD) are any such occurrences that involve dosing or administration of IDs. In addition, DRD may include the use of protocol prohibited concomitant medications. To this end, an updated medication history is necessary to ensure that prohibited concomitant medications are not administered to study subjects. In addition to preventing DRD, an accurate and comprehensive medication history can also prevent medical errors and/or adverse drug events in other types of patient encounters outside of the research setting, and are therefore important for provision of health services within the continuum of clinical care [1,3–5].

Pharmacists have been shown to decrease the number of medication discrepancies in patient health records [6] and may therefore be the ideal healthcare professionals to reconcile the subject's medication history with the protocol requirements in a clinical research setting. In a study on the accuracy of geriatric patients' medication histories, patients randomized to pharmacist-conducted histories had medication lists that were 71% correct at 48 h post admission compared to 48% accuracy for those in the control group [1]. Likewise, in a surgical orthopedic unit, researchers concluded "a clinical pharmacist performed more

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complete and more accurate drug histories than nurses." [5] Based on the results of these and other studies, it has been proposed that pharmacy personnel may be uniquely positioned to improve both the quality of clinical research through involvement in medication reconciliation activities.

This retrospective pilot project was conducted to identify potential opportunities for pharmacy personnel to improve both protocol compliance and accuracy of medication history activities in a clinical research unit setting. The specific aims were to determine the percent of patients seen in the Michigan Institute for Clinical and Health Research (MICHR) Michigan Clinical Research Unit (MCRU) who had IDs correctly added to their medication lists by the study team, and to identify whether study staff correctly identified protocol prohibited or restricted medications as indicated on the patient medication list.

2. Methods

The MICHR MCRU is an outpatient patient care unit that provides support and services for the conduct of clinical trials, and received funding from the Clinical Translational Science Awards, grant number 2UL1TR000433-06. A significant number of the projects conducted in MICHR MCRU include administration of IDs dispensed from the University of Michigan Health System (UMHS) Research Pharmacy (RP). The RP is a division in the Department of Pharmacy Services (DPS) that manages IDs in order to ensure that regulations and drug-related aspects of the protocol are followed. The design was a retrospective pilot study to evaluate opportunities for quality improvement related in provision of activities already a part of standard practice at MICHR MCRU, and was deemed by the University of Michigan Medical School Institutional Review Board (IRBMED) to be non-regulated research.

The study population was defined as those patients, 18 years of age and older, who were enrolled in an "included" clinical trial. Included clinical trials were defined as those clinical trials that were IRBMED-approved, included a drug or biologic as the test object in the study, and had study visits in which subjects were seen in MICHR MCRU during the defined time period. Since this was considered a pilot project, and there were no previous studies conducted in this setting identified, formal sample size calculations were not performed. A convenience sample of all visits during a 60-day period that met inclusion criteria was utilized.

During the study period, it was standard practice for the study team to obtain a current medication list from the patient during a MICHR MCRU visit and update the medication list in the EHR if needed. In this study, pharmacy personnel reviewed the medication list as recorded in the EHR at least 48 h after the conclusion of the visit, in order to allow adequate time for the study team to update the EHR. Information about excluded or restricted concomitant medications was identified from the study protocol and compared to the patient's medication list in the EHR. The EHR was also specifically evaluated for the inclusion of the IDs administered as a part of the MICHR MCRU visit. If the ID was included on the EHR, the accuracy of the drug name, dose, route, and frequency was compared to the original prescriber order for the ID using records maintained by the RP, and accuracy of the entry was evaluated.

3. Results

During the two-month study period, 95 MICHR MCRU patient visits involving 97 IDs were reviewed. Eleven of these were for the first study visit for the clinical trial, and 61 study visits were for double-blinded clinical trials. Characteristics of the clinical trials included in this project are summarized in Table 1, and the summary of ID listings in the EHR is presented in Table 2.

An average of 5.44 concomitant medications (range: 0 to 18) were identified during these visits (Table 3). Of the 97 investigational medications, only 20 (20.6%) were included on the EHR medication list. All 20 of these included IDs that were identified correctly by name on the EHR, but only 8 (40%) had the correct dose and 10 (50%) had the correct frequency listed. Nineteen drugs (95%) had the route correctly listed. There were 20 potential DRD due to prohibited concomitant medications found on the patients' medication lists. Since this was a retrospective study, the pharmacist was not able to confirm if prohibited medications included on the EHR were actually being taken by the patient (i.e., whether the patient's medication list was an accurate representation of current medications). Likewise, if the protocol prohibited medications at time of subject enrollment, but allowed them to be taken later (e.g. anti-emetics to be added only after patient experienced drug-related nausea and vomiting), these time-dependent restrictions could not be confirmed in real time. Therefore, these must be considered only potential DRD of prohibited medications. Additional analysis showed four IDs that were part of blinded studies erroneously included on the EHR medication list in an open-label format (i.e. without indicating treatment could be either active/placebo or treatment 1/treatment 2), potentially misleading blinded personnel and the patient regarding actual assigned treatment. Additionally, 39 concomitant medications had at least one missing characteristic (dose, frequency, route, etc.).

4. Discussion

As standard practice for patients seen in the MICHR MCRU, study team members obtain the current medication list and may or may not update it in the EHR. It is also a study team responsibility to evaluate the medication list for the presence or absence of any restricted medications. Standard RP services include tools to ensure

Table 1
Characteristics of clinical trials evaluated.

Study Design	Number of studies	Number of Visits (Number of First Visits)
Open label	8	26 (3)
Single Blinded	1	8 (3)
Double Blinded	16	61 (5)
Total	25	97 (11)

Table 2
Accuracy of IDs information listed in the EHR.

	Number of drugs (%) n = 20 total drugs
Correct Drug	20 (100)
Correct Dose	8 (40)
Correct Frequency	10 (50)
Correct Route	19 (95)
Blinded drugs listed in manner that may have compromised blinding status	4

Table 3
Concomitant medications listed in the EHR.

	Number of medications
Number of concomitant medications per visit (average)	5.44
Number of concomitant medications per patient (range)	0–18
Potential prohibited medications (%)	20 (21)
Added medication after visit	44
Deleted medication after visit	2
Lists with at least 1 potential discrepancy	39
Potential discrepancies (%)	45 (8.7)
Missing Dose (%)	28 (5.4)
Missing Frequency (%)	16 (3.1)
Missing Route (%)	16 (3.1)

safe and appropriate dispensing and administration of IDs, but at present there are no direct patient care services provided by the RP staff. However, this study demonstrated that in this and similar settings, pharmacists have the potential to improve the quality of clinical research by decreasing occurrences of DRD.

This study provided evidence of the potential opportunities pharmacists have to identify protocol-prohibited concomitant medications. Due to the design of the study (retrospective and conduction of study visits by the study team), re-questioning by pharmacy personnel regarding concomitant medications was not performed. Therefore, the deviations related to prohibited concomitant medications were unconfirmed However, because past studies [1,2,5,6] have shown pharmacists are able to identify and correct errors in patients' medication lists, the results from this pilot study support a future study to prospectively assess the direct role of pharmacists in the medication reconciliation process in the clinical trial setting.

Information regarding blinded status of IDs was also an important finding in this project. In this pilot, incidences were noted in which blinded treatments had been listed on the patient medication lists in a manner that was both misleading and potentially compromised the integrity of the blind. Since it is critical that healthcare personnel, study team members, and patients remain blinded when indicated by the protocol, the way in which IDs are listed in the EHRis important. For example, if the patient is randomized to a blinded regimen, all possible treatments should be included in the drug name on the medication list in order to maintain the blind (i.e. "Drug A __ mg OR Drug B __ mg OR placebo tablets orally once daily"). In these situations, free-text entries rather than use of the EHR drug database is required. Given the particular expertise and role of RP personnel, they may be uniquely qualified to ensure that blinded treatments are appropriately included on medication lists.

Because most IDs used in clinical trials are not yet approved or because of the blinding requirements noted above, many IDs must be entered into medication lists as free-text entries. However, in cases where the study drug is already available commercially and there are not unblinding concerns, the standard EHR medication database listings should be used. . This enables use of the EHR clinical decision support tools, such as drug-drug interactions databases. When using the standard medication database listing, it is important to include a notation that the drug is being administered as part of a clinical trial.

5. Conclusion

The results of this retrospective pilot indicate there may be gaps related to medication histories that can contribute to DRD in clinical trials. These gaps present opportunities for pharmacists to have a positive impact on research by improving the medication history process. Pharmacists engaged in the specialized practice area of research pharmacy or IDs services may be uniquely qualified to provide these services, given their specialized expertise in managing drugs used in clinical trials. Based on the results of this project, a prospective study assessing specific number and types of interventions made by pharmacists, and the potential impact of these on DRD and patient care in the clinical research setting is warranted.

Disclosure

The authors have no relevant disclosures.

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