

Hypercholesterolaemia and its Treatment in Singapore with Implications for Screening

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Abstract

The National University of Singapore Heart Study is a cross-sectional survey of the whole of Singapore from 1993 to 1995 with a random sample of 961 persons aged 30 to 69 years (response rate 71.2%). Serum lipids were measured enzymatically on an autoanalyser (Ektachem, Kodak). Hypercholesterolaemia was diagnosed if the person was on lipid lowering drugs or had a serum cholesterol ≥ 6.5 mmol/L (250 mg/dL). Results for the 40 to 64 age group are presented. The proportion and number in Singapore with hypercholesterolaemia were high, 23.7% and 186 544 persons respectively. However, they declined with the additional requirement of coronary heart disease (CHD) or risk factors (i.e. cigarette smoking, hypertension or diabetes mellitus), and were small if only hypercholesterolaemic persons with CHD were included, 1.6% and 13 126 persons respectively. For both genders, the proportions on drugs increased with the added options of CHD or risk factors, so that for persons with hypercholesterolaemia and CHD the proportion on drugs was very high i.e. 84.0%. However, 11.2% of persons with only hypercholesterolaemia (i.e. without CHD or other risk factors) had been prescribed drugs. The main conclusions were: 1) The use of different criteria for the screening and treatment of hypercholesterolaemia would involve large differences in the number of Singaporeans on lipid lowering drugs and this should be considered when deciding policy and 2) Medical practitioners currently to some extent do consider the presence of CHD or other risk factors when prescribing lipid lowering drugs for hypercholesterolaemia.

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Introduction

Coronary heart disease (CHD) has been increasing in Singapore though with recent declines^{1,2} and is now the commonest single cause of death.³ In particular, it is a major cause of premature death, accounting for 40% of deaths in men between the ages of 45 and 60 years. CHD results in high social costs such as impaired quality of life and reduced economic activity. Furthermore, it directly imparts high economic costs both on the individual and the government. The major risk factors are cigarette smoking, high blood pressure, high serum cholesterol and diabetes mellitus.⁴

Strategies for primary prevention include measures directed at the population as a whole and those directed at individuals with high risk.⁵ The "population" strategy seeks to improve the health-oriented behaviour (i.e. nutrition, smoking and exercise) of the whole population so as to reduce the risk of CHD in the

entire population. The "high-risk" strategy seeks to identify by screening the minority of persons who are at high risk of CHD, in particular those with hypercholesterolaemia and hypertension. Health education on lifestyles and possibly the use of drugs are then directed at these "high-risk" individuals so as to reduce the levels of risk factor(s). These two strategies can be complimentary.

Screening for and treatment of hypercholesterolaemia has been reviewed.⁶ The review concluded that on present evidence, screening for hypercholesterolaemia is only justified in persons over 40 years of age with CHD or at least with 2 major risk factors of family history of premature CHD, cigarette smoking, hypertension and diabetes. It also recommended that the current situation of hypercholesterolaemia in Singapore be assessed before introducing any screening programmes. The Singapore Thyroid and Heart Study showed serum cholesterol in the mid-1980s to be high in Singapore⁷ and comparable

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to Western countries,⁸ though the National University of Singapore Heart Study (NUS Heart Study) indicates a 10% fall in the mid-1990s.⁹ Serum cholesterol in Singapore has also been measured on volunteers¹⁰ and the general population.*

This paper examines current levels of hypercholesterolaemia (overall and in combination with CHD or other risk factors) and its treatment in Singapore obtained from the NUS Heart Study, and discusses the implications with regard to screening for and treatment of hypercholesterolaemia.

Materials and Methods

The NUS Heart Study is a cross-sectional survey of a random sample of persons aged 30 to 69 years from the general population of Singapore. The sample was obtained from two sources, the Singapore Thyroid and Heart Study,⁷ and 5 divisions of the 1992 electoral register, one from each part of the island (north, south, east, west and centre). There was disproportionate sampling by ethnic group to obtain an equal number of subjects in each of the 6 gender/ethnic groups. The required sample was 180 subjects in each gender/ethnic group giving a total of 1080 persons. It was assumed that 20% of the subjects would not be recruitable because of death, migration, infirmity, and relocation (which is high in Singapore due to massive urban redevelopment) and there would be a response rate of 75%, so that a total of 1800 persons were selected. In fact, of these 1800 subjects, 419 (23.3%) were found not to be recruitable and 983 responded giving a response rate of 71.2%. Of these 983 subjects, 22 were found to be 70 years of age or over and were excluded, leaving 961 persons aged between 30 and 69 years.

Morning clinics were held from June 1993 to December 1995 with the two genders and three ethnic groups seen concurrently. All measurements were standardised. Full demographic information was obtained by questionnaire. Lipid lowering drug usage with type and duration of treatment were obtained by questionnaire. Also obtained by questionnaire was current cigarette smoking status with a smoker defined as regularly smoking at least one cigarette per day. Serum lipids were measured enzymatically on an autoanalyser (Ektachem, Kodak). Hypercholesterolaemia was diagnosed if the person was on lipid lowering drugs or had a serum cholesterol ≥ 6.5 mmol/L (250 mg/dL). Coronary heart disease (CHD) was considered present if the diagnosis had been made by a doctor. Blood pressures were measured by one doctor (KH) using the standard mercury sphygmomanometer in accordance to the protocol of the MONICA project¹² with the mean of 2 readings being used, and hypertension diagnosed if the person was on treatment or had systolic pressure ≥ 160 mm Hg and/or diastolic pressure ≥ 95 mm Hg, according to the World

Health Organization classification. Diabetes mellitus was diagnosed if the person was on treatment or had a 2-hour level of plasma glucose ≥ 11.1 mmol/L on an oral glucose tolerance test (performed if the person had a fasting plasma glucose ≥ 6.0 mmol/L), according to World Health Organization recommendations.¹³ Blood samples were taken between 1000 and 1100 hours and blood pressures were measured between 0900 and 1000 hours; so there was no problem of diurnal variation.

Data for the 40 to 64 age group are presented as this is the age group likely to be considered for screening and treatment of hypercholesterolaemia. In Singapore, ethnic group differences are not present for serum cholesterol but are present for CHD, cigarette smoking and diabetes as found in the Singapore Thyroid and Heart Study⁷ and the NUS Heart Study.¹⁴ Hence, to obtain the proportions and numbers of persons in the Singapore population with combinations of hypercholesterolaemia with CHD and risk factors, and on lipid lowering drugs, the gender/ethnic group proportions obtained from the NUS Heart Study were applied to the 1995 general population of Singapore."

The proportions and numbers of persons indicate the implications of using different criteria for treatment of hypercholesterolaemia i.e. all persons with hypercholesterolaemia, or those with hypercholesterolaemia and CHD or at least one other risk factor (cigarette smoking, hypertension or diabetes), or those with hypercholesterolaemia and CHD or at least two other risk factors, or those with hypercholesterolaemia and CHD. The proportions of persons on lipid lowering drugs indicate the current situation with regard to these drugs and the extent to which doctors are considering the presence of CHD or other risk factors in persons with hypercholesterolaemia before prescribing these drugs.

Results

Table I shows that in the 40 to 64 age group, hypercholesterolaemia was higher in females than males, but as CHD and risk factors were higher in males, the combinations were similar in the 2 genders. The proportions and numbers with hypercholesterolaemia were high (slightly higher for females than males), 23.7% and 186 544 respectively for all persons. However, the proportions and numbers declined with the additional requirement of CHD or at least one risk factor (cigarette smoking, hypertension or diabetes mellitus), and declined further with the additional requirement of CHD or at least two risk factors, and were even smaller if only hypercholesterolaemic persons with CHD were included, 1.6% and 13 126 respectively for all persons.

Of persons taking lipid lowering drugs, 93.3% were in the 40 to 64 age group. Table II shows that the proportion of persons in the 40 to 64 age group taking drugs was

TABLE I: PROPORTIONS* AND NUMBERS OF PERSONS* AGED 40 TO 64 YEARS WITH COMBINATIONS OF HYPERCHOLESTEROLAEMIA,** CORONARY HEART DISEASE AND RISK FACTORS,*** SINGAPORE 1995

	Proportion (%)			Number		
	Males	Females	All	Males	Females	All
Hypercholesterolaemia	19.9	27.0	23.7	79 759	106 785	186 544
Hypercholesterolaemia with CHD or at least 1 risk factor	10.2	10.5	10.3	40 882	41 528	82 410
Hypercholesterolaemia with CHD or at least 2 risk factors	3.6	4.0	3.8	14 429	15 820	30 249
Hypercholesterolaemia with CHD	1.4	1.9	1.6	5611	7515	13 126

* Obtained by applying the gender/ethnic group proportions from the NUS Heart Study to the 1995 general population of Singapore

** On lipid lowering drugs or serum cholesterol ≥ 6.5 mmol/L

*** Cigarette smoking, hypertension, diabetes mellitus

CHD: Coronary heart disease

higher for males than females, though this was not so for hypercholesterolaemic persons with other risk factors. For both genders, the proportions on drugs increased with the added options of CHD or risk factors, so that for persons with hypercholesterolaemia and CHD, the proportions on drugs were very high in both genders, 84.0% for all persons. Of persons with only hypercholesterolaemia (i.e. without CHD or other risk factors), more males were on drugs than females, and overall, 11.2% had been prescribed drugs. Of the lipid lowering drugs prescribed, 57.1% were fibrates, 35.7% statins, and 7.1% nicotinic acid derivatives.

Discussion

This paper presents the current situation in Singapore with regard to hypercholesterolaemia and its treatment. This is the first presentation on the prevalence of hypercholesterolaemia in combination with CHD or other risk factors and on the proportion of the population taking lipid lowering drugs. It provides information relevant to screening for hypercholesterolaemia with a view to its treatment and the reduction of cardiovascular diseases.

Present evidence suggests that persons with hypercholesterolaemia should only be treated if in addition they have CHD or at least 2 other risk factors i.e. cigarette smoking, hypertension, or diabetes.⁶ Table I shows that this policy would involve the treatment of about 30 000 persons between the ages of 40 and 64 years in Singapore, while Table II shows that currently in Singapore slightly less than half of these persons are on treatment. If the policy is liberalised to treat hypercholesterolaemic persons with CHD or at least 1 other risk factor, then the numbers involved would be more than doubled to about 80 000 (Table I). Currently just less than a quarter of these hypercholesterolaemic persons are on treatment (Table II). If all persons with hypercholesterolaemia were treated this would involve six times as many persons or about 185 000 (Table I) and currently about one fifth of these are being treated (Table II). Hence, apart from the fact that overall benefit has only been proven for treatment of

TABLE II: PROPORTIONS OF PERSONS* AGED 40 TO 64 YEARS ON LIPID LOWERING DRUGS ACCORDING TO COMBINATIONS OF HYPERCHOLESTEROLAEMIA,** CORONARY HEART DISEASE AND RISK FACTORS,*** SINGAPORE 1995

	Proportion (%)		
	Males	Females	All
Hypercholesterolaemia	29.4	11.6	20.5
Hypercholesterolaemia with CHD or at least 1 risk factor	22.5	25.1	23.8
Hypercholesterolaemia with CHD or at least 2 risk factors	30.0	61.7	45.8
Hypercholesterolaemia with CHD	85.7	82.3	84.0
Hypercholesterolaemia without CHD or risk factors	19.1	3.1	11.2
All Persons	4.1	3.1	3.6

* Obtained by applying the gender/ethnic group proportions from the NUS Heart Study to the 1995 general population of Singapore

** On lipid lowering drugs or serum cholesterol ≥ 6.5 mmol/L

*** Cigarette smoking, hypertension, diabetes mellitus

CHD: Coronary heart disease

hypercholesterolaemia with CHD or at least 2 other risk factors, liberalising the screening policy would produce much less favourable cost-benefit and cost-effectiveness analyses. In Singapore, the Ministry of Health has recently warned against mass screening for hypercholesterolaemia and stressed the importance of a healthy lifestyle.¹⁶

It is reassuring that medical practitioners in Singapore are considering the presence of CHD or other risk factors when prescribing lipid lowering drugs, though this is more so in females than males (Table II). It is also reassuring that the majority of hypercholesterolaemic persons with CHD are on treatment (84.0%). The value of cholesterol lowering after an infarction is now beyond doubt as it not only reduces CHD deaths but also total mortality.⁶ This was shown in particular by an analysis of secondary prevention trials¹⁷ and confirmed by the

Scandinavian Simvastatin Survival Study.¹⁸ It is probably reasonable that nearly 50% of persons with hypercholesterolaemia and CHD or at least 2 other risk factors are on treatment though this can be improved upon. However, nearly one quarter of persons with hypercholesterolaemia and CHD or at least 1 other risk factor and about 10% of hypercholesterolaemic persons without CHD or other risk factors are being treated when on present evidence they should not be treated.

Of the lipid lowering drugs prescribed, 92.8% were fibrates or statins which is reasonable considering their efficacy. Statins are probably the most effective in reducing CHD mortality though it must be said that their long-term effect on overall mortality has not been established.

Conclusion

The use of different criteria for screening and treatment of hypercholesterolaemia would involve large differences in the number of Singaporeans on lipid lowering drugs and this should be considered when deciding policy on screening and treatment. At present, the position with regard to treatment of hypercholesterolaemia in Singapore can be considered reasonable, with the presence of CHD or other risk factors being taken into consideration when prescribing lipid lowering drugs. However, persons who would benefit from treatment are being left untreated while others, who on current evidence should not be treated, are being treated. There still seems to be a need for doctors to be better informed on the indications for screening for hypercholesterolaemia and its treatment with lipid lowering drugs.

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