Harmonisation of SEBIA Capillarys CDT results according to WG-CDT recommendations

Anders Helander[1,2] **& Helen Dahl**[2]

[1] *Department of Laboratory Medicine, Karolinska Institutet, Stockholm, Sweden.*

[2] *Department of Clinical Chemistry, Karolinska University Laboratory Huddinge, Stockholm, Sweden.*

Background

Carbohydrate-deficient transferrin (CDT) is a specific serum biomarker for long-term alcohol overconsumption. Drawbacks in CDT testing are that routine methods differ in their definition of the measurand ("CDT") and hence in reference intervals, which prompted initiation of an IFCC Working Group on CDT Standardisation (WG-CDT) (1).

This study examined the possibility to harmonize CDT results of the SEBIA Capillarys CDT method according to WG-CDT recommendations (1-4), using high-performance liquid chromatography (HPLC) as the candidate reference method.

Methods

The study involved in total 525 serum samples, including 60 with genetic transferrin variants, congenital disorder of glycosylation, or samples showing chromatographic interferences. The samples originated from the routine HPLC analysis of CDT (i.e. relative amount of disialotransferrin glycoform values; %DST) at the Karolinska University Laboratory in Stockholm (Sweden). The serum samples were analysed in parallel by the SEBIA Capillarys capillary electrophoresis (CE) assay on a Capillarys-2 system.

Results

There was good overall correlation between the %DST results obtained by SEBIA CE and HPLC (R^2=0.91. p<0.0001), but the CE values were on average 0.5% lower over the entire measuring range (Fig. 1).

Using the regression equation between the two methods, the CE %DST results were adjusted ("harmonised") to corresponding HPLC %DST equivalents (Fig. 2). At a cut-off of 1.9% DST, which is routinely used in Sweden (= mean+3SD/upper limit of reference interval), the harmonised CE values showed good agreement (sensitivity 90%, specificity 99%) with the measured HPLC values (Fig. 2).

A closer evaluation of the deviating ("false positive" or "false negative") results revealed that almost all of those showed %DST values close to the cut-off (Table 1), suggesting CE and HPLC method imprecision as a main cause.

The method imprecision of the SEBIA Capillarys CE assay was ≤6% near or above the cut-off. For a few samples, quantification of %DST was not possible by CE due to analytical interferences, but in these cases the HPLC method usually provided good results.

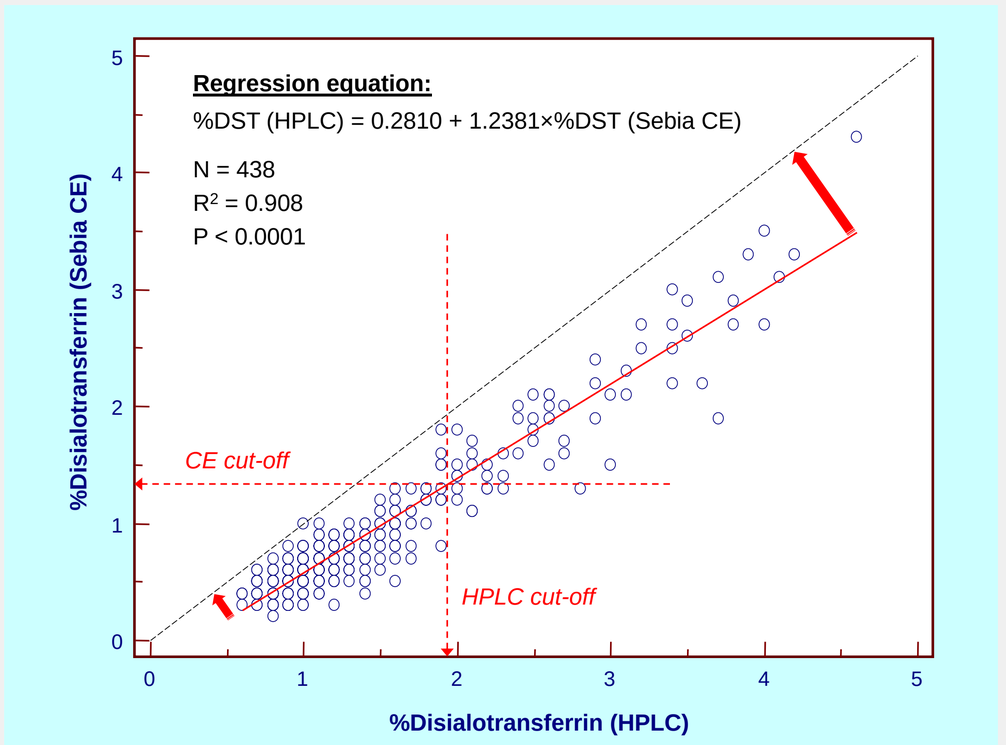

Fig. 1. Comparison of CDT (%disialotransferrin; %DST) results by SEBIA Capillarys CE capillary electrophoresis assay and by HPLC (for values <5%).

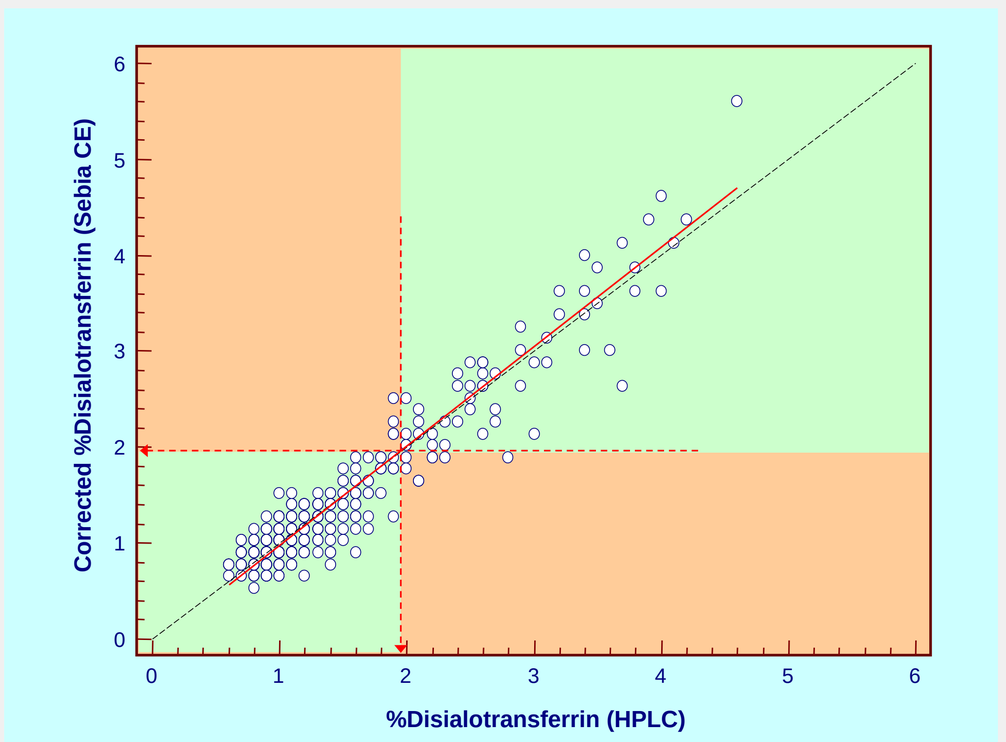

Fig. 2. Comparison of corrected CDT (%DST) values by SEBIA Capillarys CE capillary electrophoresis assay (using the equation in Fig. 1) and HPLC values.

"False positive" corrected Sebia CE	
HPLC	**Corrected Sebia CE**
1.9	2.1
1.9	2.1
1.9	2.3

"False negative" corrected Sebia CE	
HPLC	**Corrected Sebia CE**
2.2	1.9
2.2	1.9
2.1	1.6
2.0	1.8
2.3	1.9
2.0	1.9
2.1	1.6
2.7	1.9

Table 1. The "false positive" and "false negative" corrected SEBIA CE CDT (%DST) results, relative to HPLC as the reference method, were mainly due to analytical imprecision at levels close to the cut-off.

References

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Conclusions

The results demonstrated good linearity and reproducibility of CDT values by the SEBIA Capillarys CDT assay when analysed in parallel with HPLC. The results further demonstrated that routine harmonisation of SEBIA Capillarys CDT (%DST) results by way of the IFCC WG-CDT recommendation is feasible. This harmonisation strategy aims for comparable results and use of the same reference interval (cut-off), irrespective of the CDT method used. The present results further pointed at the importance of having access to HPLC as confirmative CDT method, in the few serum samples showing analytical interferences in the SEBIA Capillarys CE assay.

Karolinska University Laboratory Huddinge
C1:74. Clinical Chemistry
SE- 141 86 Stockholm. Sweden
E-mail: anders.helander@ki.se

Karolinska Institutet | KAROLINSKA Universitetssjukhuset