Is the Treatment of Hyperlipidemia as Secondary Prevention Adequate in Different Age Groups in Israel?

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Key words: hyperlipidemia, secondary prevention, coronary heart disease, elderly

Abstract

Background: Treatment of hyperlipidemia is important for secondary prevention in patients suffering from coronary heart disease. It has been proven that “young elderly” (patients aged 65–75 years) can benefit from the treatment at least as much as younger patients. The question of treatment efficacy in different age groups is especially important when consideration is given to the physiologic as well as social changes that occur around the age of 65.

Objective: To assess the adequacy of treatment as part of secondary prevention in “young elderly” and younger patients.

Methods: In this prospective study, 389 patients discharged from the hospital with the diagnosis of coronary heart disease were divided according to age groups. Data were collected regarding lipid profile examinations, dietary and drug therapy, and results of lipid profiles.

Results: Less than one-third of patients achieved target low density lipoprotein levels. More patients in the older age group achieved the treatment goals. The goals were achieved despite the fact that the percentage of patients treated with lipid-lowering drugs was lower in the older age group.

Conclusion: The percentage of patients treated for hyperlipidemia as part of a secondary prevention plan in Israel is similar to that in other developed countries. The fact that more “young elderly” patients achieve adequate lipid profiles compared to younger patients indicates that there is no age discrimination towards this patient group. The finding that less than one-third of the patients reach the treatment goals should prompt physicians to treat hyperlipidemia more aggressively.

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Atherosclerotic cardiovascular diseases are the leading cause of morbidity and mortality in industrialized countries, with coronary heart disease being the commonest cause of morbidity and mortality in the elderly [1]. Hyperlipidemia is an established major risk factor for vascular diseases. There is no doubt that treatment of hyperlipidemia is an essential intervention in secondary prevention of coronary heart disease [2,3]. Age by itself is a risk factor for CHD morbidity.

The role of hyperlipidemia as a risk factor continues also in the older age group, and several studies have demonstrated the effectiveness of intervention for lipid reduction in primary prevention in these patients [4,5]. Clinical trials demonstrated a decrease of 25–30% in the risk for major coronary events in elderly subjects treated for 5 years in lipid-lowering programs [6]. The guidelines for lipid reduction in secondary prevention are universal for all age groups (diabetic patients should be treated as patients with established CHD according to the National Cholesterol Education Program III guidelines) [7].

The purposes of this study were to assess the quality of lipid-lowering interventions in patients with ischemic heart disease and to determine if there are differences in the attitude of patients and their caregivers between “young elderly” (age range 65–74) and younger patients. Therefore we compared the plasma lipid concentrations at least 6 months after the latest coronary event as an outcome parameter, and lifestyle as well as hypolipidemic drugs consumption as process parameters.

Patients and Methods

A historical prospective study was conducted in 389 patients who were discharged from Meir General Hospital, Kfar Saba, Israel, with the diagnosis of coronary heart disease during a 6 month period. Meir General Hospital is a 700 bed regional hospital serving a population of 500,000. The diagnosis of CHD was established according to one of the following three criteria: a) patients discharged after acute myocardial infarction, b) patients after coronary artery bypass surgery, and c) patients with both angina and angiographic findings of coronary disease. All patients included in the study were functionally independent and had no evident malignancy or other chronic diseases that may shorten life expectancy.

The subjects were divided according to their age into two groups: younger than 65 years old and those aged 65–75. The younger group comprised 216 subjects (176 males and 40 females) and the older group 173 subjects (111 males and 62 females). For each subject the following data were collected:

- Duration of ischemic heart disease
- Co-morbidity (other established diagnoses of the patient)
- Functional status in basic activities of living
- Lipid profile during the study period. Since for many patients baseline lipid profile was not available, and the aim of our study was to measure the treatment outcome, baseline lipid profile was not a prerequisite for inclusion in the study (in the cases that lipid profile was not obtained after discharge the physicians were encouraged to measure the patient's current lipid profile.)
- Dietary consultation
- Pharmacologic treatment for hyperlipidemia
- Important lifestyle variables of the patient including smoking habits.

CHD = coronary heart disease
All the parameters were analyzed for statistical significance using SPSS for Windows software.

**Results**

The 369 subjects examined in the survey were predominantly males. The pertinent demographic details of study population are summarized in Table 1.

A significantly higher proportion of males (81% vs. 64%), smokers (20.6% vs. 5.2%) and a trend to receive lipid-lowering drug treatment (64% vs. 55%) was found in patients from the younger age group. The majority of the study patients were treated for hyperlipidemia: 54.7% of the subjects were treated with various statins (simvastatin, pravastatin) in different range of doses, 3.4% were treated with fibrates (bezafibrate) and 1.8% with a combination of statins and fibrates. While the percentage of patients in the elderly group who received drug therapy was smaller than in the younger population, their lipoprotein profile was more favorable (Table 2). The percentage of women increased with age, a well-recognized phenomenon, reflecting the higher rate of increase in CHD with aging in women. Total cholesterol, LDL cholesterol and triglyceride levels were higher in women than in men ($P < 0.0001$); this difference may reflect a “gender discrimination” in the treatment.

Table 2 summarizes the plasma lipid concentration according to the treatment type and age group. The total cholesterol concentration was significantly lower in the older age group, where its mean value reached the recommended levels in both treatment modalities. LDL plasma cholesterol concentration reached a significant lower mean in the older age group only in the drug-treated group. There were no significant differences with age in the mean concentrations of high density lipoproteins and triglycerides. The subjects maintaining a diet had lower triglyceride plasma concentrations only in the older age group. The mean lipid concentrations were about 20–30% above the recommended levels but were similar in all age groups and treatment modalities, reflecting uniformity in goal determination by their physicians.

Two-thirds of the patients received drug therapy, but only 25.7% and 31.2% in the older and younger age groups respectively reached the treatment goals of LDL <100 mg/dl according to the NCEP guidelines.

**Discussion**

Lipid lowering is one of the main strategies in secondary prevention of ischemic cardiovascular diseases. This study represents the treatment of hyperlipidemia as a secondary prevention measure in Israel. We found that the young elderly (65–74 years) age group reached significantly lower plasma LDL and total cholesterol plasma concentrations than the younger age group. The average LDL plasma concentration following 6 months of intervention was about 20% above the recommended target levels in both age groups. Most of the subjects had good compliance with the recommendations. In less than a third of the patients lipid concentrations were kept below the recommended levels: LDL 100 mg/dl (7). Although the success of the treatment described in our study is far from satisfactory, it is better than those of another survey conducted in the United States (8) where, in a similar cohort of 622 patients, only 37% received lipid-lowering agents. A descriptive study performed in Canada on 4,315 subjects demonstrated similar results (9,10). As can be seen in Table 2, both treatment modalities of dietary consultation alone and diet with pharmacologic lipid-lowering agents resulted in almost the same outcomes of LDL, HDL, and total cholesterol plasma concentration. It is assumed that patients treated with lipid-lowering agents did not respond sufficiently to dietary consultation. Both treatment modalities achieved the same lipids levels. Dietary treatment is more beneficial in reducing triglycerides than the combination of diet and lipid-lowering agents, and the patients receiving the combination treatment may demonstrate different as well as more severe hyperlipidemia. Therefore, the outcomes reflect not only the physicians' recognition of the importance of lipid lowering in secondary prevention in the regional medical community, but also the cooperation of their patients.

We observed a trend for the severity of risk factors to de-

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**Table 1. Study population**

<table>
<thead>
<tr>
<th></th>
<th>Younger age group (n=216)</th>
<th>&quot;Young elderly&quot; age group (n=173)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: mean and range</td>
<td>55.29 (20–66)</td>
<td>71.1 (65–75)</td>
</tr>
<tr>
<td>Women (%)*</td>
<td>40 (18.5%)</td>
<td>62 (36.0%)</td>
</tr>
<tr>
<td>Men (%)*</td>
<td>176 (81.5%)</td>
<td>111 (64.0%)</td>
</tr>
<tr>
<td>Smoking*</td>
<td>45 (20.6%)</td>
<td>9 (5.2%)</td>
</tr>
<tr>
<td>Maintaining diet</td>
<td>144 (66.7%)</td>
<td>126 (72.8%)</td>
</tr>
<tr>
<td>Combined diet and drug treatment</td>
<td>136 (63%)</td>
<td>96 (55.5%)</td>
</tr>
</tbody>
</table>

* $P < 0.001$

**Table 2. Lipid concentration according to treatment group and treatment modality**

<table>
<thead>
<tr>
<th></th>
<th>35–44 yrs</th>
<th>45–64 yrs</th>
<th>55–64 yrs</th>
<th>65–74 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>269 ± 133</td>
<td>219 ± 47</td>
<td>213 ± 35</td>
<td>197 ± 31</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>Diet only</td>
<td>Diet &amp; drugs</td>
<td>NR</td>
<td>209 ± 128</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>134 ± 33</td>
<td>140 ± 32</td>
<td>127 ± 29</td>
<td>121 ± 29</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>Diet only</td>
<td>Diet &amp; drugs</td>
<td>NR</td>
<td>128 ± 31</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>39 ± 9.8</td>
<td>42 ± 11</td>
<td>44 ± 13</td>
<td>44 ± 13.6</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>Diet only</td>
<td>Diet &amp; drugs</td>
<td>NR</td>
<td>46 ± 10.8</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>269 ± 133</td>
<td>217 ± 142</td>
<td>164 ± 91</td>
<td>150 ± 154</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>Diet only</td>
<td>Diet &amp; drugs</td>
<td>NR</td>
<td>209 ± 128</td>
</tr>
</tbody>
</table>

* $P < 0.05$ by ANOVA, all variables changed significantly with age in both the "diet only" and the "diet + drug therapy" groups.

NR = not relevant

NCEP = National Cholesterol Education Program

HDL = high density lipoprotein
crease in the older group. The lipid concentrations were lower, and the intervention results of both treatment modalities and the outcome in the older group were better. Lower risk factor levels with aging and more severe risk and disease presentation in the younger age group may explain the difference between the two age groups. The guideline goals for treatment were achieved to a greater extent in the older age group, an observation that may reflect not only the differences in disease severity but also better adherence to treatment in the older patients.

The significant increase in the prevalence of heart diseases with aging has been demonstrated by studies conducted in various population groups [11]. In recent years the benefits of both secondary and primary prevention in the elderly have been proven. In addition, due to the burden of cerebrovascular morbidity in this age group, this approach has gained popularity [11]. In our study group the outcomes of the secondary prevention efforts in women were somewhat weaker than in men. This finding was observed in both age groups. This observation may suggest that a different attitude exists regarding treatment strategies for women, as discussed elsewhere [12]. In a model for the assessment of the benefits of primary and secondary prevention in cardiovascular diseases, among those with CVD the forecasted benefits of lipid-lowering therapy were similar in both the low and high risk group, in contrast to those without CVD where different outcomes of intervention were found in the risk group [13]. We found that less than one-third of the patients reached the treatment goals, despite the fact that almost two-thirds were treated with lipid-lowering drugs. This should prompt physicians to treat their patients more aggressively by both dietary and pharmacologic modalities as well as using effective patient education strategies, in order to optimize their health and well being.

References

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Capsule

**Congenital night blindness**

Congenital night blindness (CNB) occurs when retinal rod photoreceptor cells are inappropriately stimulated so that their sensitivity to dim light is reduced. Three rhodopsin mutants are known to cause CNB in humans, but it has been unclear whether desensitization is caused by constitutive activation of the apoprotein (opsin) or activation of the holoprotein by thermal isomerization of the 11-cis-retinal chromophore to all-trans retinal. In et al resolved this by isolating photoreceptor cells containing each of the three rhodopsin mutants from transgenic frogs, and measuring their photo response before and after incubation with 11-cis-retinal. Intensity response curves and dim flash kinetics showed that all mutants were desensitized initially but recovered wild-type photo responses after incubation with 11-cis-retinal. The addition of 11-cis-retinal would not be expected to have any effect on active rhodopsin, however, it could convert active opsin to inactive rhodopsin. Thus it appears that rhodopsin mutations cause CNB by constitutively activating opsin and not by increasing thermal isomerization of the retinal chromophore. *Nature Neurosci* 2003:10:1038/mn.1070
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