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6.2.3 Quality Status of Serum Cholesterol Analysis in Iceland

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ABSTRACT

Eight laboratories participated in the first Icelandic quality assessment survey of serum cholesterol analysis in 1989. Quality control material, lyophilized animal serum and frozen human serum, was distributed three times over a period of one year and analyzed each time over 10 consecutive days. After two distributions of control material the laboratories were advised to start using a common calibrator from the U.S. National Bureau of Standards, and six months later the third lot of control material was analyzed. All laboratories use the same enzymatic methods for estimating serum cholesterol. Average total imprecision within and between laboratories improved throughout the survey, but did not reach the quality goal of the U.S. National Cholesterol Education Panel of ± 3% for imprecision and ± 3% for bias (1) leaving scope for further improvement.

INTRODUCTION

In 1988 recommendations were prepared in Iceland for the treatment of hypercholesterolemia as a preventive measure in cardiovascular disease. Since the doctors decision on treatment is based almost entirely on laboratory results of blood lipids and predetermined cut off points, accuracy and precision of blood lipid analysis is of utmost importance. Therefore it was decided to assess the status of blood lipid analysis in Iceland. All laboratories that were known to do analyses on serum cholesterol were invited to participate in a survey extending over a period of one year. The external quality assessment (EQA) services used by the individual laboratories are either Wellcome Diagnostics in England or WHO Collaborating Lipid Reference Centre in Czechoslovakia. Professional agreement on quality goals for S-cholesterol had not been made nor was information about quality status within individual laboratories available. However most of the laboratories used unofficially the guidelines of the U.S. National Cholesterol Education Panel, NCEP, (1) or guidelines from other national bodies (2).

MATERIALS AND METHODS

Methods: Eight laboratories participated in this investigation. All used the same assay procedure, an enzymatic, colorimetric assay with cholesterol esterase, cholesterol oxidase and a chromogenic compound. The reagents were purchased from 3 different manufacturers. Six different calibrators were used by the eight laboratories and six different autoanalysers were used for the analysis.

Quality assessment material: In this study freeze-dried control serum (a, b, c) of bovine and horse blood origin was used, Pathonorm high and low, from Nycomed Pharma AS, Oslo, Norway, frozen human serum (d, e) prepared locally and frozen human serum (A, B, C) with assigned S-cholesterol values, generously donated by Adam Uldall, Herlev Hospital, Denmark.

Calculations: The average within-laboratory and between-laboratory imprecision was calculated using analysis of variance techniques and expressed as coefficient of variation (CV) in per cent of the mean value of each component (3). The average bias was calculated directly by comparing the deviation of the mean measured value from the assigned value and also expressed graphically by plotting individually measured minus assigned values versus assigned values.

RESULTS AND DISCUSSION

Initially three lyophilized animal sera were distributed to the eight participating laboratories and analyzed over 10 consecutive days. S-cholesterol, S-HDL cholesterol and S-triglycerides were assessed, although only cholesterol results are reported here. A few weeks later two frozen human sera were analyzed in the same way.

	Imprecision % CV			Concentration mmol/l		
Sample	within-lab	between-lab	total	assigned	measured	% bias
a	1.1 - 4.3	5.6	6.2	3.25	3.21	-1.2
b	0.6 - 3.7	6.2	6.6	6.25	6.25	0
c	0.5 - 6.3	6.9	7.7	10.40	9.95	-4.3
average	**2.8**	**6.3**	**6.9**			
d	0.7 - 4.5	4.8	5.6		3.63	
e	0.7 - 4.8	3.8	5.2		5.25	
average	**3.2**	**4.3**	**5.4**			
A	0.7 - 4.4	2.7	3.9	5.07	5.15	1.6
B	0.8 - 10.3	1.7	4.6	6.41	6.52	1.7
C	0.6 - 6.1	2.7	4.2	3.27	3.29	0.6
average	**3.5**	**2.4**	**4.2**			

Table 1. Results from the interlaboratory quality assessment, showing imprecision within laboratories, between laboratories and total imprecision, expressed as coefficient of variation (% CV). Assigned value of samples a, b, c and A, B, C as well as mean measured value of all samples is shown. The % bias of mean measured value from assigned in samples a, b, c and A, B, C is seen in the last column of the table.

In Table 1, the results are expressed as the within, between laboratory and total imprecision and % bias from assigned values. The average total imprecision for the first three samples is 6.9 %, and the between laboratory imprecision accounts largly for this. The two frozen human samples analyzed a few weeks later show an average total imprecision of 5.4 %. Reconstitution problems with the freeze-dried material in the different laboratories could be the reason for this, since the between-lab imprecision is reduced from 6.3 to 4.3 % with the use of frozen samples. The between-lab imprecision for samples d and e is however higher than the average imprecision within laboratories indicating a need for improved calibration procedures. The average bias from assigned values in samples a, b, c is shown in Table 1 as well as in Fig. 1. Since only the animal serum had assigned values the human samples d and e are excluded from the bias calculations. As seen in Fig. 1 the spread of results is considerable although the average bias is well within the ± 3% limits of the NCEP from 1992, except at highest concentration of 10.4 mmol/l. About half of the laboratories are outside the older ± 5% limits of the NCEP.

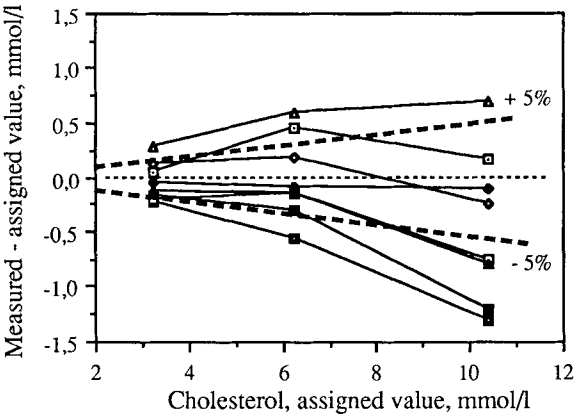

Figure 1. Absolute bias in cholesterol measurements illustrating the deviation of measured - assigned value of the control material (a, b, c) in all eight laboratories, plotted vs the assigned value (x-axis). The broken lines radiating from the zero point encompass ± 5 % bias.

After statistical treatment of the results revealed an unacceptably high total imprecision, within-lab imprecision and bias in some of the participating laboratories, all were asked to start using a common calibrator, a lyophilized human serum from the U.S. National Bureau of Standards. Six months later three frozen human sera samples A, B and C were distributed and analyzed as before. The between laboratory imprecision and bias had improved considerably from before as can be seen from Table 1 and Fig. 2. The average between laboratory imprecision decreased from 4.3% to 2.4% in the frozen human sera and even more so when the animal sera are considered. The analytical bias in different laboratories for samples A, B and C is shown in Fig. 2. The spread of results is considerably less than with samples a, b and c, indicating a great improvement in calibration in those laboratories that showed greatest deviation, before the common calibrator was taken into use.

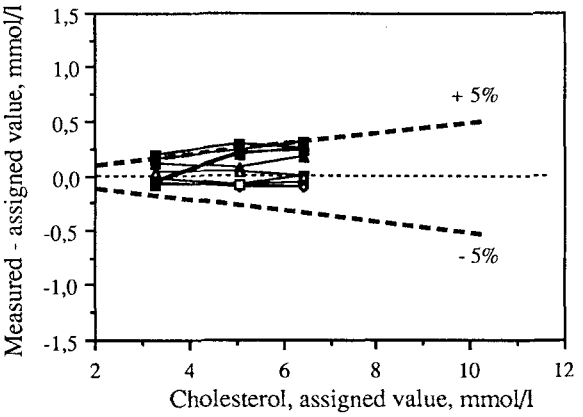

Figure 2. Absolute bias in cholesterol measurements illustrating the deviation of measured - assigned value of the control material (A, B and C) in all eight laboratories, plotted vs the assigned value (x-axis). The broken lines radiating from the zero point encompass ± 5 % bias.

Since this survey was carried out a number of Reflatron analyzers have been imported and are situated in doctors offices throughout the country. It is of utmost importance to start an EQA scheme that will assist all laboratories in the country to meet the quality standards that have been set, although unofficially.

REFERENCES

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