Medication Adherence and Attrition to Biologic Treatment in Rheumatoid Arthritis Patients

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ABSTRACT

Purpose: The objectives of this study were to assess medication adherence rate and attrition rate in first-time adalimumab (ADA) or etanercept (ETA) users in rheumatoid arthritis (RA) patients. This study also identified the risk factors associated with nonadherence and treatment abandonment.

Methods: This was a retrospective study with a 2-year follow-up. A total 2151 adult RA patients (18 years of age and older) who initiated ADA or ETA treatment in the Kaiser Permanente Southern California health plan between 2002 and 2009 were identified. Among those on treatment in the first year, continuous treatment receipt was determined by having at least 1 medication refill in the second year; otherwise treatment was considered as abandoned. Medication adherence was measured through proportion of days covered (PDC) and compared between patients continuously on treatment and those abandoning treatment. Risk factors of nonadherence (PDC < 80%) and treatment abandonment were estimated by a multinomial logistic regression model.

Findings: Patients who abandoned treatment had significantly lower PDC (37.3%) and lower average number of refills (5.1) than adherers (PDC = 88.8%; average number of refills = 12.4) and nonadherers (PDC = 53.3%; average refills = 8.2). Age, African Americans (odds ratio [OR], 1.49; 95% CI, 1.03–2.17), corticosteroids use (OR, 0.80; 95% CI, 0.63–0.98), and history of physical/occupational therapy (OR = 0.66; 95% CI, 0.46–0.93) were associated with nonadherence, whereas having a comorbidity (OR, 1.24; 95% CI, 1.01–1.57) was associated with treatment abandonment. The difference in PDC between ADA and ETA was no longer statistically significant after excluding the treatment abandonment group. A higher proportion of ADA users abandoned treatment than ETA users (42.9% vs 32.2%).

Implications: Taking into account treatment abandonment when measuring medication adherence in ADA and ETA use in RA patients can provide a fair and clinically meaningful view of patients' medication-taking behavior. (*Clin Ther.* 2015;37:660–666)

Key words: anti-TNF, medication adherence, medication attrition rate, rheumatoid arthritis, treatment abandonment.

INTRODUCTION

With the goal to improve how patients follow the directions on a prescription and minimize the avoidable medical spending related to inappropriate use of medications, the Centers for Medicare and Medicaid Services (CMS) included new metrics using prescription claims to gauge medication adherence to Medicare Health & Drug Plan Quality and Performance Ratings.[1] The medication adherence rate used to measure how well a patient adheres to the directions of a prescription in a defined time period is a key metric to understanding a patient's medication consumption behavior.[2,3]

With the increased use of pharmacy administrative databases and awareness of the medication adherence, the proportion of days covered (PDC), one of the metrics to calculate the medication adherence rate, was endorsed by the National Quality Forum as an

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indicator of quality in drug therapy management.[4] However, 2 strong assumptions are required for measuring the PDC. First, the refill records in a pharmacy administrative database are assumed to truthfully reflect the prescription directions given by physicians. It should be noted that a pharmacy administrative system and physicians may not interact directly. There are circumstances when physicians need flexibility in treating their patients, such as advising patients to use lower dose by splitting the pill or reducing the frequency of drug use if needed. These dynamics in medication use are difficult to capture. The second assumption is that patients would follow the prescription exactly. In other words, factors that may influence a patient's medication-taking behavior such as forgetfulness, side effects, and adverse events are usually not taken into account.

One conventional approach to determine the end point of medication use is to identify a patient's switch from or discontinuation of current drug use, which is referred to as treatment persistence. The criteria of treatment persistence are to specify a window of time for the occurrence of switch and/or discontinuation. This window varies significantly; in studies on biologic disease-modifying antirheumatic drug (DMARD) use in rheumatoid arthritis (RA), the time window to define discontinuation varied from 30 days[5–7] to 60 days[8] to 90 days.[9] The lack of consistency in specifying this time period leads to inconclusive results and difficulty in generalizing the results to different populations.

To avoid reinitiation of the drug use and be distinct from discontinuation, this study defines treatment abandonment as having at least a 1-year time period of having no refill records after initiating the treatment. With such a definition, it allows us to separate patients into stoppers and nonstoppers.

In addition to medication adherence rate, which tells us how well a patient takes the medication as recommended, this study includes a medication attrition rate, which reflects the proportion of patients who abandon treatment. With these 2 measures, we would be able to have a more complete picture for understanding the use of adalimumab (ADA) or etanercept (ETA) in RA patients.

The objectives of this study were to assess medication adherence rate and attrition rate in the first-time ADA or ETA users in RA patients. At the same time, this study also examined the risk factors associated with nonadherence and treatment abandonment.

PATIENTS AND METHODS

Data Source

The primary data source was Kaiser Permanente Southern California (KPSC) electronic medical records, which contain detailed information on interactions of members with the health system. KPSC has 14 medical centers and affiliated hospitals, along with 198 medical offices. The Medical Care Program of KPSC is a large group practice managed health care organization with >3.5 million members. Members receive their health care predominantly within KPSC-owned facilities throughout the 7-county regions in Southern California.

Data were extracted from research datasets created from the electronic medical records that included detailed information on inpatient and outpatient use, emergency department (ED) visits, diagnosis, and pharmacy. Patient demographic information including date of birth, sex, race/ethnicity, and health plan enrollment were obtained from KPSC membership databases.

Study Cohort

The study cohort included 2151 adult RA patients 18 to 100 years of age who initiated ADA (n = 564) or ETA (n = 1587) treatment between 2002 and 2009. The date of initiating ADA or ETA was defined as the index date. RA was defined as a patient having at least 2 medical encounters 30 days apart in an outpatient setting with International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) codes (714, 714.0, 714.1, 714.2, 714.4, 714.8, 714.81, 714.89) or 1 RA-related hospitalization record or ED visit and at least 1 prescription filled for a DMARD (ie, methotrexate, hydroxychloroquine, sulfasalazine, adalimumab, etanercept, infliximab, rituximab, abatacept, golimumab, anakinra, certolizumab, tocilizumab) within a year after the diagnosis.[5] The positive predictive value of this logic to identify RA patients was 97% based on a manual chart review resulting from a random sample of RA patients. Continuous eligibility included enrollment in KPSC with both medical and pharmacy benefit. At least 1 year continuous eligibility before the index date and no biologic DMARD use were required in this preindex (baseline) period. A 2-year continuous eligibility was applied after the index date to ensure that the patient was a member of the health plan for at least 2 years.