Barriers to Medication Adherence in Children, Adolescents, and Young Adults Prescribed Anticoagulation

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Abstract

Pediatric and adolescent and young adult (AYA) thromboembolism is treated with anticoagulation. While anticoagulation non-adherence in adults has been linked to increased morbidity and mortality, much is unknown concerning medication adherence in pediatric and AYA populations. The aims of this study were to describe barriers to adherence in anticoagulated pediatric and AYA outpatients and to explore the relationship between barriers and self-reported adherence. Nearly 75% of patients and caregivers reported barriers to anticoagulation adherence, and a greater number of reported barriers was associated with lower adherence (rpb = 0.48, p = .01). Limitations, clinical implications, and future directions are discussed.

Introduction

Venous thromboembolism (VTE) in children, adolescents, and young adults (AYAs) typically develops in the setting of multiple thrombotic risk factors, including central venous access, severe illness/inflammation, surgery, and/or high estrogen state. While rare in healthy children, VTE occurs in up to 58 cases per 10,000 pediatric hospital admissions.[1-6] Although the risk factors, associated medical conditions, and sites of thrombosis vary across children and AYAs, therapeutic anticoagulant medications (i.e., oral vitamin K antagonists, subcutaneously injected low molecular weight heparin, newer direct oral anticoagulants) are prescribed to promote thrombus resolution while preventing thrombus extension, embolization, or formation at new sites.[7] Anticoagulant adherence is presumed to be critical for maximizing health outcomes, yet emerging literature shows that 2-42% of children and AYAs demonstrate non-adherence or medication-taking that differs from the prescribed treatment regimen.[8-10]

To date, pediatric and AYA VTE research has found that younger age and lower parental education are associated with lower adherence,[8,9] but the modifiable factors, or barriers, that may lead to non-adherence have not yet been examined. A critical next step for the field and the primary aim of this project was to begin to identify barriers to anticoagulation adherence among children and AYAs. The secondary aim was to explore the relationship between barriers and adherence. If, as hypothesized, a higher number of barriers is associated with lower adherence, these data would provide support for developing adherence-promotion interventions targeting barriers. Adherence-promotion interventions in children and AYAs prescribed anticoagulants thus far have targeted general education and the promotion of self-efficacy, and produced minimal improvements in adherence rates.[11-13] Understanding barriers that could be targeted to improve anticoagulation adherence, thus, is an essential step in improving outcomes for children and AYAs prescribed anticoagulants.

Methods

This study includes a secondary analysis of data collected as part of a quality improvement (QI) initiative to assess adherence barriers within clinical care. Collection and retrospective analysis of anonymized data

were approved by the Institutional Review Board. Participants in the larger QI initiative included caregivers (of patients ages 0-18 years), children, and AYAs diagnosed with VTE who were followed for therapeutic anticoagulation in the Hematology clinic at Cincinnati Children's Hospital Medical Center (May-November 2019).

Measure

As part of the larger QI initiative, self-report measures of barriers to oral and injectable anticoagulant medication adherence were created. Items were adapted from those included in the psychometrically validated Parent and Adolescent Medication Barriers Scales[14]with author permission and used to create four versions of a barriers measure (oral anticoagulant – patient report; oral anticoagulant – caregiver report; injectable anticoagulant – patient report; injectable anticoagulant – caregiver report). Qualitative feedback from patients, caregivers, and the multidisciplinary medical team regarding item comprehension and face validity was gathered and used to inform measure refinements. The final measures are included in Supplemental Table I.

Approximately 6 weeks into the QI initiative, two items assessing adherence were added to the barriers measure. The first item, "How many anticoagulant doses did you/your child miss in the past 7 days?," was used to calculate the percentage of prescribed doses taken defined as$\left(\frac{n\ prescribed\ doses\ in\ past\ 7\ days - n\ doses\ missed\ in\ past\ 7\ days}{n\ prescribed\ doses\ in\ past\ 7\ days} * 100\right)$. The second item, "Did you/your child miss any anticoagulant doses in the past month?", was used to obtain a dichotomous (yes/no) indicator of missed doses in the past month.

Procedures

A barriers measure was completed by caregivers of children ages 0-18 years and children and AYAs ages 10-25 years during anticoagulation follow-up visits.

Clinical and Demographic Information

As this measure was completed anonymously, participant clinical and demographic information were not collected.

Analyses

Descriptive statistics were used to summarize the most frequent barriers, adherence values, and concordance of barriers within patient/caregiver dyads. Correlations were used to explore the relationships between the total number of barriers endorsed and medication adherence (percentage of prescribed doses taken; indicator of missed doses in past month). Analyses were conducted in IBM SPSS version 27.[15]

Results

A total of 130 families completed the barriers measure as part of the QI project. The sample included 62 patients (patient-report only), 37 caregivers (caregiver-report only), and 31 patient/caregiver dyads for a total of 161 participants. Seventy-nine patients (85% of patients) and 32 caregivers (47% of caregivers) reported on adherence to oral anticoagulants, with the remaining participants reporting on adherence to injectable anticoagulants (n = 14 [15%] patients, n = 36 [53%] caregivers).

Roughly three-fourths of patients (n = 67; 72%) and caregivers (n = 53; 78%) endorsed [?] 1 barrier. On average, patients reported 1.72 barriers (Range = 0-10; Standard Deviation (SD) = 1.92) and caregivers reported 2.03 barriers (Range = 0-8; SD = 2.00). The frequencies of barriers by participant and medication type (oral versus injection) are presented in Figure 1. Within the 31 caregiver-patient dyads, pain was the only barrier that all caregivers and patients agreed on whether it was present or absent (Figure 2).

On average, patients reported taking 96% of doses in the past week (Range = 57-100%; SD = 10%; n = 70) and caregivers reported that their child took 97% of doses in the past week (Range = 71-100%; SD = 7%; n = 62). Of the patients (n = 26) and caregivers (n = 24) asked about adherence in the past month, 50%

of patients (n = 13) and 50% of caregivers (n = 12) reported that they missed at least one dose. Among patients, a greater number of barriers was associated with at least one missed dose in the past month (r_{pb} = 0.48, p = .01) but not the percentage of prescribed doses taken (r = -0.20, p = .09). Among caregivers, a greater number of barriers was associated with at least one missed dose in the past month (r_{pb} = 0.52, p = .01) and a lower percentage of prescribed doses taken (r = -0.26, p = .04).

Discussion

Data collected as part of our QI initiative show that children and AYAs face a wide range of barriers to anticoagulation adherence. For patients prescribed an oral anticoagulant, the most frequently endorsed barriers included forgetting to take the medication, medication side effects, and alteration of lifestyle required secondary to taking the medication. For patients prescribed an injectable anticoagulant, the most common barriers included medication side effects, alteration of lifestyle required secondary to taking the medication, and pain. Of note, caregivers and patients reported different top barriers and when both completed measures (in the 31 dyads), 55% of the barriers endorsed differed across reporters. These data highlight the importance of assessing the barriers perceived by all stakeholders involved in adherence management, as perceptions of barriers and their impact on adherence behavior may vary across individuals.

Consistent with studies from other pediatric medical populations, a greater number of barriers was associated with lower adherence per patient- and caregiver-report.[16-18] While results are limited by the lack of demographic and clinical data, missing data, lack of objective adherence measurement, and single site design inherent in the collection of data as part of a QI initiative, they suggest that targeting barriers may be a promising avenue for improving adherence in children and young adults prescribed anticoagulants. Critical next steps include standardizing and optimizing adherence measurement and developing and evaluating interventions for this population.

Conflict of Interest Statement: The authors have no conflicts of interest associated with this publication, and there has been no significant financial support for this work that could have influenced its outcome.

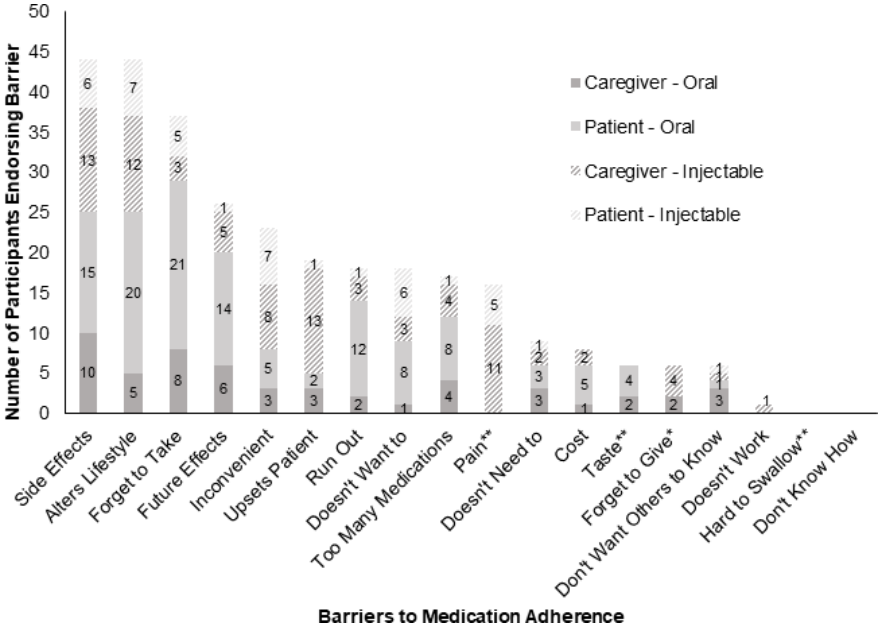

Figure 1. Barriers endorsed by reporter and medication type. *Barrier only included on the caregiver-report measure. **Barrier only included on the measure for oral medications (taste, hard to swallow) or injectable medications (pain).

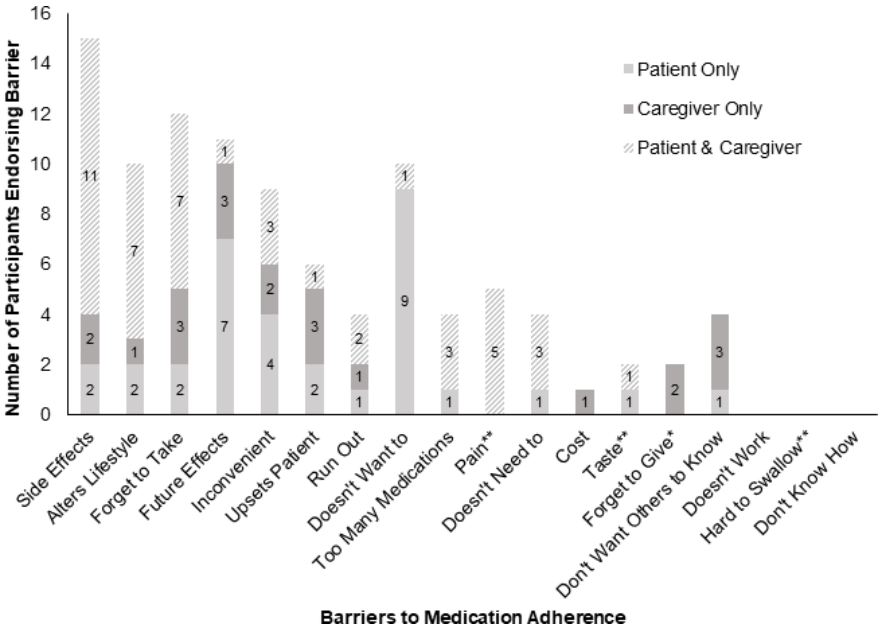

Figure 2. Barriers endorsed by dyads (n = 31). *Barrier only included on the caregiver-report measure. **Barrier only included on the measure for oral medications (taste, hard to swallow) or injectable medications (pain).

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Legend List

Figure 1. Barriers endorsed by reporter and medication type. *Barrier only included on the caregiver-report measure. **Barrier only included on the measure for oral medications (taste, hard to swallow) or injectable medications (pain).

Figure 2. Barriers endorsed by dyads (n = 31). *Barrier only included on the caregiver-report measure. **Barrier only included on the measure for oral medications (taste, hard to swallow) or injectable medications (pain).