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Adherence to Lipid-Lowering Therapy and Reaching Treatment Goals in Youth Seen in a Preventive Cardiology Clinic

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Abstract

Introduction—The efficacy of lipid-lowering therapy in reducing cardiovascular disease in adults is well-established. Unfortunately, it is also well-established that adults have inadequate adherence to lipid-lowering therapy, which is associated with increased costs and mortality. However, the adherence patterns of youth prescribed lipid-lowering therapy is not well-described.

Methods—We analyzed data that was prospectively collected from patients <27 years-old who were referred to a large regional preventive cardiology clinic from 2010–2017. Adherence to lipid-lowering therapy was self-reported at the patient's most recent clinic visit and categorized as either adequate adherence (≥80%) or inadequate adherence (<80%). We compared adherence rates by demographic factors, class of lipid-lowering therapy, length of time on lipid-lowering therapy, family history, lipid parameters, and laboratory measures of adverse effects.

Results—In our cohort, we had 318 patients prescribed a lipid-lowering medication over a seven-year period. Of those, 235 (75%) had adequate adherence. Those with adequate adherence had an improved LDL-C (123 mg/dL [standard deviation (SD) 32.3] vs. 167 mg/dL [SD 50.4], $p<0.05$), total cholesterol (198 mg/dL [49.5] vs. 239 mg/dL [SD 53.2]), and non-HDL-C (148 mg/dL [SD 38.7] vs. 193 mg/dL [SD 43.9]). In addition, patients with adequate adherence were more likely to reach goal LDL-C of <130 mg/dL than those with inadequate adherence (130 vs. 25, $p<0.01$). The relationship between LDL-C and adherence remained statistically significant after controlling for

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Contributors' Statement Page

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Dr. de Ferranti conceptualized the study, designed the data collection instruments, maintained the dataset, and reviewed and revised the manuscript.
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age, gender, and the length of time on therapy (β = −0.66, p <0.01). Adherence level did not differ by gender, class of lipid-lowering therapy, length of time on lipid-lowering therapy, or presence of a family history of an atherosclerotic event. The findings were similar when we only analyzed those prescribed a statin.

Conclusions—Self-reported adherence to lipid-lowering therapy in youth is excellent and was associated with achieving goal LDL-C goals. Obtaining adherence data from patients may help more patients reach LDL-C goals.

INTRODUCTION

Lipid-lowering therapies, in particular statins, reduce the risk of atherosclerotic cardiovascular disease (ASCVD) and mortality in adults.[1] However, adherence to lipid-lowering therapy in adults is reported to be as low as 50%,[1, 2] and lower adherence rates are associated with worse outcomes and increased costs.[1] Randomized controlled trial data show lipid-lowering therapies reduce low density lipoprotein cholesterol (LDL-C) in children and adolescents[3, 4] and decrease surrogate markers of ASCVD, such as carotid intima-media thickness.[5] In addition, more youth and young adults are presenting with a combined dyslipidemia associated with obesity.[6] However, limited pediatric data suggests that adherence rates may also be low, thus preventing patients from reaching goal LDL-C levels.[7, 8] The purpose of this study is to evaluate the characteristics of those with high adherence rates to better understand how to improve adherence to lipid-lowering therapy in youth and young adults.

METHODS

Eligibility Criteria

As part of this project, clinical and demographic data were prospectively collected from patients who were under the age of 25 years at the time of their first encounter and cared for at a large regional medical center from September 1, 2010 to December 31, 2017. Please note, that subjects up to the age of 27 years old were included in this analysis. While all patients who presented to the clinic with a concern for dyslipidemia were eligible for inclusion in the quality improvement project, Patients were eligible for this particular analysis only if they were prescribed a bile acid sequestrant, ezetimibe, fibrate, omega-3 fatty acid supplement, or statin and had at least two visits, separated by at least 12 months during the observation period. To be eligible, adherence had to be measured within three months of the most recent fasting lipid panel. This study was approved by the Boston Children’s Hospital research ethics board with a waiver of individual participant consent.

Assessment of Adherence and Covariates

Adherence was self-reported to the visit provider as the proportion of doses taken of those prescribed over the previous seven days, as standardized in the quality improvement form. Assessing adherence by proportion of days prescribed and medication possession ratio was not possible given the limitations of the dataset. The most recently captured value was used. For this analysis, “adequate” adherence was defined as taking >80% of prescribed doses to be consistent with previous studies[9, 10] and with findings that adherence above this level

in adults may be associated with improved outcomes. Family history of hypertension, type II diabetes mellitus, obesity, and ASCVD events were collected as part of clinical care. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and LDL-C were obtained as part of clinical care from peripheral blood samples using standard enzymatic assays.

Statistical Analysis

Multivariable linear regression models were used to assess for an association between adherence and 1) the length of time since the initial prescription; 2) the LDL-C recorded immediately prior to the adherence measurement; and 3) a family history of ASCVD, controlling for age and gender. All statistical calculations were done with R statistical package.[11]

RESULTS

In our cohort of 317 patients prescribed a lipid-lowering medication over a seven-year period, 235 (75%) had adequate adherence (Table 1). Patients with adequate adherence were more likely to reach goal LDL-C of <130 mg/dL than those with inadequate adherence (85% vs 15%, $p<0.05$). The relationship between LDL-C and adherence remained statistically significant after controlling for age, sex, and duration of therapy ($\beta=-0.66$, $p \leq 0.01$). Subjects who reported lower adherence did not differ by age at initiation of therapy (16.7 years [3.1] vs. 17.3 years [3.7], p=0.16), female sex (49% vs 43%, p=0.47), or family history of ASCVD (82% vs 18%, p=0.09). However, the presence of a high-risk family history was associated with initiating a statin at a younger age (Odds Ratio 1.2, p=0.004). These findings were similar when we restricted the analysis to just those patients prescribed statins, which was a majority of our patients in this cohort (vs. other lipid-lowering therapies).

DISCUSSION

In this unique, single cohort study of patients prescribed lipid-lowering therapy, we found that overall adherence was relatively high, with 75% of youth and young adults having adequate adherence (i.e., >80% of prescribed doses taken), regardless of class of lipid-lowering therapy. Further, improved adherence was associated with a higher likelihood of reaching goal LDL-C.

Adherence rates in this cohort were higher than seen in other chronic diseases in childhood, such as asthma (49–71%)[12] and human immunodeficiency virus (28–70%).[13] We also found adherence rates to lipid-lowering medications in youth and young adults were higher than those published in the adult literature.[14] Although methodologic differences make directly comparing results difficult, our adherence rate was substantially higher than reported by Joyce et al.[7] In the study by Joyce et al, the authors used an administrative database to report the proportion of patients failing to fill one or more prescriptions for lipid-lowering therapy over a 10-year period and found 87.9% of eligible youth and young adults had at least one 90-day period of not filling a prescription during the study period.[7]

In addition, our results suggest that ensuring patients have adequate adherence may lead to a higher proportion of patients reaching LDL-C treatment goals. In our analysis, only 25 (30.1%) of patients with poor adherence reached goal, whereas 139 (59.1%) of those with adherence >80 percent reached LDL-C goal. In a previous analysis of this cohort in which adherence data was not captured, only 60 percent of subjects reached goal level of an LDL-C less than 130 mg/dL.[15] This suggests that adequate adherence, in addition to diet and physical activity, may be an important factor associated with achieving goal LDL-C levels. However, adherence may be not captured accurately using self-reported data. Other study designs can take advantage of more objective measures of adherence, such as the proportion of days prescribed, medication possession ratio, or directly observed therapy, which was not captured in as part of this quality improvement project.

Adverse effects are often cited as a causes of nonadherence;[1] however, adverse effects are rare in randomized trials of youth and young adults taking lipid-lowering therapy, occurring at similar rates to placebo.[4] Increased understanding of one's disease process has been shown to improve adherence;[16] thus, we expected a family history of ASCVD would be associated with improved adherence, but this did not bear out. However, a positive family history of ASCVD did increase the length of time that a patient was on a statin (odds ratio 1.2, p=0.004), suggesting that a family history of ASCVD may promote earlier initiation of a statin.

Our findings are limited by the fact that adherence rates were self-reported to the subject's provider, likely biasing towards a higher reported adherence. The correlation between adherence rates and LDL-C values suggests that true adherence may not be that dissimilar to the reported rate. Even given the likely reporting bias, one in four youth reported an adherence rate that insufficiently lowers their LDL-C.

CONCLUSION

In conclusion, self-reported adherence was relatively high, with 75% of youth and young adults having adequate adherence. Qualitative and quantitative research is needed to further our understanding of the factors leading to higher adherence rates, in particular socioeconomic and environmental factors, and to develop strategies to improve adherence in youth and young adults.

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Abbreviations:

HDL-C	high density lipoprotein cholesterol

LDL-C	low density lipoprotein cholesterol
CK	creatine kinase
ALT	alanine aminotransferase

REFERENCES

1. Maningat P, Gordon BR, Breslow JL. How do we improve patient compliance and adherence to long-term statin therapy? Current Atherosclerosis Reports. 2013;15:1–12.
2. Avorn M J, Lacour A, Bohn RL, et al. Persistence of Use of Lipid-Lowering Medications: A Cross-National Study. JAMA. 1998;279(18).
3. Wiegman A, Gidding SS, Watts GF, et al. Familial hypercholesterolaemia in children and adolescents: gaining decades of life by optimizing detection and treatment. European Heart Journal. 2015;36(36):2425–2437. [PubMed: 26009596]
4. Vuorio A, Kuoppala J, Kovanen PT, et al. Statins for children with familial hypercholesterolemia. Cochrane Database Syst Rev. 2019;2019(11).
5. Braamskamp MJAM. Effect of Rosuvastatin on Carotid Intima-Media Thickness in Children With Heterozygous Familial Hypercholesterolemia: The CHARON Study (Hypercholesterolemia in Children and Adolescents Taking Rosuvastatin Open Label). Circulation. 2017;136(4):359–366. [PubMed: 28592434]
6. Cook S, Kavey RE. Dyslipidemia and pediatric obesity. Pediatr Clin North Am. 2011;58(6):1363–1373, ix. [PubMed: 22093856]
7. Joyce NR, Wellenius GA, Eaton CB, Trivedi AN, Zachariah JP. Patterns and predictors of medication adherence to lipid-lowering therapy in children aged 8 to 20 years. J Clin Lipidol. 2016;10(4):824–832.e822. [PubMed: 27578113]
8. Braamskamp MJ, Kusters DM, Avis HJ, et al. Long-term statin treatment in children with familial hypercholesterolemia: more insight into tolerability and adherence. Paediatr Drugs. 2015;17(2):159–166. [PubMed: 25644328]
9. Bansilal S, Castellano JM, Garrido E, et al. Assessing the Impact of Medication Adherence on Long-Term Cardiovascular Outcomes. Journal of the American College of Cardiology. 2016;68(8):789–801. [PubMed: 27539170]
10. Karve S, Cleves MA, Helm M, et al. Good and poor adherence: optimal cut-point for adherence measures using administrative claims data. Current Medical Research and Opinion. 2009;25(9):2303–2310. [PubMed: 19635045]
11. Team RC. R: A language and environment for statistical computing. In: R Foundation for Statistical Computing, editor. Vienna, Austria2021.
12. Desager K, Vermeulen F, Bodart E. Adherence to asthma treatment in childhood and adolescence - a narrative literature review. Acta Clin Belg. 2018;73(5):348–355. [PubMed: 29228891]
13. Reisner SL, Mimiaga MJ, Skeer M, et al. A review of HIV antiretroviral adherence and intervention studies among HIV-infected youth. Top HIV Med. 2009;17(1):14–25. [PubMed: 19270345]
14. Yeaw J, Benner JS, Walt JG, Sian S, Smith DB. Comparing Adherence and Persistence Across 6 Chronic Medication Classes. Journal of Managed Care Pharmacy. 2009;15(9):728–740. [PubMed: 19954264]
15. Mendelson MM, Regh T, Chan J, et al. Correlates of Achieving Statin Therapy Goals in Children and Adolescents with Dyslipidemia. J Pediatr. 2016;178:149–155 e149. [PubMed: 27592099]
16. Yilmaz MB, Pinar M, Naharci I, et al. Being well-informed about statin is associated with continuous adherence and reaching targets. Cardiovascular Drugs and Therapy,. 2005;19(6):437–444. [PubMed: 16435071]

Highlights

1. In youth, self-reported adherence to lipid-lowering therapy, in particular statins, is high (75%).
2. Adequate adherence (i.e., >80%) was associated with reaching low-density lipoprotein cholesterol level goals.

Table 1.

Characteristics of patients prescribed any lipid-lowering therapy at assessment of adherence.

	All (N=317)	Adherence >80% (N=235, 73.9%)	Adherence ≤80% (N=82, 26.1%)	P Value
Age at measurement (years)	17.3 (3.7)	17.5 (3.9)	16.7 (3.1)	0.16
Age at medication start (years)	14.0 (3.8)	14.1 (3.9)	13.5 (3.2)	0.14
Years on medication	3.3 (2.6)	3.4(2.6)	3.1(2.4)	0.40
Female (N, %)	152 (48%)	116 (49%)	36 (43%)	0.47
Type of Medication				
Statin	284 (89.3)	215 (75.7)	69 (24.3)	0.12 **
Bile Acid Sequestrant	8 (2.5)	5 (62.3)	3 (37.7)	0.43
Ezetimibe	3 (0.9)	1 (33.3)	2 (66.7)	0.16
Fibrates	18 (5.7)	12 (66.7)	6 (33.3)	0.42
Omega-3 fatty acid *	4 (1.3)	2 (50.0)	2 (50.0)	0.27
Total Cholesterol (mg/dL), mean (SD)	210 (62.2)	199 (51.4)	242 (77.3)	<0.05
non-HDL-C (mg/dL), mean (SD)	162 (55.7)	150 (40.0)	196 (76.2)	<0.05
Triglycerides (mg/dL), mean (SD)	165 (288.8)	153 (233.3)	197 (406.1)	0.21
HDL-C (mg/dL), mean (SD)	47 (13.4)	47 (14.0)	47 (11.8)	0.58
LDL-C (mg/dL), mean (SD)	133 (42.2)	123 (33.3)	161 (52.0)	<0.05
Proportion reaching goal, N (%)	164 (51.6)	139 (59.1%)	25 (30.1%)	<0.05
Family History				
Atherosclerotic Event (N, %) †	158	129 (54.9%)	29 (34.9%)	0.09
Elevated cholesterol (N, %)	208	160 (68.1%)	48 (57.8%)	0.44
Hypertension (N, %)	127	102 (43.4%)	25 (30.1%)	0.13
Type II diabetes mellitus (N, %)	88	70 (29.8%)	18 (21.7%)	0.67

* Omega-3 fatty acid supplements were either prescribed or obtained over-the-counter.

** Yates correction was used.

† Family history of atherosclerotic event was defined as a myocardial infarction, treated angina, interventions for coronary artery disease, sudden cardiac death, or stroke in a first or second degree relative. High density lipoprotein cholesterol, HDL-C; low density lipoprotein cholesterol, LDL-C.