Follow-Up in a Lipid Clinic Improves the Management of Risk Factors in Cardiovascular Disease Patients

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Abstract

Background: The implementation of treatment guidelines is lacking worldwide.

Objectives: To examine whether follow-up in a specialized lipid clinic improves the achievement rate of the treatment guidelines, as formulated by the National Cholesterol Education Program and the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

Methods: The study group included patients who were referred to the lipid clinic because of hyperlipidemia. At each of five visits over a 12 month period, lipid levels, liver and creatine kinase levels, body mass index, and adherence to diet and medications were measured, and achievement of the NCEP target level was assessed.

Results: A total of 1,133 patients (mean age 61.3 years, 60% males) were studied. Additional risk factors for atherosclerosis included hypertension (41%), type II diabetes mellitus (21%), smoking (17%), and a positive family history of coronary artery disease (32%). All patients had evidence of atherosclerotic vascular disease (coronary, cerebrovascular or peripheral vascular diseases). The low density lipoprotein target of < 100 mg was present in only 22% of patients before enrollment, with improvement of up to 57% after the follow-up period. During follow-up, blood pressure control was improved (from 38% at the time of referral to 88% after 12 months, $P < 0.001$), as was glycemic control in diabetic patients (HgA1C improved from 8.2% to 7.1% after 12 months, $P < 0.001$). Improved risk factor control was due to increased compliance to medication treatment (from 66% at enrollment to more than 90% after 12 months), as well as careful attention to risk factor management that translated into a change in the treatment profile during the follow-up. There was an increase in the use of the following medications: aspirin from 68% to 96%, statins from 42% to 88%, beta blockers from 20% to 40%, and angiotensin-converting enzyme inhibitors from 28% to 42%; while calcium channel blocker use decreased from 40% to 30% in patients during follow-up.

Conclusion: Follow-up of patients in a specialized clinic enhances the achievement of LDL-cholesterol treatment goals as well as other risk factor treatment goals, due to increased patient compliance and increased use of medications.

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Atherosclerotic vascular disease and its sequelae still remain the number one cause of death in the western world. In the United States alone, there are 900,000 new cases of acute myocardial infarction annually, and the death rate from coronary artery disease is 225,000 per year [1]. Numerous studies have searched for ways to reduce the number of vascular events [2–4] and, based on these studies, the new National Cholesterol Education Program guidelines were updated in 2001 [5]. While the benefits of cardiovascular disease prevention have been proven many times, adherence to the NCEP guidelines for primary as well as secondary prevention is far from desirable [6–11].

Schectman and Hiatt [6] studied the rate of low density lipoprotein-cholesterol target goal achievement in a specialized lipid clinic and found that only 55% of their patients managed to reach the NCEP target LDL after adhering to the guidelines for primary and secondary prevention. The authors also found that several factors contributed to the success rate in treating hyperlipidemia, such as high baseline LDL and triglyceride levels (both are predictors of failure) and combination of hyperlipidemia medications. In another study, Marcelino and Feingold [7] reported that only 33% of patients on statin monotherapy reached target LDL-C goals; most of the patients did not receive appropriate doses of statins. The HERS (Heart and Estrogen/Progestin Replacement Study) research group [8] published data regarding adherence to the NCEP goals in post-menopausal women with coronary artery disease across the United States. They found that 53% of the women were not receiving any hypolipidemic medication and that 91% of all the volunteers enrolled in the study did not reach the LDL target level recommendation of < 100 mg/dl [8]. The L-TAP study [9] also surveyed the success rate of achieving LDL target goals among patients treated in general practice and in family and internal medicine clinics. Among the patients surveyed, only 18% of the patients in need of secondary prevention reached the LDL target goal of < 100 mg/dl.

The reasons for this problem are complex. All researchers state that patient compliance is a major factor in reaching target levels. Schectman and Hiatt [6] and the investigators in the L-TAP study state that adherence to a low fat diet is a good marker for patient compliance, though it is not the only factor. Undoubtedly, a close physician-patient relationship or a multidisciplinary approach can also improve patient compliance. Another factor that has major impact on the ability to reach treatment target levels is the physicians' follow-up of their patients' lipid levels. In 1999, Sueta et al. [10] published data from the Quality Assurance Program, a nationwide U.S. endeavor to treat patients suffering from coronary heart disease. These researchers found that 44% of the patients with ischemic heart disease did not have even one LDL measurement noted in their clinic chart. Of the patients who did have LDL measured, only 25% had LDL levels < 100 mg/dl, and of the patients

NCEP = National Cholesterol Education Program
LDL = low density lipoprotein

receiving statins 65% had not had the dose adjusted since the beginning of the treatment.

The need for solutions to this worldwide problem is evident. We present our study to examine whether follow-up in a specialized lipid clinic can increase the level of LDL target achievement in patients requiring secondary prevention.

Patients and Methods

Our study group comprised patients with atherosclerotic vascular disease in need of secondary prevention. The patients were referred by general practice clinics from the two major health maintenance organizations in Israel (Maccabi Health Services, Dan district, and Meuhedet Health Services, Jerusalem district) to the central lipid clinic of each HMO, both of which were supervised by the same physician. The reasons for referral were difficulty in achieving lipid control (62%) and at the patients' request (38%). Referrals to the specialized lipid clinics have been in practice since June 1996.

All patients had a full history, risk factor evaluation, as well as lipid profile, liver and kidney function tests at baseline. The patients were followed regularly every 12 weeks, and before each visit were asked to undergo routine blood tests, including complete lipid profile and blood chemistry, and for diabetic patients HbA1C and fasting glucose levels as well. At each visit, the head of the clinic supervised the evaluation and treatment of the risk factors in accordance with the updated guidelines, including lipid levels, blood pressure levels and weight, as well as glucose and HbA1C for diabetics.

Patients were asked to complete a diet diary for the 3 days preceding each visit, which was used to assess dietary compliance. Drug compliance was monitored by comparing the percent of prescribed drugs to the actual percent of drugs taken from the pharmacy. Patients were also reminded by phone to bring all medications and used packages to each visit, when pills were counted.

Table 1. Patients' demographic characteristics

	Male (n=671)	Female (n=462)	Total n=1,133)
Age (range)	60 (42–71)	64 (49–78)	61 (42–78)
Evidence of atherosclerotic vascular disease			
Prior myocardial infarction or angina	308 (46%)	220 (48%)	528 (47%)
Angiographic evidence	200 (30%)	42 (9%)	242 (21%)
Peripheral vascular disease	60 (9%)	50 (11%)	110 (10%)
Stroke/transient ischemic attack	90 (13%)	130 (28%)	220 (19%)
Type of dyslipidemia at referral			
Hypercholesterolemia*	154 (23%)	92 (20%)	246 (22%)
Hypertriglyceridemia**	121 (18%)	107 (23%)	228 (20%)
Combined dyslipidemia***	396 (59%)	263 (57%)	659 (58%)
Distribution of risk factors			
Hypertension	240 (36%)	222 (48%)	462 (41%)
Obesity (BMI > 26)	196 (29%)	200 (43%)	396 (35%)
Diabetes mellitus type II	100 (15%)	142 (31%)	242 (21%)
Positive family history	204 (30%)	160 (35%)	364 (32%)
Smoking history	210 (31%)	208 (45%)	418 (37%)
Current smoker	100 (15%)	98 (21%)	198 (17%)

* Hypercholesterolemia: cholesterol $\geqslant$ 220 mg/dl

** Hypertriglyceridemia: triglycerides $\geqslant$ 200 mg/dl

*** Combined dyslipidemia: triglycerides $\geqslant$ 200 mg/dl + cholesterol $\geqslant$ 220 mg/dl.

BMI = body mass index

Table 2. Achievement of treatment goals during follow-up period

	Visit 1	Visit 3	Visit 5
Treatment goals			
LDL < 100 mg/dl	254 (22%)	362 (32%)	645 (57%)
Controlled blood pressure	176 (38%)	380 (82%)	407 (88%)
HgA1C (%)	8.2 ± 2.0	7.5 ± 1.8	7.1 ± 1.5
Compliance	66%	82%	90%
Lipid levels			
Total cholesterol (mg/d)	252 ± 50	212 ± 55	208 ± 48
Triglycerides (mg/d)	238 ± 70	185 ± 86	165 ± 82
High density lipoprotein cholesterol (mg/dl)	43 ± 14	44 ± 16	45 ± 15
LDL-C (mg/dl)	161 ± 30	124 ± 38	119 ± 36

Results

Between 1996 and 1999, a total of 1,133 patients (671 males and 462 females, with a mean age of 61, range 42–78 years) were followed for one year (five office visits). The expression of the atherosclerotic vascular disease is specified in Table 1. All patients suffered from hyperlipidemia, and 58% of the patients had combined dyslipidemia (a total cholesterol level > 220 mg/dl and triglyceride level > 200 mg/dl). The type of dyslipidemia at referral is specified in Table 1. Most of the patients had additional risk factors, hypertension being the most prevalent (42%). Females were more obese and had more type II diabetes mellitus (32% as compared to 15% of males). The distribution of risk factors is shown in Table 1.

During the follow-up period there was a marked improvement in the number of patients who had achieved the LDL target goal of < 100 mg/dl (57% as compared to 22% at the beginning of the study) [Table 2]. This improvement was due to an increase in the number of patients receiving hypolipidemic medication and to more aggressive hypolipidemic treatments. The percentage of patients receiving statins increased twofold from 42% to 88% during the follow-up period [Figure 1]. The combination of hypolipidemic medications was also used more often: the frequency of statin and resin combination therapy increased from 3% to 21% after one year of follow-up and the combination of a statin and a fibrate increased from 0 to 10% [Figure 1].

The type of statin used at the beginning of the follow-up was subject to clinical judgment. Patients who did not reach the LDL target goal using one statin were either switched to a more potent statin or had their statin dose increased, again according to clinical discretion. During follow-up, patients who had achieved the NCEP goal for LDL-C levels (< 100 mg/dl) had usually been given higher doses of statins. For patients with resistant hypercholesterolemia or patients with combined hyperlipidemia, the combination of a statin

HMO = health maintenance organization

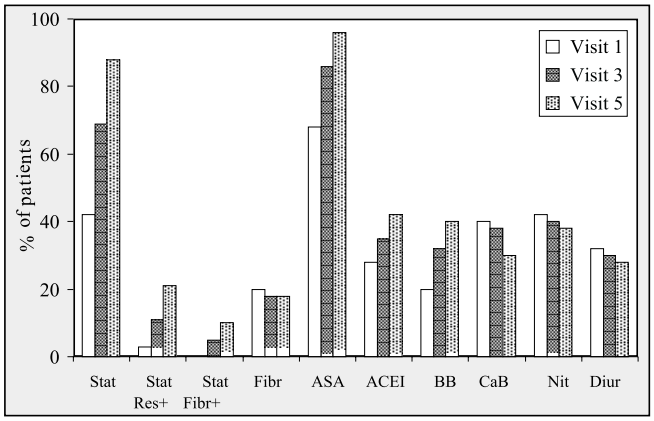

Figure 1. Percent of patients treated with medications. There was a marked increase in the percent of patients treated with statins (either as single drug or in combination), as well as an increase in the use of aspirin, ACE inhibitors and beta-blockers.
Stat = statin, Fibr = fibrate, Res = resin, ASA = aspirin, ACEI = ACE inhibitor, BB = beta-blocker, CaB = calcium channel blocker, Nit = nitrates, Diur = diuretics.

Table 3. Hypolipidemic treatment in relation to target LDL levels

Treatment	Visit 1		Visit 5	
	Goal achieved		Goal achieved	
	No. (%)	No. (%)	No. (%)	No. (%)
Fluvastatin				
20 mg	22 (2)	0	20 (2)	15 (75)
40 mg	20 (2)	1 (5)	26 (2)	21 (81)
Pravastatin				
10 mg	102 (9)	2 (2)	10 (1)	5 (50)
20 mg	80 (7)	10 (12)	192 (17)	60 (31)
40 mg	62 (5)	32 (52)	146 (13)	99 (68)
Simvastatin				
10 mg	110 (10)	28 (25)	246 (22)	79 (32)
20 mg	36 (3)	16 (45)	132 (12)	74 (56)
40 mg	30 (3)	25 (83)	88 (8)	60 (68)
Combination				
Statin + resin	33 (3)	25 (76)	131 (12)	126 (96)
Statin + fibrate	0	–	110 (10)	106 (96)
No treatment	638 (56)	115 (18)	32 (3)	0
Total	**1,133**	**254 (22.4)**	**1133**	**645 (56.9)**

with either a resin or a fibrate had a high rate of success in achieving LDL target levels [Table 3]. Other statins like atorvastatin and cerivastatin were not used and therefore were not included in the table.

During the follow-up period, careful attention was paid to controlling other risk factors. Among the hypertensive patients, blood pressure was poorly controlled at the beginning of the follow-up (only 38% of patients with hypertension had blood pressure levels < 140/85 mmHg). This percentage increased to 88% after one year of follow-up [Table 2]. The improvement was achieved by adjusting the anti-hypertensive medications and changing the treatment profile of the patients [Table 2]. Patients received angiotensin-converting enzyme inhibitors and beta-blockers more frequently and at higher doses than at the beginning of the study [Figure 1]. Glucose control also improved, and HbA1C levels decreased from 8.2% at the beginning of the study to 7.1% after one year of follow-up. Although body mass index did not change significantly (27.6 $\pm$ 10.0 at baseline and 27.2 $\pm$ 8.2 after 5 visits), better adherence to a low fat, low carbohydrate diet was achieved, as well as increased compliance to the medication protocol [Table 2].

During the follow-up we encountered very few side effects. Twenty-six patients (2.3%) had mild creatine kinase elevation (less than threefold above normal limits), while only 7 (0.6%) had CK levels more than threefold above the normal limits needed for the discontinuation of treatment. Two patients from the group that stopped the treatment were given a combination of statin and fibrate (2% of the combination treated patients). None of our patients had liver function tests more than twofold the normal limits.

Discussion

Reduction of LDL has become a mainstay in the treatment strategy of patients with ischemic heart disease. Although the new NCEP guidelines have proven to be highly beneficial in reducing the morbidity and mortality from this disease, failure to implement these guidelines is one of the major downfalls in the treatment of cardiovascular conditions today [6–11].

Similar evidence is emerging concerning other risk factors. The UKPDS (UK Prospective Diabetes Study) showed that the ability to achieve blood pressure control is crucial in secondary prevention among patients with diabetes. The UKPDS research group also showed that treating type II diabetes mellitus with a single medication has a low probability of achieving glucose control [12], and that most patients with diabetes mellitus do not have adequate risk factor control. The EUROASPIRE II study demonstrated that blood pressure control was poor and that the population had gained weight as compared to previous years [13].

The reasons for this problem are complex, and include low patient compliance, physician unawareness of the new guidelines, inadequate follow-up of risk factor status, and resistance to medical treatment. Taken together, the above reasons result in a low rate (less than 20%) of patients who reach the target goals for lipid control [8]. However, the contribution of each of the above factors to this lack of success is not clear.

Recently, we presented our findings on the reasons for lack of implementation of the NCEP guidelines among family practitioners [14]. Despite the small number of patients who reached the LDL target goals, physicians stated that most patients did not need further medical treatment. Eighty percent of the physicians included in the survey were fully aware of the NCEP guidelines, and the remaining 19% were partially aware of the recommendations.

Shaffer and Wexler [15] attempted to resolve this issue in a multidisciplinary, goal-oriented and collaborative study that involved a clinical nurse, physiologist and social workers. Although

CK = creatine kinase

their study was based on the NCEP 1 guidelines from 1988, their results can still be considered valid. They found that by using this multidisciplinary approach, they were able to increase the rate of target LDL level achievement to more than 44%, as compared to only 11% of the patients treated by the general practitioner.

In our study, we investigated the efficacy of following cardiovascular disease patients attending a specialized hyperlipidemia clinic, including an emphasis on multiple risk factor control. We found that a designated clinic emphasizing risk factor control not only can improve the level of lipid control significantly (57% of all patients achieved target LDL-C levels) but exerts a positive impact in other areas as well, such as improved control of blood pressure and HbA1C levels. The success of treatment can be attributed to an increase in compliance (from 66% at enrollment to more than 90% after 12 months). Among our diabetic patients 75% reached the recommended HbA1C levels of < 7% and 62% achieved blood pressure goals.

The treatment profile was changed for better secondary prevention: aspirin use increased from 68 to 96% statins from 42 to 88%, beta-blockers from 20 to 40% and ACE inhibitors from 28 to 42%. Calcium channel-blocker use decreased from 40% to 30%, and nitrate treatment did not change. Better control of blood pressure levels was achieved by increasing the doses of anti-hypertensive medications for each patient and adding more anti-hypertensive medications (45% of the hypertensive patients received three medications as compared to 18% at baseline, $P < 0.01$).

One can ask why only 57% of the patients achieved the recommended LDL-C target levels. There are probably several reasons. Some of our patients have resistant hypercholesterolemia that should be treated with potent drugs and/or a combination of anti-hyperlipidemic medications. Despite the increased use of combination therapy and higher doses of statins, several patients still received low doses of statins even though they did not reach the target levels for LDL-C. Even in our clinic, some patients were reluctant to take higher statin doses because they feared the side effects, and this reluctance affected the physicians. It is also possible that changes in lipid levels were due to inadequate adherence to a low fat diet. Nonetheless, we believe that a specialized lipid and risk factor clinic and a longer follow-up will result in a better outcome in the long run.

Another question to be asked is whether such a clinic is cost-effective. Is it feasible to send all patients with risk factors to a specialized facility? We did not do cost-benefit calculations, so we cannot answer this question as yet. Perhaps this type of follow-up unit can be used in another way: for example, in an advisory capacity working within the HMOs to guide the actual control of risk factors for each patient. With the proper management, this unit could cut costs on specialized clinics by using a computerized feedback evaluation system on each patient, guiding the physician to order the necessary tests and help them to make the adjustments needed to achieve the treatment goals. We think this "Risk-factor Control Unit" should and can guide in multiple risk factor control, since most of the physicians dealing with a specific risk factor (like hyperlipidemia) tend to pay attention to other risk factors as well.

ACE = angiotensin-converting enzyme

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