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Some data about laboratory bias

Last year, the CSCQ organised a clinical chemistry external quality assessment (EQA) survey with a commutable serum sample in which the concentrations of six analytes were assessed by reference methods (assigned value, table 1). The CSCQ performed the usual statistics and evaluations based on the consensus values and sent the report to the laboratories. The report included the assigned values as well, so that each participant was able to compare the reported results with the expected ones. The results of this survey coupled with the commutability and the reference values made it possible to get additional information, mainly the calculation of the bias [1]. The bias is a component of the total laboratory error and corresponds to the distance between the "true" value (as measured by the reference method) and the result obtained by the laboratory with its routine analytical system. This study aims at summarising and discussing the laboratory biases.

Methods and results

The frozen commutable samples were purchased from the LNE (Laboratoire National de Métrologie et d'Essais, Paris, France, ISO 15195 and ISO 17025 accredited) and sent in dry ice to the 250 participating laboratories during the spring 2015 EQA survey (15-05-CH).

Each participating laboratory kept the sample frozen before analysing it like any patient sample with its routine analytical system, and returned the results to the CSCQ. Hospital and private laboratories obtained the results with large analytical systems, while medical offices chiefly used small analytical systems and Targa devices. For each result, the CSCQ calculated the bias (in %) according to the corresponding assigned value. For each analyte, the biases were first grouped by analytical systems (peer groups), and then the median bias (MB) of each peer group was calculated. Finally, the biases were compared with the Westgard desirable specification for analytical bias (table 1) available online [2]. For each analytical system and analyte, the percentage of biases that were included in the desirable analytical bias range (DABr) was calculated.

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In order to illustrate the percentage of biases included in the DABr, the «+» symbol was used: + was assigned to 1–25% of biases that fell inside the DABr, ++ to 26–50%, +++ to 51–75, and ++++ to 76–100%. When all the biases were outside the DABr, a 0 (zero) was assigned. Table 2 shows the data from large analytical systems, and table 3 those from small analytical systems.

Discussion

Although the bias is an important component of the total laboratory error [3], few studies dealt with it. The CSCQ organised this specific EQA survey to allow the quantification of laboratory biases in field conditions. Most small analytical systems obtain bigger MB and lower percentages of biases inside the DABr, even if, in some cases, very good performances are observed. When the desirable analytical bias is low (for glucose and creatinine), many analytical systems (both small and large) have low percentages of biases inside the DABr (i.e. the large number of + and ++ results). It is interesting to observe that even if some analytical systems have a MB close to zero, they could have a low percentage of biases within the DABr. This indicates a wide result dispersion, with many biases being too high and many others too low. Some biases are as high as 20%, and can even reach 40%, which could potentially affect the clinical decision. Another observation is that, for a given analytical system, the MB and the percentage of biases within the DABr are different for the six analytes. This suggests that the biases not only depend on the analytical system but also on the analyte considered. Additional information regarding the distribution of the results (min, max, CV) and individual biases (graphs) is available on our EQAcom website (for CSCQ members only). Two facts account for these findings: first, the individual laboratory variability (technician, reagent lot, calibration), and second, the assay standardisation by the manufacturer. Both of them should be improved in order to reduce the analytical bias, as already suggested [4, 5].

However, the conclusion of this work cannot be generalised at this stage. Indeed, the commutability was demonstrated by the LNE with large analytical systems only. Second, the MB calculated for each peer group of devices is based on a single survey, with a limited number of results, and in a limited period of time (May 2015). Third, the results reported by Targa devices were obtained with reagents from different manufacturers, thus adding variability. Finally, this paper does not include the results obtained by glucometers since the latter are not primarily designed to measure serum glucose, but blood glucose; nevertheless, these results are available in our EQAcom member area.

Further similar studies should thus be conducted to have a clearer picture of the laboratory biases. Unfortunately, it might be difficult due to the high logistic requirements and costs it implies.

Conclusions

This survey proves to be very interesting to assess the analytical biases of six analytes with several types of analytical systems used in the laboratory routine. It shows that the MBs of the small analytical systems are often big-

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Analyte	Assigned value	Desirable analytical bias
S-Glucose	11.898 ± 0.165 mmol/L	± 2.34 %
S-Creatinine	550.54 ± 6.12 µmol/L	± 3.96 %
S-Triglyceride	1.607 ± 0.047 mmol/L	± 9.57 %
S-Cholesterol, total	5.934 ± 0.127 mmol/L	± 4.10 %
S-Cholesterol, HDL	1.531 ± 0.053 mmol/L	± 5.61 %
S-Cholesterol, LDL	3.518 ± 0.126 mmol/L	± 5.46 %

Table 1: Assigned values from the LNE and desirable analytical bias from Westgard.

		Architect 4000, 8000	Beckman Coulter AU	Cobas 6000, 8000	Cobas Modular	Dimension EXL, Vista, X Pand	Integra 400, 800	Synchron UniCel DxC 600, 800	Targa
Glucose	N	11	7	40	8	16	42	14	-
	MB	+2.5	+0.9	–1.7	–1.7	+0.1	–0.8	–3.3	-
	P	++	++++	+++	++	++	+++	++	-
Creatinine	N	11	-	18[a]; 21[b]	-	16	11[a]; 33[b]	15	-
	MB	+2.1	-	–0.9[a]; –4.3[b]	-	+1.0	–2.3[a]; –8.8[b]	–1.0	-
	P	+++	-	++++[a]; ++[b]	-	++++	+++[a]; +[b]	++++	-
Triglyceride	N	9	-	39	8	9	37	14	7
	MB	–1.1	-	–3.5	–6.7	–4.2	–2.3	+0.5	–0.4
	P	++++	-	++++	++++	++++	++++	++++	++
Total cholesterol	N	9	-	40	8	14	37	15	7
	MB	+4.5	-	+1.1	–0.2	–3.9	+2.8	+0.9	+1.8
	P	++	-	++++	++++	++	+++	++++	+++
Cholesterol HDL	N	9	-	38	8	14	35	14	7
	MB	+11.0	-	–8.6	–2.0	–2.0	–4.6	+2.2	+11.0
	P	+	-	++	+++	++++	+++	++++	++
Cholesterol LDL	N	8	-	28	8	8	27	12	-
	MB	–0.5	-	+6.9	+3.2	+0.5	+6.0	+3.0	-
	P	++++	-	++	++++	++++	++	+++	-

Table 2: Large analytical systems. MB: median bias (%); P: percentage of biases in the DABr (desirable analytical bias range): 0 (0%), +(1–25%), ++(26–50%), +++(51–75%), and ++++(76–100%); [a]PAP; [b]Jaffe

		Fuji dri-chem	Reflotron	SpotChem D-Concept	SpotChem EZ SP 4430	SpotChem SP 4410, 4420
Glucose	N	10	34	8	8	10
	MB	–3.3	–5.0	–3.3	+3.4	–1.2
	P	++	+	++	++	++
Creatinine	N	10	41	8	8	9
	MB	–1.0	+5.9	–7.4	–14.0	–12.6
	P	++++	++	+	+	+
Triglyceride	N	10	27	8	7	7
	MB	+4.5	–12.9	+4.9	–5.4	–9.8
	P	++++	++	++++	++++	++
Total cholesterol	N	11	30	8	7	10
	MB	+4.8	+0.2	–0.2	+0.9	+3.6
	P	++	++++	+++	++	++
Cholesterol HDL	N	10	18	8	7	7
	MB	+3.5	–22.3	–11.2	–8.6	–13.8
	P	+++	0	0	++	+

Table 3: Small analytical systems. For the legend, see table 2.

ger than those of the large analytical systems and that many results (obtained either by small or large analytical systems) have high biases, outside the DABr. Such biases could potentially mislead the clinical decision. Efforts should be made to reduce the individual laboratory variability and to improve the assay standardisation.

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Einige Daten über Laborabweichungen

Das Schweizerische Zentrum für Qualitätskontrolle (CSCQ) hat einen Ringversuch zur externen Qualitätskontrolle (EQA) mit einer austauschbaren Probe organisiert, in der die Konzentration von sechs Parametern (Glukose, Kreatinin, Triglyzeride, Gesamtcholesterin, HDL- und LDL-Cholesterin) mithilfe von Referenzmethoden gemessen wurde (festgelegter Referenzwert). 250 Laboratorien (Privat, Spital und Arztpraxis) übermittelten ihre Ergebnisse.

Nach Berechnung der Abweichung jedes Ergebnisses vom Referenzwert wurden die Abweichungen nach Analysesystem gruppiert (klein und gross) und die mittlere Abweichung berechnet. Diese ist bei kleinen Analysesystemen oftmals höher als bei grossen. Alle Abweichungen wurden mit der anzustrebenden analytischen Abweichung verglichen. Mehrere Ergebnisse – sowohl von kleinen als auch von grossen Systemen – liegen ausserhalb dieses Toleranzbereichs und können möglicherweise zu einer falschen klinischen Entscheidung führen. Die Variabilität zwischen den Laboratorien sollte deshalb reduziert und die analytische Standardisierung angepasst werden.

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