Risk assessment and treatment of dyslipidemia in primary health care

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ABSTRACT

Introduction: The aim was to evaluate the practices of routine management of dyslipidemia performed by general practitioners in a large geographic area.

Metohodology: Patients were identified by three or more plasma cholesterol measurements registered in the electronic laboratory information system (LIS) covering the total geographic area, and the study population was characterised by information from general practitioners' records, and from a questionnaire sent to the patients. Further information on ischaemic heart disease (IHD) was obtained from the National Hospital register, and information on prescriptions on lipid lowering medications from the National Health Service.

Participants: A sample of 1163 subjects, monitored by 134 different general practices.

Results: One third of the patients monitored for dyslipidemia had IHD, and two thirds were monitored as part of primary intervention. Dietary counselling was reported by 76%, and 54% were treated with lipid-lowering medications. The treatment frequency was related to cardiovascular risk, increasing from 25% of those with the lowest risk to 72% of the patients with IHD. The treatment goal was not reached in 74% of the cases, but overall a 20% reduction in plasma cholesterol was achieved.

Conclusions: Subjects monitored for dyslipidemia were relevantly monitored because of IHD or high risk of IHD, and initiated treatment of dyslipidemia was clearly related to the individual assessed risk of IHD. Only a minority reached the treatment goals (<5 mmol/l), and the statin doses used were generally lower than the doses used in clinical trials.

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Ischaemic heart disease is a major cause of death in the western countries implying that effective prevention and treatment of coronary arteriosclerosis is a major issue in public health promotion.

Elevated cholesterol levels are associated with an increased risk of ischaemic heart disease, and large randomised clinical trials have shown that correction of dyslipidemia reduces this risk (1-3) Also the risk of progression of coronary heart disease in patients with already known ischaemic heart disease can be modified by cholesterol lowering (4-6).

In Denmark an increasing number of lipid measurements are registered (7), but it is not known whether the increasing efforts concerning cholesterol-lowering activities are targeted the right subjects, or whether interventions towards lowering cholesterol levels are sufficient. Former studies from other countries have revealed a poor adherence to guidelines on treatment of dyslipidemia, and to the evidence obtained from clinical trials (8, 9).

The majority of lipid measurements are prescribed by general practitioners (7) indicating that a substantial part of the monitoring activities take place in general practices, and primary physicians play an important role in achieving the recommended goals set in guidelines. This study addresses practices of routine management, performed by general practitioners, regarding elevated plasma cholesterol. The survey was carried out one year after a new national guideline, from the Danish Society of General Practicioners (DSAM) (15), based on the European guideline (10) was distributed. Subjects monitored for dyslipidemia were identified by the electronic laboratory information system (LIS), and the aim was to evaluate the treatment of dyslipidemia in the complex routine situation, outside the randomised-controlled trials.

METHODS

IDENTIFICATION OF STUDY POPULATION

The survey was carried out in three municipals (Aarhus, Hørning and Hinnerup), comprising 304,000 inhabitants, served by 134 general practices with 227 general practitioners.

Laboratory testing is a necessity for monitoring dyslipidemia, and blood samples from all the general practitioners (GP) and the hospital departments were analysed at hospital laboratories, where the results were registered and kept for years in the electronic laboratory information system (LIS). Results were stored together with date of blood test, patient identification (civil personal registration number, CPR), and an identification code for the physician or hospital department ordering the blood test. All plasma cholesterol measurements were extracted from LIS from August 1, 1995 until January 31, 2001.

Registration of three or more cholesterol measurements during one year was chosen to identify subjects monitored for dyslipidemia. During a year August 1, 1998-July 31, 1999, 6821 subjects were monitored (**Figure 1**), and in 3332 subjects the three plasma cholesterol measurements were ordered from GPs. A sample of 1200 consecutive subjects were identified for further analysis, and in May 2000, 1163 were alive and resident in the area, and they formed the study population, and were followed by cholesterol measurements in LIS until July 31, 2000. Civil personal registration numbers (CPR) were used to follow patients in LIS and to collect additional information.

INFORMATION FROM GP'S RECORDS

Beside information from LIS further information was obtained from the GPs' records, and after achieving the GPs' permission, as demanded by Danish law, a questionnaire was sent to the patients. Data collection including a reminder took place between May and August 2000. Prior to the study the patient questionnaires and the registration sheets for the GPs were tested in pilot projects. Information from general practitioners' records was obtained partly by the general practitioners and partly by one of the authors (HK).

The following information from the medical records was tabulated for each patient: History of cardiovascular disease (CVD) and family history of ischaemic heart disease (IHD), diagnosis of hypertension and diabetes, smoking status, weight and height. Actual or former treatment of dyslipidemia, lipid levels before treatment, and whether treatment was initiated in general practice, in specialist practice or at the hospital.

PATIENT QUESTIONNAIRES

The patient questionnaires also included family and personal history of CVD, coronary risk factors including hypertension, diabetes mellitus and smoking status, as well as information on height and weight. Patients reported whether they had received dietary counselling, and whether they were treated with lipid-lowering drugs.

The data presented on smoking, height and weight, and data on lipid-lowering diet, originate from patients, as it was difficult to get valid information from GPs' records. Information on lipid-lowering medications, IHD and other risk factors was collected from medical records and if not available from patient questionnaires.

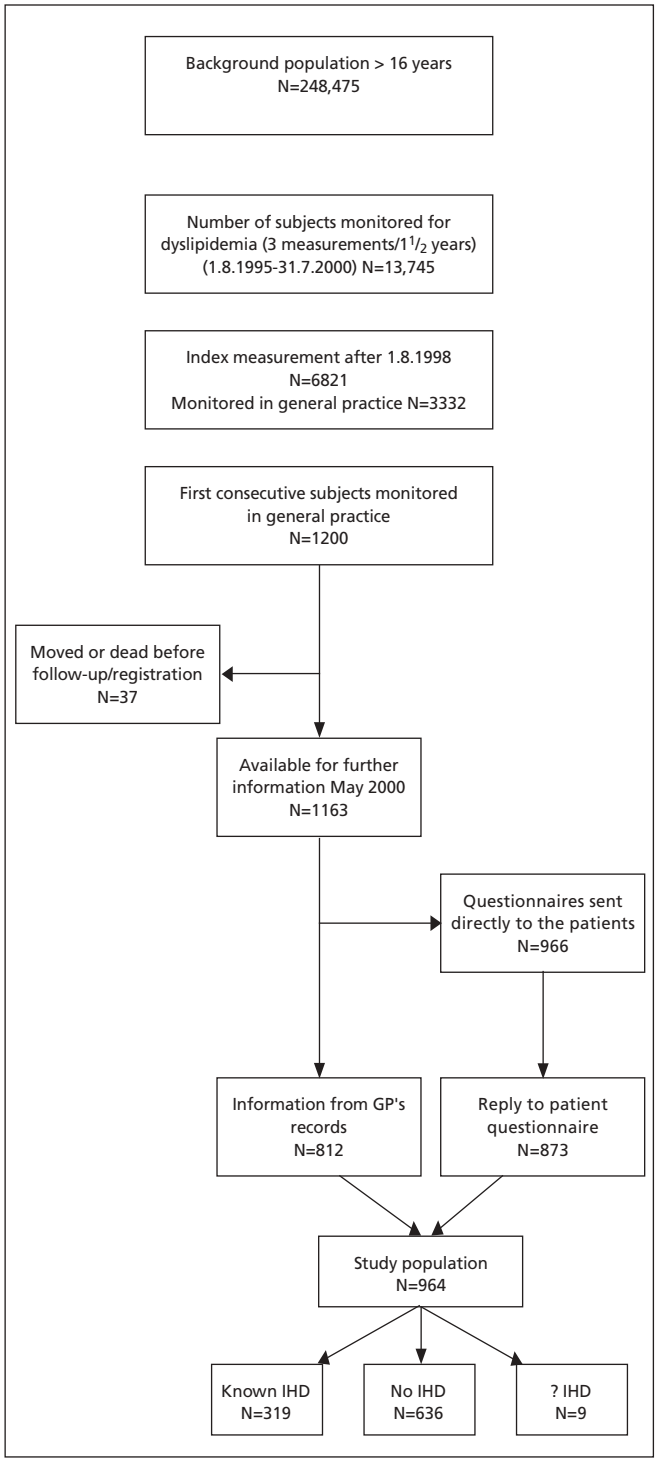

Figure 1. Flowchart.

NATIONAL HOSPITAL REGISTER AND PRESCRIPTION REGISTER

By use of CPR the information on lipid-lowering medications was cross-validated with information on prescriptions on lipid-lowering medications from the National Health Service. The National Health Services receive information from all the pharmacies on prescriptions on reimbursable medicine (11, 12).

Furthermore the information on IHD was compared to discharge diagnoses in the National Hospital register (January 1, 1990 – December 31, 1999), for all study patients hospitalised prior to or during the study period.

RISK ASSESSMENTS

For subjects without IHD an absolute ten year risk of an IHD event was estimated by using the coronary risk charts as enclosed by the European guideline (10). For the risk estimation the plasma cholesterol values before treatment were used (GP), and if they were missing the first value in LIS was applied. If a systolic blood pressure was not available, but hypertension was ticked by yes, the systolic blood pressure was noted in the category 150-170 mmHg, and if hypertension was ticked no or missing it was noted in the category <130 mmHg. If information on height or weight was missing and the patient was ticked as overweight, BMI was categorised as >25 kg/m^2, the remaining were categorised as <25 kg/m^2. If information on smoking was missing the patients were categorised as non-smokers. All estimations tending towards the lowest risk.

DATA PROCESSING AND STATISTICS

Double data entry was carried out for all data by SPSS data-entry, and SPSS was used for data processing (SPSS for Windows, Rel. 8.0. 1998. Chicago). Mann-Whitney test was used for comparing continuous variables between groups, and Wilcoxon's signed rank test for comparing related samples within groups. Differences between groups in categorised variables were analysed with chi square test. All analyses were two-sided, and results were considered statistically significant at the level of $P < 0.05$.

ETHICS

The Scientific Ethical Committee of Aarhus County and the Danish Data Protection Agency gave approval and permission to conduct the study. The committee for multicentre studies of the Danish College of general practitioners also recommended the study.

RESULTS

Out of 1163 subjects monitored by 134 different general practices, the general practitioners provided information on 812 subjects (70%) (Figure 1). The GPs accepted that a questionnaire was sent directly to 966 subjects (83%), and 873 (90%) filled in the questionnaires. In total the survey gave information on 964 different subjects (83%), monitored by 117 different general practices.

Table 1. Data sources.

	LIS	GPs' records Yes/total (N=812)	Patient questionnaires Yes/total (N = 873)	Combined Yes/total (N = 964)	%
IHD		+ 269/792	(+) 269/854	319/955	33.4
Other atherosclerotic manifestations		+ 96/793	(+) 113/813	122/949	12.9
Hypertension (yes/no)		+ 438/786	(+) 413/864	512/955	53.6
- systolic blood pressure		+ 749/812			
Diabetes		+ 124/809	(+) 122/871	149/962	15.5
BMI > 25 kg/m^2		(+) 255/421	+ 516/867	533/908	58.7
Family history of CVD		(+) 144/253	+ 276/768	296/799	37.0
Smoking		(+) 123/341	+ 271/872	288/910	31.6
Dietary counselling		(+)	+ 658/867		75.9
Lipid lowering medications		+ 432/804	(+) 479/861	517/958	54.0
P-Cholesterol value before treatment	(+)	+ 760/812		939/964	
Further lipid analyses (-31/7 00)	+			1200	

LIS (electronic laboratory information system).
+ The primary data source. (+) Used if the primary data source was missing.

There were no differences between the study population (964) and the non-responders (199) concerning age, gender or last measured cholesterol values.

In total 76% (658/867) of the patients reported that they had received dietary counselling (**Table 1**), and 87% of the patients treated with lipid-lowering medications also received dietary counselling compared to only 60% of those not treated with lipid-lowering medications. Most frequently the counselling was given by the general practitioners 65% (424/649) or by a dietician 32% (206/649), and less frequently by other health personnel or private organisations. Use of alternative medicine was reported by 11% of the patients (97/850), most frequently fish oil or cod-liver oil (36/97), garlic (31/97) or Guarmin (23/97).

In total 54% (517/958) were treated with lipid lowering medications, and 4.3% (41/958) had previously been treated with medications but had stopped. The most frequent reason for discontinuation of medication was side effects (20/41), the price of the medication (7/41), or normalisation of lipid values (6/41).

Only four patients were treated with combination therapy and 94.0% (483/515) were treated solely with statins, 4.7% (24/515) were treated with fibrates, and four patients treated with bile acid sequestrants (Type not recorded in two cases). Average daily doses for the most frequent prescribed statins were Simvastatin 17.1 mg, Pravastatin 23.2 mg, and Atorvastatin 16.1 mg.

According to the general practitioners 82% (297/362) of the subjects treated with lipid-lowering medications had initiated the treatment in general practice, and most of the remaining subjects had initiated treatment at the hospital and were now monitored by the GP.

PRESCRIPTIONS ON LIPID-LOWERING MEDICATIONS

The information on treatment with lipid-lowering medication was by use of CPR cross validated with information from the Danish National Health Service, on subjects claming lipid-lowering medication January 1, 2000–July 31, 2000. In 517 subjects recorded as treated with lipid-lowering medications 96% (494/517) also claimed a prescription on lipid-lowering medication during the period. Further 11 subjects claimed a prescription (ten had stopped treatment, one unknown treatment status). The dispensed dose showed agreement with records in 90% (358/400) of the cases, when data was compared for the three most frequent used statins. When the prescription information was examined for both responders and non-responders (1163), the treatment rate was 53% (611/1,163).

SECONDARY INTERVENTION

In total 33% (319/955) had known ischaemic heart disease, mainly reported as AMI, angina, former PTCA or Coronary artery by-pass grafting (Table 1). If the information on IHD from GP records and patient questionnaires was compared to discharge diagnoses in the Danish National hospital register, 204/318 had been discharged with a diagnose of IHD during the preceding ten years. Ten patients recorded as no IHD had been discharged with a diagnosis of angina pectoris.

The patients with ischaemic heart disease were significantly older than the subjects without IHD (median age 68 and 61 years, P=0.000) (**Table 2**). In total 72% of the patients with IHD were treated with lipid lowering medications. Despite the high frequency of treatment only 42.3% had a plasma-cholesterol lower than the recommended 5 mmol/l, when the last registered plasma cholesterol before August 1, 2000 was used, and 62.4% had plasma cholesterol levels lower than 5.5 mmol/l.

PRIMARY INTERVENTION

The subjects without ischaemic heart disease were more often women (58%) than men, and the median age for women was 64 years compared to 57 years for men.

The risk charts based on Framingham data were used to evaluate the absolute risk for IHD as described in methods. Only 16% had an absolute ten year risk of a IHD event lower than 10%, half the subjects (319/645) had an absolute risk between 10 and 20%, and the remaining 34% (220/645) of the subjects had an absolute risk higher than 20% for the next ten years, and only nine subjects were categorised in the highest risk group (>40%). In addition 76 patients (12%) had other atherosclerotic manifestations, e.g. claudicatio, transient ischaemic attack (TIA), or apoplexia cerebri.

In total 45% of the subjects without IHD were treated with lipid-lowering medications, and the treatment frequency increased with cardiovascular risk (**Figure 2**). Among subjects with a risk of IHD higher than 20%, 53% of the patients were treated with lipid-lowering drugs. In this group 76% (167/220) still had plasma-cholesterol values higher than 5 mmol/l (median 5.8, 75 and 90 percentiles 6.6 and 7.4), but comparing plasma cholesterol value before treatment with the last measured it had decreased significantly by 1.6 mmol, corresponding to a 21% reduction. (**Figure 3**) (Median 3.4 years between last measured plasma cholesterol and plasma cholesterol before treatment).

Table 2. Distribution of age, gender and plasma cholesterol values before treatment and latest measured.

	N	Median age years	P-cholesterol before,mmol/l median (75/90 PC)	P-cholesterol latest, mmol/l median (75/90 PC)
IHS				
Men	198 (62.1%)	67	6.6 (7.3/8.0)	5.1 (5.7/6.4)*
Women	121 (37.9%)	69	7.1 (8.2/9.4)	5.5 (6.0/6.6)*
Total	319	68**	6.8 (7.5/8.5)	5.3 (5.8/6.4)*
No IHD				
Men	271 (42.0%)	57	7.1 (7.8/8.7)	5.8 (6.5/7.2)*
Women	374 (58.0%)	64	7.5 (8.3/9.2)	6.0 (6.7/7.4)*
Total	645	61**	7.3 (8.1/9.0)	6.0 (6.7/7.3)*

Before, is the plasma cholesterol before eventual treatment, and latest is the last registered plasma cholesterol in LIS (August 1-July 31, 2000).
*) Wilcoxon's Signed Rank Test P<0.000. **) Mann-Whitney U Test P<0.000

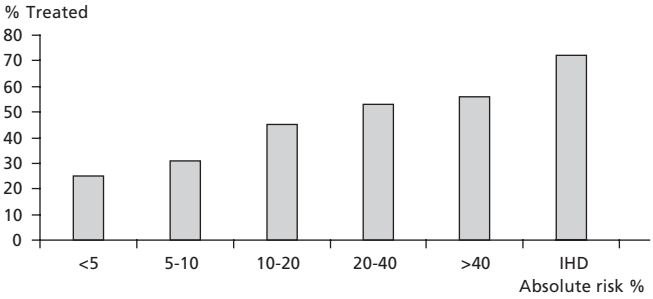

Figure 2. Treatment with lipid-lowering medications, related to the absolute ten years risk of an IHD event.

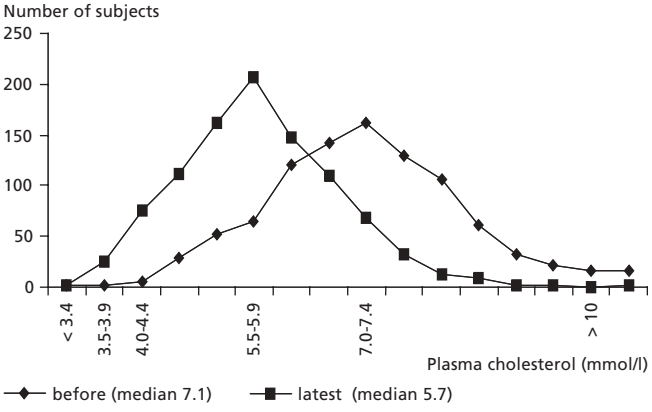

Figure 3. Plasma cholesterol before treatment and latest measured (N=964). Before, is the plasma cholesterol before treatment, and latest is the last registered cholesterol in LIS (August 1-July 31, 2000).

DISCUSSION

This study showed that patients followed and treated for dyslipidemia in primary health care mainly were patients at increased risk or with manifest ischaemic heart disease. Approximately three fourth of the patients had received information on lipid lowering diet, and 54% were treated with lipid-lowering medications. Only a minority reached the goals as recommended in guidelines, but mean plasma cholesterol was reduced significantly by 19.4% in the total population.

Compared to most former studies this survey included all types of patients from a representative part of all general practices (87%) in a large geographic area, instead of only focusing on subsets of patients (e.g. those with CHD) from selected centres. A pitfall of the method is that the best-controlled subjects could be monitored more often, resulting in a selection for the best-controlled subjects, and furthermore there is no information on those who were never tested. Another selection bias could be the location of the study population in an area with special interest in dyslipidemia, but official medicinal statistics did not indicate that this county was more aggressive in prescribing lipid-lowering medications, compared to other Danish counties.

Based on European recommendation (10), the Danish College of General Practitioners in December 1998 published new guidelines for the prevention of ischaemic heart disease (13). Treatment of dyslipidemia in healthy subjects should depend on absolute risk of IHD, and risk charts based on Framingham data were attached to the guideline. The treatment goals for patients with coronary heart disease and healthy subjects with high risk of CHD were total cholesterol lower than 5 mmol/l and LDL cholesterol lower than 3.0 mmol/l.

The cardiovascular risk charts are not taking all risk factors into account, and those with a family history of premature cardiovascular disease, other atherosclerotic diseases than IHD, high BMI, high triglycerides, or low HDL cholesterol have a higher risk than registered. Therefore the estimated risk will tend to be higher than recorded here.

This survey demonstrated that a large number of subjects were treated with statins, but they did not achieve the recommended target levels for plasma cholesterol. Maximal doses were used infrequently, and the doses used were generally lower than the doses used in the studies that showed reduction in morbidity and mortality, which might be one of the reasons for the low level of success in meeting treatment goals. The average dose of Simvastatin was 17 mg compared to 27 mg in the 4S study, and average Pravastatin dose was 23 mg compared to 40 mg in CARE and LIPID (4-6). The low doses and a substantial number of patients staying at starting doses are consistent with the findings in other studies (14). Other explanations for not achieving the goals set in guidelines might be multiple (other goals, compliance?), and further investigations to answer that will be necessary.

Even though the specified targets were not achieved, the plasma cholesterol levels for the population were lowered considerably with a reduction in mean plasma cholesterol of approximately 20%. A decrease in total cholesterol of 20% is expected to result in a reduction in IHD events of approximately 40% (15, 16) , which is an important relative risk reduction in this high-risk population. The extremely valuable achievements in risk reductions, despite poor adherence to target levels for plasma cholesterol, indicate that it might not be sufficient solely to evaluate if target levels are reached, if the quality of treatment is to be evaluated adequately. However, more recent studies (HPS, Prove it) (17, 18), indicates that lipid-lowering treatment should be even more aggressive, and most recent guidelines aims at LDL cholesterol levels below 2.5 mmol/l.

CONCLUSION

The laboratory information system is a valuable tool in assessment of the quality of treatment of dyslipidemia in large geographic areas. Subjects monitored for dyslipidemia were relevantly monitored because of IHD or high risk of IHD, and treatment was clearly related to degree of cardiovascular risk as recommended by both European and National guidelines. In total 54% of the monitored subjects were treated with lipid-lowering drugs. The statin doses used were often lower than the comparable doses used in randomised trials. A significant reduction in plasma cholesterol resulted in an important risk reduction, but the majority of patients did not attain the suggested targets for plasma cholesterol.

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