Similar Medication Compliance and Control of Dyslipidemia With Simvastatin or Atorvastatin in a Staff-Model HMO Medical Clinic

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ABSTRACT

OBJECTIVE: The primary objective of this study was to determine medication compliance rates and dyslipidemia control in a patient population receiving simvastatin or atorvastatin (statins) in a unique staff-model health maintenance organization (HMO). The secondary objective of this study was to measure the effect of gender and statin regimen on the success rate of dylipidemia control and medication compliance.

METHODS: This was a retrospective chart review conducted for patients with a diagnosis of dyslipidemia who received monotherapy with a statin for cholesterol reduction. Patients received care at an outpatient clinic during a 12-month study period (December 1998 through December 1999). Patients were excluded if they did not have a low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) concentration obtained in 1999, did not have a statin prescription filled at least twice the during study period, discontinued statin therapy, or received a statin other than simvastatin or atorvastatin. Patient medication compliance was assessed using the medication possession ratio (MPR). Dyslipidemia control rates were determined according to the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) II guidelines.

RESULTS: A total of 819 patients met inclusion criteria for study enrollment (55% male, 45% female). The mean age of the patients was 68.5 years. The mean MPR for the entire study group was 0.96 ± 0.23. Men and women had similar mean MPR values (0.97 ± 0.23 vs. 0.96 ± 0.22, respectively; $P = 0.76$). A nearly identical proportion of patients who received either atorvastatin or simvastatin achieved their LDL-C goal, 70.0% vs. 69.6%, respectively. Gender was not related to success rate, with 73.0% of women and 66.9% of men achieving their NCEP-directed LDL-C goal ($P = 0.06$). The rate of attainment of ATP II LDL goal was 43.2% (92 of 213) for patients with goal <100 mg/dL, 69.1% (226 of 327) for <130, and 90.7% (252 of 279) for patients with goal <160 mg/dL.

CONCLUSIONS: Patients enrolled in a unique staff-model HMO who received either simvastatin or atorvastatin exhibited high medication compliance and dyslipidemia control rates. Gender did not affect medication compliance or attainment of LDL-C goal, and the success of achieving dyslipidemia control was not different between atorvastatin and simvastatin.

KEYWORDS: Hyperlipidemia, Statins, Health maintenance organizations, Patient compliance, Physician-patient relations

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Coronary heart disease (CHD) is responsible for more than 20% of American deaths, making it the leading cause of death in the United States.[1] This year, an estimated 1.2 million Americans will suffer a coronary attack, and approximately 25% of men and 38% of women will die within a year of an initial event.[1] The estimated cost of CHD for 2005 is $142.1 billion.[1] Efforts to reduce mortality and costs associated with CHD is targeted at prevention through lifestyle modification and drug therapy.

Numerous studies have confirmed the link between elevations in total cholesterol and low-density lipoprotein cholesterol (LDL-C) with an increased incidence of atherosclerotic cardiovascular disease.[2-5] In the 1980s, several interventional trials demonstrated that lowering cholesterol with bile acid sequestrants, niacin, or fibric acids significantly reduced the risk of cardiac mortality and CHD.[6-10] It was not until the 1990s that primary and secondary prevention trials demonstrated decreased morbidity and mortality with the most common cholesterol-lowering agents prescribed today, the statin drugs.[11-14] More-recent trials have extended these findings by demonstrating benefits for other high-risk patient populations and for patients with lower baseline cholesterol levels.[15-17] Statins reduce LDL-C and total cholesterol to a greater extent than other agents and are the lipid-lowering drugs of choice for prevention of CHD.[18] The more potent the statin, the greater the LDL-C reduction. Prior to 1997, the only high-potency statin on the market was simvastatin. Since then, 3 additional high-potency statins have been introduced to the market: atorvastatin, cerivastatin, and rosuvastatin.

Despite the availability of effective medications to lower cholesterol, approximately two thirds of patients with dyslipidemia do not achieve their LDL-C goal.[19,20] Variability in medication adherence likely contributes to the discrepancy in outcomes between clinical trials and clinical practice.[21] Only 40% to 70% of patients comply with their medication regimen, which limits the success of lipid reduction and, ultimately, CHD prevention.[22-24] However, it has been demonstrated that medication compliance can be enhanced through a positive patient-provider relationship.[25-27]

This study was implemented in a unique health care model that provided medical care to the same patient population for decades using the same providers. Similar to the creation of Kaiser Permanente, which developed medical services in California to manage workers of the Aqueduct project, a medical and dental clinic was developed to manage health care of employees, retired employees, and their families of a large industrial company in Denver. This company was created in 1911

and was one of the largest employers in Denver. The company realized the benefit of developing and maintaining a loyal workforce and keeping that workforce healthy by providing health services as a benefit. Subsequently, around 1920, the company developed a small on-site medical clinic to address the flu epidemic. Sometime prior to the 1940s, the clinic expanded services, employed physicians, employed trained professional staff, and created a health maintenance organization (HMO) to provide comprehensive health care for members (i.e., employees, retired employees, families of employees). Throughout the existence of the clinic, extensive services were offered to the members at one location, including pharmacy, laboratory, X-ray, physical therapy, urgent care, primary care, specialty care, dental care, ophthalmology care, etc. Although the corporate headquarters continues to operate, the large industrial component of the company no longer operates out of Denver. As a result, few active employees and their families continue to receive medical care in Denver.

At the time of the study, the majority of patients (more than 70%) were retirees who had been receiving health care from the same clinic providers for up to 50 years. It was speculated that this continuity of care might result in enhanced patient-provider relationships, which, in turn, may positively impact medication adherence rates. In addition, as a result of a favorable drug manufacturer contract, simvastatin was the only statin on formulary. Based on patient-specific factors (i.e., formulary selection for secondary insurance) and formulary guidelines (i.e., intolerance to simvastatin), other statins could be dispensed upon prior authorization approval. The most common non-formulary drug dispensed was atorvastatin (7.6%), followed by lovastatin (2.6%) and pravastatin (0.6%). Based on the unique factors of long-term patient-provider relationships and use of high-potency statin agents, this study was conducted to determine if rates of compliance and dyslipidemia control were greater than those of other clinical practices cited in the literature.

Since previous landmark trials (i.e., Scandinavian Simvastatin Survival Study [4S], West of Scotland Coronary Prevention Study [WOSCOPS], Cholesterol and Recurrent Events [CARE], and Long-term Intervention with Pravastatin in Ischaemic Disease [LIPID] studies)[11-14] primarily included men, this study also sought to explore the effect of gender on medication compliance and achievement of LDL-C goals. Therefore, the primary objective of this study was to describe medication compliance rates and dyslipidemia control in a patient population receiving simvastatin or atorvastatin (statins) in a unique staff-model HMO. The secondary objective of this study was to measure the effect of gender and statin regimen on the success rate of dylipidemia control and medication compliance.

Methods

A retrospective chart review was conducted in an outpatient clinic during a 12-month study period (December 1998 through December 1999). Patients receiving monotherapy with

a statin for cholesterol reduction were identified through the pharmacy claims database for study inclusion. Medical charts of any patient who had a prescription filled for simvastatin or atorvastatin were then reviewed to collect demographic and laboratory data, including age, gender, race, and presence of cardiac risk factors (hypertension, diabetes, smoking, family history, and cholesterol levels). LDL-C was used as the measure of dylipidemia control, consistent with the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) II guidelines.[28] The LDL-C concentration was considered to be representative of the individual's overall control. High-density lipoprotein cholesterol (HDL-C) was used to assess cardiovascular risk since HDL-C < 35 mg/dL is a cardiovascular risk factor based on the NCEP ATP II guidelines, independent of LDL-C. Each patient's last-recorded LDL-C concentration as well as the HLDL-C concentration was used to determine the LDL goal under NCEP ATP II guidelines. Patients were excluded if they (1) did not have an LDL-C and an HDL-C concentration obtained in 1999, (2) did not have a statin prescription filled at least twice during the study period, (3) discontinued statin therapy, or (4) were receiving a statin other than simvastatin or atorvastatin.

Data collected from chart review was imported into a database for analysis. The pharmacy claims database was used to perform medication utilization analysis and included medication name, medication strength, quantity dispensed, day's supply, refill data, number of prescriptions filled per patient, and acquisition cost for each patient. Information from the chart review and pharmacy claims database was merged for final analysis.

The medication possession ratio (MPR) was used to measure patient medication compliance.[29,30]

$$MPR = \frac{\text{number of days supply of medication received by patient}}{\text{number of days supply of medication required for continuous treatment}}$$

This ratio (range 0.0-1.1) has been validated in several studies and provides numerical inference to therapy adherence.[29,30] The generally accepted cut-off point for "poor compliance" is an MPR lower than 0.8, whereas "good compliance" is defined as an MPR of 0.8 to 1.1, and an MPR greater than 1.1 is considered to be the result of excessive medication fills.[30] LDL-C goals and risk factors for patients were determined as per recommendations for that time period set forth in NCEP.[28] Patients were considered to be controlled and at LDL-C goal if their LDL-C concentration was less than or equal to their individual goal based on risk factors.

Statistical analysis: Differences in medication compliance (based on MPR) between men and women were analyzed using the Student's t test. The Pearson chi-square test was used to detect the effect of gender and type of statin on the attainment of goal LDL-C. Significance was set at a P value < 0.05. Statistical analyses were performed using SPSS version 11.0.

Results

A total of 963 patients were identified in the pharmacy claims

database for initial review. One hundred forty-four were excluded (15.0%, Table 1), resulting in 819 patients who met the criteria for study inclusion. Patient demographic data are shown in Table 2. The mean age of patients was similar for men and women, at 66.5 years (range 19-90) and 68.7 (range 36-97), respectively, with an overall mean age of 68.5 years. The study population was 60.8% white, 6.3% Hispanic, 1.5% African American, and 0.1% Asian. Ethnicity was not documented for 31.2% of the patients. Simvastatin was the preferred formulary drug at the time of this study and was prescribed to 91% of the study population, with atorvastatin making up the remaining 9%. Twenty-six percent of patients were diagnosed with CHD and 74% had CHD risk factors. The most common risk factor identified was age/gender (Figure 1).

Overall, 76.9% of the study population demonstrated "good medication compliance" as defined by an MPR between 0.8 and 1.1. Fifteen percent of the study group had a calculated MPR lower than 0.79, indicating "poor" compliance, and 8% had a calculated MPR greater than 1.1, indicating "excessive compliance" (Table 3). The mean MPR for the entire study group was 0.96 ± 0.23. A significant difference was not detected in medication compliance between men and women (mean MPR = 0.97 ± 0.23 versus 0.96 ± 0.22, respectively; $P = 0.76$).

The mean LDL-C concentration for the study population was 114 ± 32.1, with a mean of 113 ± 30.7 for males and 115 ± 33.9 for females. The majority of patients (70%) were at their NCEP-directed LDL-C goal (Table 4). Forty-three percent of women and 44% of men with an NCEP-directed LDL-C goal of <100 mg/dL reached their therapeutic goal. Sixty-six percent of women and 72% of men with an NCEP-directed LDL-C goal of <130 mg/dL reached their therapeutic goal, and 91.5% of women and 90% of men with an NCEP-directed LDL-C goal of <160 mg/dL reached their therapeutic goal (Table 5).

There was not a statistically significant difference between the 2 statin groups in the success rate in achieving LDL-C goal; 70% of patients receiving atorvastatin and 69.6% of patients receiving simvastatin achieved their LDL-C goal. There was not a statistically significant effect of gender on success rate, with 73% of women and 67% of men achieving their NCEP-directed LDL-C goal ($P = 0.06$) (Table 5).

Discussion

This retrospective analysis demonstrated that patients receiving care at a unique staff-model HMO medical practice had high statin compliance, with a mean MPR of 0.96. Additionally, the majority of patients (70%) achieved their NCEP-directed LDL-C goal. There was an apparent but not statistically significant higher LDL-C success rate for women.

The rates of dyslipidemia control in this study were much higher than those previously published in the literature.[19,20] The Lipid Treatment Assessment Project (L-TAP) reported that only 38% of patients treated with lipid-lowering agents reached their

TABLE 1 Reasons for Exclusion From the Study

| Exclusion Criteria	N* (%)
Did not have an LDL-C concentration obtained in 1999	20 (2.1)
Did not have a statin prescription filled at least twice during the study period	42 (4.4)
Discontinued statin therapy	51 (5.3)
Received a statin other than simvastatin or atorvastatin	31 (3.2)
Total excluded	144 (15)

N is the total number of patients excluded; (%) is the percentage of the initial study population (N=963) initially identified from pharmacy claims as having received a statin drug. LDL-C=low-density lipoprotein cholesterol.

TABLE 2 Characteristics of the Study Group

	Atorvastatin N* (%)	Simvastatin N* (%)	Total N* (%)
Gender			
Male	40 (54)	414 (56)	454 (55)
Female	34 (46)	331 (44)	365 (45)
Total	74 (9)	745 (91)	819 (100)
Treatment			
Primary prevention	54 (73)	552 (74)	606 (74)
Secondary prevention	20 (27)	193 (26)	213 (26)
Total	74 (9)	745 (91)	819 (100)
Average dose (mg/day)	16.9	18.6	
Average days of drug therapy	274.0	295.9	293.7

N is the total number of patients in each subgroup.

FIGURE 1 National Cholesterol Education Program Risk Factors Other Than Low-Density Lipoprotein Cholesterol of Patient Population[28]
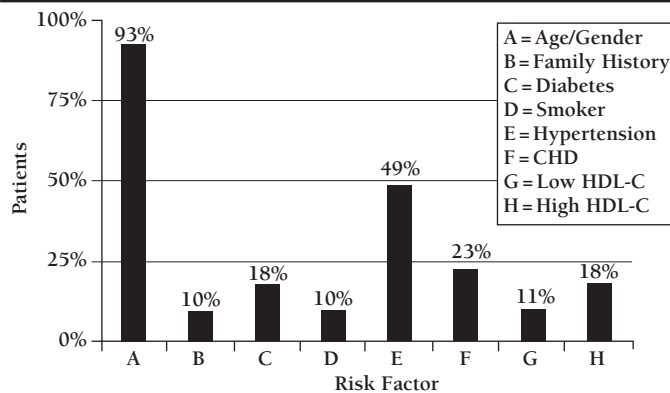
Definitions of Risk Factors[28]
Positive Risk Factors:
Age: men ≥45 years; women ≥55 years or premature menopause without estrogen replacement.
Family history: premature coronary heart disease (CHD) (myocardial infarction or sudden death before the age of 55 years in father or male first-degree relative or before the age of 65 years in mother or other female first-degree relative).
Hypertension: 140/90 mm Hg (confirmed on several occasions) or antihypertensive medication.
Low high-density lipoprotein cholesterol (HDL-C): <35 mg/dL.
Negative Risk Factor:
High high-density lipoprotein cholesterol (HDL-C): ≥60 mg/dL.

TABLE 3 Relationship of Gender to Medication Compliance as Measured by the Medication Possession Ratio (MPR)[30]

Compliance Category	MPR Value Range	Male %	Female %	Total %
Poor	0.1-0.79	8.3	6.7	15.0
Good	0.8-1.1	43.2	33.7	76.9
Excessive	Greater than 1.1	4.8	3.3	8.1

TABLE 4 Actual Mean LDL-C Concentration Based on NCEP-Directed LDL-C Goal

LDL-C Goal (mg/dL)	Male Mean LDL-C Concentration (N)	Female Mean LDL-C Concentration (N)	Male and Female Mean LDL-C Concentration (N)	Standard Deviation ±
<100	105 (158)	109 (55)	106 (213)	32.1
<130	113 (170)	117 (157)	115 (327)	33.0
<160	123 (126)	116 (153)	119 (279)	31.0

Data are presented as the mean LDL-C concentration for each LDL-C goal subgroup; N is the total number of patients in each subgroup.
LDL-C = low-density lipoprotein cholesterol.

TABLE 5 Success of Achieving NCEP-Directed LDL-C Goal Based on Lipid-Lowering Agent and Gender

LDL-C Goal (mg/dL)	Lipid-Lowering Agent	Male % (N)	Female % (N)	Total % (N)	P Value*
<100	Atorvastatin	42.9 (6/14)	16.7 (1/6)	35.0 (7/20)	0.26
<100	Simvastatin	43.7 (63/144)	44.9 (22/49)	44.0 (85/193)	0.88
<100	Total	43.7 (69/158)	42.8 (23/55)	43.2 (92/213)	0.81
<130	Atorvastatin	80.0 (12/15)	73.3 (11/15)	76.7 (23/30)	0.67
<130	Simvastatin	71.0 (110/155)	65.4 (93/142)	68.3 (203/297)	0.31
<130	Total	71.8 (122/170)	66.2 (104/157)	69.1 (226/327)	0.28
<160	Atorvastatin	90.9 (10/11)	92.3 (12/13)	91.7 (22/24)	0.90
<160	Simvastatin	89.6 (103/115)	91.4 (128/140)	90.6 (231/255)	0.61
<160	Total	89.7 (113/126)	91.5 (140/153)	90.7 (253/279)	0.60

Data are presented as the percentage of patients achieving goal; N is the number of patients reaching LDL-C goal/total number of patients in each subgroup.
* P value for the comparison of males and females reaching their LDL-C goal.
LDL-C = low-density lipoprotein cholesterol.

LDL-C goal. Success rates were particularly low in patients with CHD (18%).[19] Similar findings were demonstrated in a smaller retrospective analysis in which only 33% patients were found to be at their LDL-C goal.[20]

The rates of compliance in this study were also much higher than those previously published in the literature. For example, in a study of 29,534 managed care members receiving statin therapy, only 46% were still taking a statin at the end of the 2-year study period.[31] Abughosh et al. demonstrated low persistence rates (57% discontinuation at 18 months) with statins among older patients regardless of drug benefit plans.[32] Studies that specifically assessed MPR rates for statin use have also demonstrated lower real-world adherence than what was seen in this study. White et al. found a mean statin MPR of 0.84 for patients enrolled in a large HMO.[33] When patients have poor medication compliance, the benefits from drug therapy are limited and can potentially result in poor health outcomes and a financial burden to the patient and health care system.

Many factors influence patient compliance, including (1) health condition(s) of the patient, (2) complex drug regimens, (3) patient perceptions, and (4) patient-provider relationship.[25] Patients who have a good relationship with their health care provider tend to be more compliant with their medications and management. Both low patient satisfaction with their physician and frequent breaking of physician appointments have been correlated with decreased adherence to lipid-lowering therapy.[26,27] Conversely, patients' perception of the time spent by the physician explaining cholesterol management has been associated with higher compliance to treatment.[26]

The staff-model HMO described in this study allowed patients to receive comprehensive medical care at one location and thereby made possible a long-term patient-provider relationship. Based on the history of promoting long-term patient-provider relationships at this study site, we speculate that the unique practice model was a contributing factor to the high statin medication compliance rate described in this study. However, it is also possible that compliance was higher secondary to the fact that the study population was older and likely taking more medications than the study populations previously reported in the literature. According to a study by Grant et al., compliance improved in patients taking more medications.[34] In addition, a study by Valuck et al. also evaluated an older patient population, and results demonstrated an 85% to 89% compliance rate.[35] It follows that high adherence to treatment was likely a major contributing factor in achieving LDL-C goals, but the reasons for compliance may warrant further investigation.

A second factor that may have contributed to treatment success in this population was the primary use of high-potency statins. These results are similar to LDL-C success rates reported by Andrews et al., who demonstrated that more patients on atorvastatin and simvastatin achieved NECP-directed LDL-C concentrations than patients receiving lovastatin, pravastatin, or fluvastatin.[36]

Landmark trials (i.e. 4S, WOSCOPS, CARE, and LIPID studies)[11-14] primarily evaluated the dyslipidemia control in men, with fewer than 20% of women represented.[11-14] Since 44% of the population in the present study was female, the effect of

gender on success rates of attaining cholesterol goals and effect of gender on rates of compliance could be evaluated. Although more females achieved their LDL-C goals than males, this difference was not statistically significant. In terms of compliance, both men and women had similar compliance rates. This is in contrast with a previously reported study by Schultz et al., which demonstrated that, compared with women, men were more likely to be compliant with statins and achieve cholesterol goals.[37] Additional research is needed to further clarify the influence of gender on dyslipidemia control.

Limitations

There are several limitations to this study that should be mentioned. First, we excluded 42 patients (4.4% of the original sample) who did not have at least 2 pharmacy claims for either of the statin drugs, and we excluded 51 patients (5.3%) who discontinued statin therapy during the study period, Therefore, we excluded 9.7% of the patients on statin therapy who would have otherwise been defined as noncompliant with statin therapy.

Second, while using pharmacy claims and calculating MPR is a common practice to assess medication compliance, it is a proxy measure and only provides an estimate of compliance. Interestingly, 8% of the study group demonstrated an MPR of greater than 1.1. This MPR value could represent excessive utilization (i.e., patients filled their prescription early) or represent appropriate utilization following a verbal change in dose that was not reflected in the pharmacy claims database (i.e., physician verbally instructed the patient to increase the dose from 1 tablet to 2 tablets daily). However, because medication compliance was based on pharmacy claims data, definitive utilization is unknown. In addition, even though patients received an average 294 days of therapy during the study period, persistence with therapy was not measured because of the difficulty of tracking the population secondary to demise or patients leaving Colorado for the winter months. As a result, it is not known how many patients remained on statin therapy at the end of the study period.

Third, this study was designed based on the NCEP ATP II guidelines. Since the inception of the study design, data collection, and analysis of this report, the NCEP ATP III guidelines have been published. Consequently, generalization of these results to current practice is limited. However, when our results are compared with other studies that used the NCEP ATP II guidelines as the practice standard, the results continue to illustrate a high rate of compliance and control, suggesting that further study using the NCEP ATP III guidelines is warranted. There would be some reduction in LDL-C success rate if the ATP III guidelines were applied to our population. In fact, Quilliam et al. assessed the impact of replacing the NCEP ATP II guidelines with the NCEP ATP III recommendations and demonstrated that, while 59.8% of the study population was at the LDL-C goal based on the NCEP ATP II criteria, only 53% were at their LDL-C goal with the application of the current NCEP ATP III

recommendations.[38] Nevertheless, since the average LDL-C concentration was 115 mg/dL for this study population, it is likely that most patients would still be at their LDL-C goal based on the current guidelines.

Fourth, while 77% of patients were at or below their LDL-C goal under ATP II guidelines, the rate of goal attainment was lower (43.2%) for patients with the lowest LDL-C goal (< 100 mg/dL) versus patients (69.1%) with a higher LDL-C goal (< 130 mg/dL).

Fifth, this patient population was older and had higher rates of CHD than previously reported studies examining LDL-C reduction. Therefore, it is not known if responses of a younger patient population with a lower degree of CHD managed in this setting would be similar to the patient population studied.

Sixth, although the majority of our patients had the same primary care physician and pharmacist for many years, patient-provider satisfaction was not explicitly measured.

Seventh, although utilization of other prescription cholesterol-reducing agents was controlled for through the database claims inclusion and exclusion process, use of over-the-counter niacin or other supplements was not. Concomitant use of these products with a statin could have skewed the results by decreasing LDL-C concentrations to a greater extent than with simvastatin or atorvastatin monotherapy. In addition, we used only the patient's last recorded LDL-C concentration as representative of the individual's overall control. Lastly, this analysis was not designed to evaluate the reduction of cardiovascular events, which is the ultimate goal of LDL-C reduction.

■ Conclusions

Patients who received care in a unique staff-model HMO medical clinic exhibited high treatment adherence and dyslipidemia control rates (based on NCEP ATP II guidelines). Gender was not a factor in medication compliance or attainment of LDL-C goal. Additional studies are needed using ATP III guidelines and to determine if long-term patient-provider relationships positively affect treatment adherence.

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