ORIGINAL ARTICLE

Is A Desk-Top Analyzer The Answer To Cholesterol Screening ?

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Abstract

This is the first evaluation study on the acceptability and accuracy of the Reflotron, a desk-top analyzer for cholesterol screening in general practice in Hong Kong. Patients aged 21-60 attending a Government general outpatient clinic in Hong Kong were randomly selected. The acceptance rate of screening was 69%. A total of 1113 subjects had their cholesterol levels screened by the Reflotron. The accuracy of the Reflotron was assessed by comparing its results to laboratory blood cholesterol (BC) results in 125 subjects. The mean error of the Reflotron cholesterol measurements was 6% which was larger than that recommended by the American National Cholesterol Education Programme. Therefore, the diagnosis or treatment of hypercholesterolaemia should not be based on the Reflotron result alone. There was a good linear correlation between the Reflotron cholesterol (RC) and blood cholesterol (BC) with a negative bias in the Reflotron results. Blood cholesterol could be predicted from RC by the regression equation: BC = 0.8395 + 0.8995 × RC. The Reflotron is useful as an initial screening test for hypercholesterolaemia in the low risk population. The threshold levels need to be adjusted accordingly, and abnormal results should be confirmed by standard laboratory tests. It is estimated that one could save H.K.$51.6 million if the Reflotron instead of the laboratory were used to screen all people aged 40 to 60 years old in Hong Kong once.

Introduction

Hypercholesterolaemia is one of the most important risk factors of coronary heart disease (CHD).[1-6] The WHO Expert Committee on prevention of coronary heart disease recommended that identifying and helping individuals at special risk is an important preventive strategy.[7] The detection of hypercholesterolaemia is important for the overall evaluation and reduction of the CHD risk of an individual.

An earlier study found that only 30% of the Chinese in Hong Kong accepted blood tests for cholesterol screening.[8] Many refused because they were afraid of venepuncture and some found it too inconvenient to return on another day for a blood test. The use of a desk-top dry chemistry analyzer may improve the acceptability of screening by saving a venepuncture and an extra visit.[9-11]

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The Answer to Cholesterol Screening

The Reflotron is the most popular desk-top analyzer among general practitioners in Europe.[12] It measures cholesterol with a drop of capillary blood obtained by finger-prick and the result is known within a few minutes. Many general practitioners in Hong Kong also use the Reflotron in their offices but there is no published data on its acceptability and accuracy locally.

This is the first evaluation study on the acceptability and accuracy of the Reflotron for opportunistic cholesterol screening on Chinese patients in general practice in Hong Kong. All the published data on the Reflotron was obtained from Western populations, and some had contradictory conclusions.[11,13-16]

Method

The study was carried out between June 15 and September 15, 1990 at a four-doctor Government general outpatient clinic in Hong Kong. Two trained interviewers sampled the subjects from patients attending two of the four doctors. The doctors were selected in rotation during the study period so that their patients had equal chance to be sampled.

One in every four patients consulting the selected doctors were approached by the interviewers in the waiting hall before their consultations. Chinese patients aged 21 to 60 years old were invited to take part in the study. The next patient was invited if the original subject was outside the age range, was not Chinese, was sampled before, or refused to participate. Each participant was interviewed with a structured questionnaire on personal demography and CHD risk factors. Each subject was then seen by the second author (M.G.C.) who measured his/her weight, height, blood pressure, and serum cholesterol. Serum blood cholesterol was measured by the Reflotron desktop analyzer (Boehringer Mannheim, W.

Germany, 1988) on a drop of capillary blood obtained by a finger prick. All the tests were performed by the second author (M.G.C.) who received a training session from the supplier before the study. The test procedures listed in the operation manual were closely followed. The machine was calibrated with the check strips from the supplier before the screening tests each day. Quality checks using standard sera from the supplier were performed once a week.

All patients with total cholesterol levels > $6.2mmol/l$, and those with levels > $5.2mmol/l$ and two additional CHD risk factors were invited to have further blood tests for cholesterol and lipoprotein analysis. The CHD risk factors included male sex, family history of premature (before the age of 55) coronary heart death or sudden death, current smoking of ≥ 10 cigarettes per day, hypertension on treatment or a blood pressure measurement > 160/90, diabetes mellitus, history of definite stroke or occlusive peripheral vascular disease, and BMI ≥ 30.[17]

Subjects who required further blood tests were asked to return within three days of the initial screening following a 12 hours fast. Their venous blood samples were sent to the Sai Ying Pun Government Biochemistry Laboratory for the assay of total cholesterol (TC), triglyceride (TG) and high density lipoprotein (HDL) by the Beckman Synchron CX5 analyzer. The Laboratory carries out quality checks twice a month by an international quality control programme, the NUREX Diagnostic Clinical Chemistry Quality Assessment Programme.

The low density lipoprotein (LDL) level was calculated by the Friedewald formula: LDL = TC − HDL − (TG / 2.2) $mmol/l$.[18] Those found to have elevated LDL according to their relative CHD risks were called back for further assessment and management.

All the data were analyzed using the SPSS-PC+ (Statistical Packages for Social Science — Personal Computer) programme.[19]

Results

Sample

There were 1616 (56% females and 44% males) eligible patients approached, 1113 (69%) completed the questionnaire and Reflotron cholesterol screening. These 1113 subjects made up the total sample for further analysis. There were 622 (56%) females and 491 (44%) males. The sex ratio of the screened sample was the same as that of the initial eligible population. The mean age of the sample was 38.7 years (S.D. 11.2). The distribution of the social class by occupation[20] and the CHD risk factors of the sample is shown in **Table 1**. Twenty-one percent of them had two or more CHD risk factors. Nine percent had previously had their blood cholesterol checked.

Table 1: Distribution of the Social Class and Coronary Heart Disease (CHD) Risk Factors

Proportion of Sample (N=1113)

Social Class	
I	1%
II	11%
III	61%
IV	17%
V	10%
CHD Risk Factors	
Current Smoker	9%
Ex-smoker	3%
CHD	1%
Family History of CHD	5%
Hypertension	14%
BMI $\geq$ 30	5%
Diabetes Mellitus	4%
Hyperlipidaemia	2%
Stroke	1%
Other atherosclerosis	0.4%

A total of 143 (13%) subjects required further cholesterol and lipoprotein tests according to our study criteria. Sixty-nine (6%) individuals had RC > 6.2*mmol/l* and 74 (7%) had RC 5.2 to 6.2*mmol/l* and two additional CHD risk factors. One hundred and twenty-five (87%) of them returned for the blood tests.

Accuracy of Cholesterol Tests by the Reflotron

The accuracy of the cholesterol measurements by the Reflotron was assessed by comparing the Reflotron and blood test results of 125 subjects who had both tests. The blood test results by the laboratory were used as the gold standard.

Correlation analysis showed that there was a strong positive correlation between the two results with a correlation coefficient of 0.805 (p < 0.0001). Figure 1 shows the correlation plot of blood cholesterol (**BC**) by Reflotron cholesterol (**RC**) of the 125 subjects. The BC value could be calculated from the RC by the regression equation : BC = 0.8395 + 0.8995 × RC. The three *threshold levels of RC that corresponded to the* three commonly used thresholds of hypercholesterolaemia of 5.2, 6.2 and 7.8*mmol/l*[19-21] were 4.8, 6.0 and 7.7*mmol/l*, respectively.

Figure 1: Correlation Plot between Reflotron Cholesterol and Blood Cholesterol

Serum Total Cholesterol by Reflotron

▼ - 3   ∗ - 2   . - 1
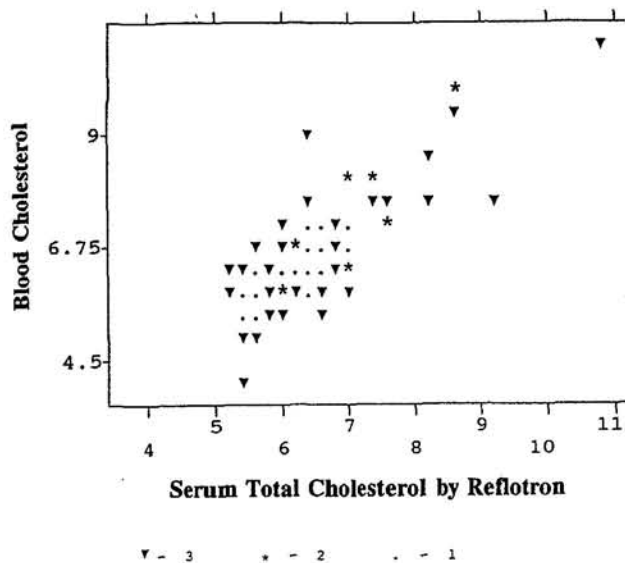
The Answer to Cholesterol Screening

The mean cholesterol level of the 125 subjects was 6.4 (S.D. 0.86, range 5.2 – 10.8) *mmol/l* by Reflotron and 6.6 (S.D. 0.96, range 4-10.7) *mmol/l* by blood test. The difference between the means was 3%. The difference between each paired results ranged from 0 to 35%. Five subjects had differences of more than 20%. If these five subjects were excluded from the analysis, the mean error was 6% (S.D. 0.045, range 0 – 18%). If they were included, the mean error became 7% (S.D. 0.057). The classification of individuals by cholesterol levels either the Reflotron, or blood tests are compared in **Table 2**. **Table 3** shows the sensitivities, specificities, and the predictive values of the Reflotron in detecting blood cholesterol levels of > 6.2*mmol/l* by using a RC threshold of 6.0*mmol/l* or 6.2*mmol/l*.

Table 2: Accuracy of Cholesterol Measurement by the Reflotron

| | Laboratory Cholesterol | |
	> 6.2 mmol/l (N=83)	≤ 6.2 mmol/l (N=42)
Reflotron Cholesterol		
> 6.2 mmol/l (N=70)	59	11
≤ 6.2 mmol/l (N=55)	24	31
> 6.0 mmol/l (N=81)	68	13
≤ 6.0 mmol/l (N=44)	15	29

Table 3: The Sensitivity, Specificity, Predictive Values of the Reflotron for blood cholesterol > 6.2*mmol/l*

| | Reflotron Threshold Level | |
	>6.0 *mmol/l*	>6.2 *mmol/l*
Sensitivity	82%	71%
Specificity	69%	74%
Positive prediction	84%	84%
Negative prediction	66%	56%

Discussion

The Reflotron cannot replace standard laboratory tests for the diagnosis of, or monitoring the treatment of, hypercholesterolaemia. The mean error of Reflotron measurements in our study was greater than the 5% recommended by the expert panel of the American National Cholesterol Education Programme (NCEP). The NCEP actually recommended that the error should ideally be no greater than 3%.[21]

We found a negative bias in the Reflotron measurements as reported by Koch *et al*,[15] but different studies have reported different results.[11,13-16] The accuracy of most desk-top analyzers has not been fully established. The error and bias of different desk-top analyzers, even of the same model and brand, may be different. The possible causes of error are multiple: calibration, assay technique, reagent strip characteristics, and possible difference between cholesterol concentration in capillary and venous blood samples.[14,15] Therefore, it is essential to check the accuracy of and calibrate a desk-top analyzer against standard laboratory results before it is used clinically. Regular quality checks should also be done to assure the accuracy of the test results.

The Reflotron results had good linear correlation with laboratory results but the values needed to be adjusted according to the regression equation. According to our results, a RC threshold levels of 4.8*mmol/l* and 6*mmol/l* should be used to identify those with blood cholesterol levels of >5.2*mmol/l* and >6.2*mmol/l* respectively. Using a RC threshold of 6.0*mmol/l*, the Reflotron had a sensitivity of 82% and specificity of 69% in detecting persons with blood cholesterol of >6.2*mmol/l*.

The negative predictive value in our validation sample was relatively low (66%) because a high proportion (66%) of subjects had cholesterol > 6.2*mmol/l*. If this were applied to

the total sample of which 96 (9%) persons had RC > 6.0$mmol/l$ (corresponds to blood cholesterol > 6.2$mmol/l$), then the negative predictive value would be 97%. This means that the Reflotron is useful as an initial screening test to exclude hypercholesterolaemia in a low-risk population. It can save a lot of unnecessary blood tests because only one in six persons requires further tests.

The biggest advantage of the Reflotron is its high acceptability which is essential for a screening test to be useful.[22] The acceptance rate was improved from 30% by blood test[8] to 69%. People were also much more motivated to return for further blood tests when the initial abnormal cholesterol results were fed back to them.

The Reflotron is cheaper than blood test for initial screening for possible cases of hypercholesterolaemia. Excluding the capital cost of the machine each Reflotron cholesterol reagent strip costs about H.K.$17 (1994 price quoted by supplier). A cholesterol test done by a private laboratory in Hong Kong costs about H.K.$60.[23] If the 1.2 million people aged 40 to 60 years old in Hong Kong were to be screened once,[24] it could save 51.6 million HK$(1.2 million × ($60 − $17)).

Conclusion

The Reflotron cannot replace laboratory tests for the diagnosis or monitoring the treatment of hypercholesterolaemia because the mean error in measurement was as big as 6%. The main use of the Reflotron is for initial case finding, it is well accepted by patients and can save a lot of unnecessary blood tests. It is more cost-effective than standard laboratory test for initial cholesterol screening in a population with relatively low prevalence of hypercholesterolaemia like ours.

It must be stressed that any abnormal Reflotron cholesterol result must be confirmed by standard laboratory blood tests before the diagnosis of hypercholesterolaemia is made. The

LDL and HDL levels should also be measured in these individuals so that treatment can be guided by the LDL and HDL levels.[25] Otherwise, the assay error may cost much more in terms of patient anxiety and unnecessary treatment than the saving from the screening tests.

Acknowledgements

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