Original Research

Frequency and Impact of Pharmacist Interventions in Clinical Trial Patients With Diabetes

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ABSTRACT

Purpose: The objective of this study was to describe the interventions and impact made by pharmacists during clinical trials.

Methods: A specialty contract research organization that used clinical trial research pharmacists to communicate with patients to support clinical trial protocol adherence, retention, and health outcomes performed a retrospective, descriptive analysis of 12 clinical trials that involved 2 noninsulin glucose-lowering medications. Pharmacists called study participants at specific timepoints during the trials as per protocol. During each telephone call, the number and types of interventions were documented. Descriptive statistics (frequencies) were performed to determine the number and type of interventions by call and by patient across all noninsulin glucose-lowering medication drug A and drug B studies.

Findings: Overall, 25,829 calls were made across all studies. Of these calls, 11,765 calls (45.5%) had at least one intervention that involved 3573 patients (92.3%). The most frequent interventions addressed adverse events (3774 [14.6%]), protocol violations for medication use (3341 [12.9%]), concurrent medications (1630 [5.9%]), and miscellaneous concerns (1269 [4.6%]). The greatest numbers of interventions were high-impact interventions (4772 [18.5%]) (eg, serious adverse events) that would seriously affect trial outcomes and patient adherence.

Implications: Pharmacists were able to identify, support, and address multiple types of interventions related to medication management during clinical trials, including those related to concurrent medication use, adverse events, and other medication-related issues. These pharmacist interventions can result in better patient outcomes and, ultimately, more reliable study results for review and approval by regulatory agencies. (*Clin Ther*. 2017;39:714–722) © 2017 The Authors. Published by Elsevier HS Journals, Inc.

Key words: clinical trials, diabetes, medication adherence, pharmacist.

INTRODUCTION

In 2016, the National Institutes of Health reported >200,000 ongoing clinical trials with locations in all 50 states and 193 countries.[1] New medications and health interventions are constantly being explored to improve the health and outcomes of patients. For these trials to produce valuable results, it is important for patients to remain adherent to the treatments and protocols being studied. Adherence is defined as "persistence in practice or tenet; steady observance or maintenance" (Aronson JK. Compliance, concordance, adherence. *Br J Clin Pharmacol*. 2007;63(4):383–384). This term is preferred over the term *compliance*, and the term *adherence* will be used hereafter.

Studies have found that adherence to medication therapies in ambulatory clinical trials is suboptimal. In 2012, Blaschke et al[2] examined a cohort of 16,907 patients enrolled in 95 clinical trials. The authors found that the number of patients taking the prescribed therapy decreased by up to 40% over time. At day 100, 20% of

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patients had discontinued treatment, and another 12% of patients had omitted doses. By the end of the 12th month, the number of patients who had discontinued use of the drug increased to 40%.[2] Improper adherence stems from many causes and may be related to patient characteristics, psychological phenomena, severity of health problems, complexity of treatment regimens, drug-drug interactions, and adverse effect profile.[3]

Nonadherence occurs for a variety of reasons (ie, adverse effects, missed doses, misunderstanding of directions) and is especially concerning in medical conditions that are chronic and prevalent, such as diabetes. Adherence in diabetes is important to minimize patient morbidity and mortality. In 2010, the TRIAD (Translating Research Into Action for Diabetes) study group found that in cases in which treatment goals were not met, 20% to 23% of patients with diabetes were found to have poor treatment adherence.[4] In addition to the consequences in diabetes specifically, the consequences of poor adherence can be considered on individual and community levels. At the individual level, patients with poor medication adherence have increased morbidity and mortality, as well as decreased quality of life, as noted above. In addition, poor adherence may also have a negative impact on the community, such as increased antimicrobial resistance and increased transmission of disease.[3]

Although nonadherence may have devastating consequences in the community setting, nonadherence within the scope of clinical trials proves to be even more problematic. Nonadherence in clinical trials may lengthen studies, increase costs, confound study results, and threaten researchers' abilities to complete statistical analyses and draw valid scientific conclusions. It is estimated that mean adherence rates for short- and long-term medication adherence within the scope of clinical trials investigating treatment regimens is 78% and 59%, respectively.[3] These percentages offer room for much improvement with respect to medication adherence within clinical trial research.

Factors for poor adherence may be related to treatment complexity, treatment adverse events, and drug-drug interactions, particularly in diabetes in which these issues commonly occur. Pharmacists have a unique opportunity as the medication experts to manage poor adherence during clinical trials. In 2012, Ali et al[5] examined the impact of a pharmacist-managed program for individuals with diabetes in the community setting on hemoglobin A_{1c} and other cardiovascular risk factors. Patients in the intervention group received diabetes education as well as monitoring and counseling every 2 months for a 12-month period. Patients in the intervention group had significant reductions in hemoglobin A_{1c}, blood pressure, blood glucose, and body mass index. Patients in the intervention group also experienced significant increases in quality of life, belief about the need for medication, and diabetes knowledge. In addition, these patients had fewer concerns about medication therapy.[5]

In 2014, Chung et al[6] examined the impact of a pharmaceutical care model on glycemic control and medication adherence in patients with type 2 diabetes. Participants in the control group received standard pharmaceutical services, including dispensing of the medication and brief instruction on how to take the medication. Participants in the intervention group were provided more extensive education and follow-up telephone calls to help them resolve any drug-related problems or issues. The authors found that the pharmaceutical care intervention was associated with significant reductions in hemoglobin A_{1c} and improvement in medication adherence.[6]

These studies found positive impacts that pharmacists have made on important markers of health, including laboratory values, quality of life, and medication adherence related to diabetes in the community setting. These findings should be explored further because these same health markers are also important in clinical trials, particularly because proper adherence is essential to ensure quality data and to minimize clinical trial costs. By using the knowledge and skills of pharmacists, researchers in clinical trials may be able to improve clinical trial retention, medication adherence, and, ultimately, patient outcomes. For example, pharmacists may be able to provide health care support by identifying and addressing medication therapy issues with patients and addressing patient questions regarding medication therapy in a timely manner.

There are currently no studies examining the types of pharmacist interventions made regarding medication use in patients with diabetes in the clinical trial setting. Understanding the types, frequency, and impact of the interventions made will help elucidate whether pharmacists provide important pharmaceutical interventions that affect the data of clinical trials. Therefore, the objective of this study was to describe the interventions and impact made by pharmacists during multiple clinical trials.