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RESEARCH NOTES

Relationship between medication synchronization and antiretroviral adherence

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ABSTRACT

Objectives: To compare antiretroviral adherence (measured as the proportion of days covered [PDC]) and change in viral load in insured, HIV-infected, adult outpatients enrolled and not enrolled in a medication synchronization program.

Methods: This was a multicenter, retrospective, pilot cohort study. Fifty-eight insured, HIV-infected, outpatients at least 18 years of age receiving antiretroviral therapy (ART) for at least 3 months as of August 2015 were included. PDC, viral load, PDC dichotomized into adherent or nonadherent, and viral load dichotomized into detectable or undetectable were collected for each patient. Study data were compared in those with (enrolled) and without (not enrolled or control) medication synchronization. The study end points were analyzed between the 2 groups retrospectively after 3 months.

Results: PDC in patients undergoing medication synchronization was significantly higher than in control patients: mean ± SD 96 ± 9% versus 71 ± 27%, respectively ($P < 0.0001$). The medication synchronization group was also more likely to be adherent to ART than the control group (odds ratio 10.67, 95% confidence interval 2.63−43.31). In the medication synchronization group, 75.9% of patients had an undetectable baseline viral load, and 83.3% had an undetectable viral load at study completion. In the control group, 62.1% and 64.7% had an undetectable viral load at baseline and completion, respectively. No statistically significant change in viral load was observed between groups ($P = 0.34$).

Conclusion: In insured, HIV-infected, adult outpatients, implementation of a medication synchronization program was associated with improved ART adherence. Future studies are needed to better assess the impact of medication synchronization on clinical outcomes.

Medication adherence to antiretroviral therapy (ART) is important in patients living with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) to achieve viral suppression, minimize drug resistance, and improve survival.[1] The Department of Health and Human Services Panel on Antiretroviral Guidelines identifies many factors that may influence adherence. These factors include the prescribed regimen, health literacy, substance abuse, poverty, inconsistent access to medication, and psychosocial hurdles (such as depression or HIV stigma). A supportive clinical setting with multidisciplinary care, including providers, pharmacists, and behavioral health clinicians, was associated with higher adherence.[2]

ART can be costly, which may affect a patient's access to medication. Uninsured HIV-infected adults may be eligible to receive ART and other associated medications at no cost through the nationwide AIDS Drug Assistance Program (ADAP).[3] Insured patients with HIV/AIDS are not eligible to receive their medications through ADAP or similar programs, which could affect medication adherence.

A number of surrogate endpoints have been used to measure medication adherence in previous studies, including refill adherence, pill counts, electronic monitoring devices, medication possession ratio, and proportion of days covered (PDC). The PDC calculates the number of days supplied of a medication class (such as ARTs) obtained over a specified time period.[4] A variety of techniques and interventions have been

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proven to affect adherence. These include compliance packaging and educational interventions, such as counseling.[5] More recently, medication synchronization has been used in areas such as chain, independent, and mail-order pharmacy, most often targeting polypharmacy patients and the nonadherent.

Medication synchronization is the process of refilling all maintenance medications on the same date for each fill cycle and is intended to improve medication adherence as well as pharmacy operation efficiency.[6] In a traditional model, the pharmacy staff prepares medications only when prompted, for example, by a patient requesting refills or a provider ordering a new prescription. In medication synchronization, a date is deliberately scheduled for the pharmacy staff to fill all of a patient's chronic medications. This model is advantageous for pharmacy workflow. By scheduling and synchronizing medications, pharmacy staff are able to perform medication reviews, identify any potential therapeutic concerns, and complete patient counseling on all medications during 1 scheduled date.[7] In addition, the synchronization model is advantageous for patients by reducing trips to the pharmacy and allowing 1 convenient day to pick up all medications. Medication synchronization and improved adherence may also have a cost benefit with reduced disease-related medical costs.[8] Holdford et al. published 2 studies to assess the impact of appointment-based medication synchronization (ABMS) and adherence to chronic medications in the general population. Both studies found a higher odds of adherence in the ABMS groups compared with control groups.[9,10] Data on medication synchronization and adherence are limited, and to date no published studies have investigated medication synchronization for ART. Therefore, the purpose of the present study was to determine if enrollment in medication synchronization was associated with improved adherence to ART.

Objectives

The primary objective of this investigation was to compare ART adherence (as measured by PDC) in insured, HIV-infected, adult outpatients enrolled and not enrolled in medication synchronization. The secondary objective was to describe viral load in both medication synchronization and control groups before and after medication synchronization.

Methods

Study design and period

This was a multicenter, retrospective, pilot cohort study. The study period was August 2015 to April 2016.

Setting and medication synchronization program

The study site was a Federally Qualified Health Center in eastern North Carolina. Patients were identified and divided into "medication synchronization" (enrolled into the medication synchronization program) and "control" (not yet enrolled in the medication synchronization program). Because of the retrospective, observational nature of this study, the groups were predetermined by the pharmacy's ongoing medication synchronization implementation and no matching or randomization was performed by the investigators. The medication synchronization group differed from the control group in timing of refills for chronic medications. When patients in the control group required a refill for a chronic medication, the patient would prompt the pharmacy to refill each medication individually at the time it was due, whereas all chronic medications were refilled on the same date for patients in the medication synchronization group.

Patient eligibility

Patients were eligible for inclusion in the study if they were outpatients at least 18 years of age, diagnosed with HIV (based on medical records) as of August 2015, using any one of the 3 Carolina Family Health Centers, Inc. pharmacies, prescribed a consistent ART regimen for at least 3 months, and insured, either publicly or privately. ART regimen was defined as the combination of antiretroviral medications prescribed for the treatment of HIV. Patients were excluded for any missing or incomplete data for calculation of the primary end point (PDC) and for any ART regimen change during the study period. Patients were identified for study eligibility by a "Ryan White" group identification code in the pharmacy dispensing software system. All patients eligible for enrollment in the medication synchronization program at data collection were eligible for inclusion in the study (enrolled group). A group of individuals meeting the same inclusion criteria, but not enrolled in the medication synchronization program, were randomly selected and identified as the control group and received no intervention.

Outcome measures

The primary end point (PDC) was determined for each patient with the use of the following equation: PDC equals the number of days supplied in the given period divided by the number of days in the given period times 100%. Though not validated, PDC is a common measure of adherence in the literature. After its determination, the PDC is often dichotomized as adherent or nonadherent. Andrade et al. found 38 studies in which PDC was categorized into levels of adherence. Of the studies that dichotomized PDC, adherence was determined by a PDC of 80% or higher in 24 (75%) of the studies and 90% or higher in 4 (13%).[11] Consistent with previous studies, the present investigation defined adherence by a PDC of 80% or higher. ART and PDC data were collected from the electronic medical record and pharmacy dispensing system software. Viral load data were collected from the electronic medical record. If available, 2 viral loads were recorded for each patient, a pre–medication synchronization viral load, which was drawn before the start of the synchronization program, and a post–medication synchronization viral load, which was drawn 3 months after the start of the program. Viral load was considered to be undetectable at fewer than 20 copies/mL.

Other independent variables

Three months of data were collected retrospectively from the electronic medical record. Data collected included demographic data (age, gender, ethnicity, and race) and clinical data (comorbidities and medications, including single-drug vs.