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6.1.2.6 Quality Specifications in Primary Health Care

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INTRODUCTION

Patients are diagnosed and treated at various levels of the health service organization in Finland according to the level of clinical facilities required. The laboratory test results should therefore be transferable over time and between laboratories in hospital and in primary health care. That is also a prerequisite for the use of common reference intervals. The quality goals of the laboratory test results should be the same, if possible, at all levels of the health service oganization.

About 80 % of all laboratory services needed in primary care are provided locally by health center laboratories. Their activity covers simple urinary and haematological tests, a variety of qualitative tests and about 5 - 10 different quantitative chemical tests, performed mainly manually. Automated chemistry and haematological analyzers are also used in bigger laboratories. The personnel usually consist of 2 - 6 medical technologists with good theoretical and practical education. Every laboratory participates monthly in the national external quality control (QC) surveys.

Small laboratories meet several practical difficulties in organizing their internal quality assurance. Medical technologists seldom have adequate experience in the use of statistical methods for assessing the target values and error limits for the internal quality control sample. That is why the internal quality control system is very simple, usually consisting of one control sample in each assay series (often the so called *long-term known control of external QC survey*). Until now the goal has been to maintain the results within the nationally decided, quite narrow error limits of ±3, ±5 or ±10%, depending on the test. The error limits are calculated from the national consensus mean. Such goals do enable simple judgement of the test results obviating the need for complex calculations. However,

such goals are not based on any statistical calculations.

Primary health care laboratories need quality goals for imprecision as well as bias. Their internal quality control system has to be established and more efficient QC rules are needed. To evaluate the possibilities to use the same quality goals in primary care and in hospital laboratories we studied the state of art of health center laboratories, and compared it with different quality goals for clinical laboratories.

METHODS

The day-to-day analytical performance of serum glucose and creatinine analyses in 12 health center laboratories was studied in one central hospital district during two months.Two samples were used, both of which were lyophilized commercial control sera of animal origin.The known, so called "long-term sample from the national QC scheme", with a national mean of 5.00 mmol/l for glucose and 123 umol/l for creatinine, and an unknown sample. The unkown sample was later used as a control sample in a national QC survey. The national means observed were 4.92 mmol/l and 127 umol/l for glucose and creatinine, respectively. The known sample was dissolved, divided in small aliquots and frozen for one to two weeks use in each health center laboratory. The unkown sample was dissolved and distributed by the central hospital and sent to health centers during the same day. The sample was to be treated like an unknown clinical sample, together with the known control sample. Both samples were analyzed during two months in each run, or at least twice a week. In the central hospital the samples were analyzed in daily runs.

All laboratories use glucose dehydrogenase method for serum glucose assays, calibrated with an aqueous glucose solution (5 mmol/l), provided by the central hospital. Kinetic Jaffe' reaction is used for serum creatinine except in one laboratory using the endpoint Jaffe' method. Creatinine assays were calibrated in health centers with the same lot of Seronorm™ quality control serum (203 umol/l), (Nycomed AS, Oslo, Norway), except in two health center laboratories using a commercial aqueous standard (Orion Diagnostica, Helsinki, Finland).

RESULTS

Serum glucose levels determined in the health center laboratories during the two-month

period were 4.94 mmol/l (mean, range 4.5 - 6.1 mmol/l, CV 3.4 %, n = 470) and 5.00 mmol/l (mean, range 4.2 - 6.1 mmol/l, CV 3.7 %, n = 470) for the known and unknown samples, respectively. The creatinine levels were 123.2 umol/l (mean, range 94 - 140 umol/l, CV 3.9 %, n = 438) and 128.9 umol/l (mean, range 98 - 152 umol/l, CV 4.6 %, n = 438) for the known and unknown sample respectively.

Table 1. shows the deviations of the laboratory means from the national mean (bias), intralaboratory coefficients of variation and correlation coefficient between known and unknown samples for glucose. Table 2. shows the corresponding results for creatinine. The mean day-to-day coefficient of variation of serum glucose were 2.7 and 3.1 % for the known and unknown samples, respectively. Corresponding figures for serum creatinine were 2.6 and 2.9 %.

When the results of each laboratory were calculated separately for the two months, there were quite small differences in the monthly mean values. For glucose the medians of the differences of monthly means were 1.2 and 0.8 %, and for serum creatinine 1.2 and 0.9%, for known and unknown samples, respectively. In serum glucose assays, significant differences (t-test, two-tailed, $p < 0.05$) was observed in four cases. In creatinine assays the differences of the monthly means of both samples were significant ($p < 0.001$) in two laboratories. The monthly coefficients of variation differed considerably. In glucose asssays the differences in CVs were 1.04 to 2.4 fold, in creatinine 1.0 to 2.1 fold. In glucose assays the differences were statisticaly significant (F-test, two-tailed, $p < 0.05$) in three and two cases, for known and unknown samples, respectively. In creatinine assays, the differences in monthly CVs were significant in two cases, both in the known and in the unknown sample.

Tables 1 and 2. Total number of results (n), number of results $\geq$ 3 s from the laboratory mean, deviation of the laboratory mean from the national mean (Bias %) and day to day coefficient of variation (CV %) of the central hospital (CH) and 12 health center laboratories during two months. r = Pearsons correlation coefficient between results of known and unknown samples. The results of laboratories are ranked according to the CV % for the known sample.

Table 1. Glucose

	Known sample			Unknown sample				
Lab	**n**	**(>3s)**	**Bias %**	**CV %**	**N**	**(>3s)**	**Bias %**	**CV %**	**r**	**p**
CH	208	(3)	-2.4	2.5	208	(1)	-0.1	2.5	0.475	<0.001
07	42		-1.1	1.7	42		+1.0	2.9	0.285	NS
09	23		-0.6	1.9	23		+1.3	2.5	0.166	NS
10	42	(2)	-2.8	2.0	42		-0.1	2.0	0.154	NS
12	41		-1.7	2.3	41		+1.2	3.6	0.647	<0.001
04	42		-0.2	2.3	42	(2)	+3.7	2.9	0.304	NS
11	41		-3.1	2.5	41	(1)	+0.4	1.9	0.084	NS
05	42	(1)	-2.2	2.5	42	(1)	+1.4	3.2	0.495	<0.001
06	43		-1.8	3.2	43		+1.2	3.5	0.590	<0.01
01	42		-0.1	3.3	42		+1.4	3.3	0.440	<0.05
03	41		-0.4	3.6	41	(1)	+2.4	3.7	0.375	<0.05
02	38		-2.0	3.8	38		-0.2	3.7	0.809	<0.001
08	33	(1)	+2.4	3.8	33	(1)	+4.5	3.4	0.794	<0.001

Table 2. Creatinine

	Known sample			Unknown sample				
Lab	**n**	**(>3s)**	**Bias %**	**CV %**	**N**	**(>3s)**	**Bias %**	**CV %**	**r**	**p**
CH	144	(1)	+1.2	3.1	144	(1)	+0.1	2.6	0.401	<0.001
09	25		-0.7	1.0	25	(1)	-2.4	2.1	0.372	NS
12	42		+0.4	1.7	42		+0.4	1.8	0.283	NS
11	34		+0.8	2.0	34	(1)	+0.1	2.1	0.139	NS
04	42		+1.6	2.1	42		+5.0	2.5	0.430	<0.01
05	41		-0.2	2.3	41	(2)	+3.5	2.8	0.295	NS
03	42	(2)	+1.3	2.4	42	(1)	+3.8	3.0	0.658	<0.001
02	32	(2)	-1.7	2.4	32		0.0	2.6	0.584	<0.001
01	40	(3)	-2.1	2.8	40	(1)	-0.8	3.4	0.607	<0.001
10	17		-0.6	2.8	17		+1.1	2.8	0.001	NS
06	43		+2.9	3.5	43		+5.7	3.9	0.739	<0.001
07	42		-3.3	4.3	42		-2.2	3.7	0.532	<0.001
08	38		+2.2	4.3	38		+7.5	3.9	0.474	<0.01

DISCUSSION

The sources of total variation in clinical samples may not be similar in the primary care to those in hospitals. There might be differences in intraindividual biological variation. The preanalytical variation is presumably larger in outpatients. The analytical variation may also be larger in health center laboratories due to manual methods . However, the quality goals for precision and accuracy should be on the level that enable adequate monitoring of the patiens, and the use of same reference intervals at all levels of health care.

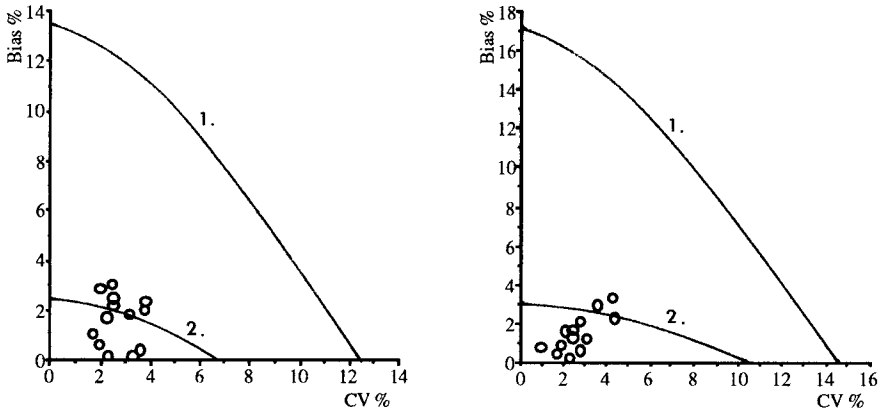
The proposed analytical goal for imprecision, i.e. not more than half of the within subject biological variation 4.4 %, for glucose and creatinine (1), appear realistic for most health center laboratories. Three to four of the 12 health center laboratories reached the analytical goal of 2.2 % and in about two-thirds of the laboratories the CV:s were less than 3 %. Some of the laboratories should improve their performance to acchieve this goal for precision. This study shows that a period of one month may be too short for assessing the true performance of small health center laboratories. There are too few results and thus even minor variations in technical performance of manual methods may cause differences in analytical variation between the periods. Also the significant correlation between the results of known and unknown sample probably indicates slight systematic variations, due e.g. to calibration process. Data should be accumulated over extended periods for assessing the performance of laboratories.

The analytical performance in the health center laboratories seems to be mostly adequate, if the results of this study are compared with the clinical decision limits, as reported e.g. by Scendzel et al. (2) and are shown as line 1. in Fig. 1. However, as discussed by Fraser et al. (3), the reported clinical decision limits generally do not take into consideration different confidence levels required in various clinical situations.

The goal for total analytical error that is based merely on intraindividual biological variation seems to be much more difficult to achieve. The maximum allowable bias between two methods, that allow optimal patient monitoring, is one-third of the within-subject biological variation, which is 1.4 % for glucose and creatinine (4). Common reference intervals can be used in laboratories, which fulfill appropriate analytical performance. Gowans et al (5) have suggested such criteria. Provided no bias exists, the

maximum allowable imprecision is 0.6 of total biological variation. Maximum allowable bias, provided no imprecision exists, is 0.25 of total biological variation (Line 2. in Fig. 1.)

The bias in the known sample ranged from -3.1 to +2.4 % and -3.4 to +2.9 % of the national means in serum glucose and creatinine, respectively. The bias in the unknown sample, expressed in presentage of the national mean obtained in a quality control survey, ranged from -0.2 to +4,5 % and -2.4 to +7.5 % for glucose and creatinine, respectively. Animal sera were used in this study, which might not necessarily give a correct estimate. E.g. the high bias of creatinine obtained in some laboratories was later recognized to be a matrix effect. Native patient samples with different concentrations should be preferred in the evaluation of the regional transferability.



Glucose Creatinine

Figure 1. The coefficient of variation and the bias of the known sample for glucose and creatinine in each laboratory combined. Line 1. represents the maximum clinical error limits based on report of Scendzel et al (2), calculated for one point testing ($p < 0.05$) (6). Line 2. is calculated according to proposed goals fo acceptance of common reference interval (5), the total biological CVs calculated using the reference interval of 3.5 - 5.5 mmol/l for fasting glucose and 55 - 115 umol/l for creatinine.

Central hospitals have a responsibility of supervising the quality assurance of the primary care laboratories in Finland. The test menu, which can be done in health center laboratories is most often agreed between hospital and primary care laboratories. Test menus should be decided according to clinical needs as well as according to quality specifications for different laboratory tests. Glucose and creatinine are examples of

analyses having quite a narrow intraindividual biological variation, thus demanding high quality method for analysis. The quality goals for other components, e.g. enzymes are not so strict. They are quite easily reached even in small laboratories. Some other commonly used tests, especially calcium, should probably always be centralized in hospital laboratories, to quarantee the necessary analytical quality.

CONCLUSION

The performance of primary health care laboratories is necessarily not much worse than in hospital laboratories. It seems possible to apply commonly agreed analytical goals, and error limits based on clinical needs also in primary care laboratories. However, also in small laboratories it is most important to use robust analytical methods with high accuracy, and to keep the imprecision as low as possible. That is the only means for effective error detection in the internal quality control using simple quality control rules based on statistical calculations.

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