LETTER TO THE EDITOR

An Improvement on the Criterion of the State of the Art to Estimate the Maximal Allowable Imprecision

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Sir,

Repeatability is one of the more important metrological properties that characterizes a measurement procedure. In clinical laboratory sciences imprecision is the metrological property usually used to represent repeatability, because the former is directly related to the value of the metrological coefficient of variation.

One criterion recommended (1, 2) for establishing the maximal allowable imprecision is derived from the biological variability data. According to this criterion, the metrological coefficient of variation must be equal to or less than one-half of the within-subject biological coefficient of variation. When information about biological variability is not available, or when current procedures give better results for imprecision than the goals set with this criterion, the so-called "state of the art" criterion is generally used. According to this criterion, the maximal allowable imprecision for physiological concentrations must be less than the 0.20 fractile of the between-run imprecision (CV) of the laboratories in an external quality assessment scheme.

The use of this criterion has already been refused for various reasons. One reason is that maximal allowable imprecision obtained with this criterion changes with time, owing to technological improvements. Another objection is that in some external quality assessment schemes the between-run coefficient of variation is calculated from a very small number of data, and these data are obtained from three or four control materials of different values (3). In this letter we present a further argument against the way in which the "state of the art" is currently used as criterion to establish the maximal allowable imprecision.

Coefficients of variation corresponding to between-day imprecision from the laboratories included in two external quality assessment schemes (International Chemistry Programme Dade and Q.C.S. Boehringer Mannheim) have been used. From these data, the 0.20 fractiles in each scheme have been calculated for each quantity. Only quantities whose values are within the physiological range have been considered. Quantities have also been chosen from assessment schemes involving more than ten participant laboratories, in which each laboratory was sent more than twenty results.

For each quantity the two 0.20 fractiles (one for each scheme) have been compared using an appropriate statistical test (4). The 0.20 fractiles obtained in the two schemes are shown in table 1. The comparison fractile statistical test shows significant differences (α = 0.05) for each quantity.

We cannot establish with certainty the origin of the differences observed between fractiles. This could be due to the heterogeneity of the measurement procedures between schemes or to the different number of laboratories participating in each one.

Considering that different external quality schemes produce different 0.20 fractile values, the maximal allowable imprecision established using the criterion of the "state of the art" will depend on the external quality scheme used for its estimation. The fact that different maximal allowable imprecision values can be estimated (one for each scheme), and that information about these values is not available to every laboratory, are objections to the way in which the "state of the art" is currently used.

This problem could be solved if the 0.20 fractile values were made available from as many external quality schemes as possible. If the 0.20 fractile values from the different schemes were known, the criteria for estimating only one maximal allowable imprecision value from all these fractiles might be established, and the resulting value would not depend on one scheme only. This unique value could be the mean or the median of these fractiles or just the smallest 0.20 fractile, i.e. the most restrictive.

Thus, it would be convenient if the 0.20 fractile values from each external quality scheme were published by their organisers.

Tab. 1 0.20 fractile values ($x_{0.20}$) of the between-day metrological coefficient of variation of measurement procedures for serum quantities from the laboratories included in two external quality assessment schemes (Dade and Boehringer Mannheim (BM))

<table>
<thead>
<tr>
<th>Serum component</th>
<th>$x_{0.20}$ Dade (%)</th>
<th>$x_{0.20}$ BM (%)</th>
<th>nBM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin esterified</td>
<td>9.85</td>
<td>3.01</td>
<td>80</td>
</tr>
<tr>
<td>Protein</td>
<td>1.70</td>
<td>1.15</td>
<td>95</td>
</tr>
<tr>
<td>Phosphate non-esterified</td>
<td>3.40</td>
<td>2.11</td>
<td>80</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>1.90</td>
<td>1.68</td>
<td>145</td>
</tr>
<tr>
<td>Potassium ion</td>
<td>1.40</td>
<td>1.28</td>
<td>30</td>
</tr>
<tr>
<td>Iron (II + III)</td>
<td>2.60</td>
<td>1.85</td>
<td>64</td>
</tr>
<tr>
<td>Chloride</td>
<td>1.60</td>
<td>1.05</td>
<td>150</td>
</tr>
<tr>
<td>Calcium (II)</td>
<td>1.80</td>
<td>1.30</td>
<td>80</td>
</tr>
<tr>
<td>Urea</td>
<td>3.00</td>
<td>1.86</td>
<td>80</td>
</tr>
<tr>
<td>Urate</td>
<td>2.80</td>
<td>1.74</td>
<td>80</td>
</tr>
<tr>
<td>Glucose</td>
<td>2.30</td>
<td>1.75</td>
<td>150</td>
</tr>
<tr>
<td>Triacylglycerols</td>
<td>2.50</td>
<td>1.75</td>
<td>80</td>
</tr>
<tr>
<td>Sodium ion</td>
<td>0.90</td>
<td>0.77</td>
<td>124</td>
</tr>
<tr>
<td>Magnesium (II)</td>
<td>4.00</td>
<td>2.19</td>
<td>75</td>
</tr>
</tbody>
</table>

n = number of data
References


Received January 24, 1996

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LETTER TO THE EDITOR

Serum Dipeptidyl Peptidase IV Activities in Czernobyl Zone Inhabitants Exposed to the Power-Station Catastrophe

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Sir,

Dipeptidyl peptidase IV is widely distributed in various mammalian cells and tissues. It is thought to be involved for example in complex processes of cell adhesion, signal transduction and cell activation/differentiation (1). However, dipeptidyl peptidase IV also has soluble counterpart in blood plasma, which is speculated to be either a product of a single gene, perhaps allowing alternative splicing, or a product of a second dipeptidyl peptidase IV gene (2). Recently, both cellular as well as blood plasma dipeptidyl peptidase IV forms have been shown to be important regulators of the immune response (3).

We tested dipeptidyl peptidase IV activity in blood sera from inhabitants living in the zone between 30 and 60 km from the Czernobyl power-station. Only persons without apparent clinical pathology and subjective complaints at the time of blood collection were involved in this study. They were examined four (31 persons, group 1) and eight (40 persons, group 2) years after the nuclear catastrophe. All subjects had lived in the same zone for four years. Due to administrative problems in the region, only eight persons are common to both tested cohorts. Serum samples from healthy blood donors, living 1000 km from Czernobyl were used as controls (46 persons). Dipeptidyl peptidase IV activity was measured by a fluorometric method according to Schrapé (4), modified for a microplate reader, with glycyl-prolyl-7-amino-4-methylcoumarin as the substrate. A set of routine clinical biochemistry assays (alanine aminotransferase, aspartate aminotransferase, γ-glutamyltransferase, alkaline phosphatase, bilirubin) was used to exclude patients with concomitant hepatic diseases. Since experimental data were normally distributed, t-test was used for statistical comparisons.

The results are summarised in figure 1. Serum dipeptidyl peptidase IV activity in patients four years after the catastrophe was significantly increased (mean = 2443 nkat/l; ranges: 506—3481 nkat/l; SD = 1014 nkat/l; p < 0.0001) when compared with controls (mean = 640 nkat/l; ranges: 399—828 nkat/l; SD = 68 nkat/l). However, after a further four years, the dipeptidyl peptidase IV serum activity of Czernobyl district inhabitants was considerably decreased, and was even lower than that in the control group (mean = 463 nkat/l; ranges: 326—799 nkat/l; SD = 88 nkat/l; p < 0.0001).

Blood serum dipeptidyl peptidase IV activity is believed to be a non-specific marker of immunological status. It has been previously reported that serum dipeptidyl peptidase IV activity is significantly decreased in patients with various solid and blood cancers (5), in immunosuppressed patients (6), pregnant women (7) and in major depression, also probably as a result of immune system disregulation (8). An increase of dipeptidyl peptidase IV serum activity during successful therapy of cancer patients has been reported (9). In contrast, increased dipeptidyl peptidase IV serum activities have been reported in patients with hepatobiliary diseases, including hepatic cancers (5), in some autoimmune diseases (10, 11), hyperthyreosis (12) and prior to transplant rejection (10). Unfortunately, it is difficult to attribute the serum dipeptidyl peptidase IV activity changes observed in our study by any particular mechanisms; immune system markers as well as thyroidal status in the studied population were not tested. We will continue our studies, particularly with regard to the cancer incidence in patients with decreased dipeptidyl peptidase IV activity.

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1) Funding: This work was supported by the Grant Agency of Czech Republic, grant No 303/93/0541
2) Enzymes:
   - Alanine aminotransferase; (EC 2.6.1.2); L-Alanine : 2-oxoglutarate aminotransferase
   - Alkaline phosphatase; (EC 3.1.3.1); Orthophosphoric-monooester phosphohydrolase (alkaline optimum)
   - Aspartate aminotransferase; (EC 2.6.1.1); L-Aspartate : 2-oxoglutarate aminotransferase
   - Dipeptidyl peptidase IV; (EC 3.4.14.5); Dipeptidyl-peptide hydrolase IV
   - γ-Glutamyltransferase; (EC 2.3.2.2); (5-Glutamyl)-peptide : amino-acid 5-glutamyltransferase
Acknowledgements

This work was supported by the Grant Agency of Czech Republic, grant No 303/93/0541.

References


Received January 22, 1996

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