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Original Article

Patterns and predictors of medication adherence to lipid-lowering therapy in children aged 8 to 20 years

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BACKGROUND: The American Academy of Pediatrics recommends lipid-lowering therapy (LLT) for children at high risk of cardiovascular disease. However, the use of LLT in children is rare, and rates of nonadherence are unknown.

OBJECTIVE: To identify patterns of use and predictors of nonadherence to LLT in children aged 8 to 20 years and the subgroup with dyslipidemia.

METHODS: Commercially insured patients with a new dispensing for an LLT were included. Nonadherence was defined as a gap of >90 days between the last dispensing plus the medication days supply and the next dispensing or censoring. Descriptive statistics characterize the patterns of LLT adherence and class-specific drug switching. Kaplan–Meier curves and multivariable Cox proportional hazard models identified time to, and predictors of, nonadherence for the cohort and the dyslipidemia subgroup.

RESULTS: Of the 8710 patients meeting inclusion criteria, 87% were nonadherent. Statins were the most common index prescription, and patients with an index statin dispensing were more likely to have multiple comorbidities and other prescription drug use. In multivariable analyses, nonadherence was inversely associated with dyslipidemia (hazard ratio [HR] = 0.61, 95% confidence interval [CI] = 0.57–0.65), chronic kidney disease (HR = 0.69, 95% CI = 0.54–0.88), higher outpatient (HR = 0.87, 95% CI = 0.77–0.98), and inpatient (HR = 0.83, 95% CI = 0.70–0.97) use. When limited to patients with dyslipidemia, nonadherence was related to age (HR = 1.21, 95% CI = 1.07–1.38) and obesity (HR = 1.23, 95% CI = 1.02–1.49).

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CONCLUSIONS: Despite recommendations to begin continuous treatment early for high-risk children, nonadherence to LLT is frequent in this population, with modestly higher adherence in children with dyslipidemia.

Introduction

The National Heart, Lung, and Blood Institute and American Academy of Pediatrics (AAP) recommend lipid-lowering therapy (LLT) for treatment of severe dyslipidemia in children aged 8 to 10 years when diet and exercise have failed to sufficiently reduce low-density lipoprotein cholesterol (LDL-C).[1,2] However, these recommendations are controversial, and the use of LLT in children and adolescents is rare.[3,4]

In adults, the benefit of LLT in reducing the risk of cardiovascular disease (CVD) depends considerably on medication adherence. Yet, adherence to LLT is low or moderate with long-term rates between 36% and 88%.[5–11] Similar to adults, there is evidence to suggest that in children, the benefits of LLT require consistent use and that the risk of CVD in children and adolescents is cumulative.[12–14] For example, a recent study by Ference et al., found that subjects who had prolonged exposure to lower LDL-C levels early in life as a result of a gene-variant had fewer coronary events relative to subjects who began LDL-C lowering with statins later in life. These findings were consistent even when the same LDL-C levels were achieved, suggesting that early treatment may reduce the risk of CVD by preventing the early and irreversible buildup of plaque.[13]

To date, however, the only study of adherence to LLT during childhood is a 10-year follow-up study of 214 children who participated in a 2-year clinical trial for the safety and efficacy of pravastatin.[15] Although the authors found that 88.8% of study subjects were still using LLT after 10 years, the generalizability of the results to the population outside the clinical trial setting is limited.[16]

Interest in population based measures of medication adherence during childhood has grown as the prevalence of chronic conditions in childhood has increased over the past two decades.[17] However, studies have found mixed results with rates of adherence ranging from 25% to 88%.[18,19] Furthermore, research has tended to focus on childhood conditions in which nonadherence can result in serious acute effects, such as asthma or diabetes.[19–21] In contrast, the benefits of LLT during childhood are unlikely to be realized for another 20 to 30 years, resulting in substantially different incentives for medication adherence. Thus, studies of other chronic medications during childhood may not be applicable, and additional work is needed to identify possible avenues for improvement in very high-risk children, especially those with genetic dyslipidemias.

The objective of this study was to describe patterns of prescribing and adherence to LLT in a population of commercially insured children aged 8 to 20 years in both the full cohort of children prescribed LLT during the study period as well as the subgroup of patients with a diagnosis for dyslipidemia. To achieve this objective, we used a large national database of private insurance claims between 2003 and 2013, a period in which the recommendations for pharmacologic treatment transitioned from the 1992 NCEP and 1998 AAP guidelines recommending bile acid sequestrants as first line agents to the 2008 AAP and 2011 NHLBI guidelines, which recommended statins as a first line treatment.

Methods

Data sources and study population

All data are from the Marketscan Research Database for calendar years 2004 to 2013. The Marketscan Research Database is a database of employer-based health insurance claims that contains all reimbursable health care claims, including prescription medication dispensings, filled for employees and their dependents.

Our study population consisted of all enrollees aged 8 to 20 years who met two criteria: (1) a new LLT dispensing, defined as the first ("index") dispensing after a minimum of 12 months of continuous enrollment (the baseline period), and (2) a minimum 12 months of follow-up time after the index dispensing. We assessed the presence of the following clinical conditions before the index dispensing: dyslipidemia, diabetes, obesity, hypertension, metabolic syndrome, asthma, chronic kidney disease (CKD), depression, and attention deficit hyperactive disorder. A condition was considered present if the patient had two outpatient claims within a 24-month period, with the first occurring before the index dispensing, or a single inpatient claim before the index dispensing. Additionally, we measured the following prescription drug dispensings and measures of health care utilization in the year before the index dispensing; prescription dispensings for diabetes, hypertension, asthma, depression, and antipsychotics; the presence of a recorded screening for diabetes or a lipid panel; and the number of outpatient, inpatient, and prescription drug dispensings other than LLT.