RESPONSE TO COMMENT ON LI ET AL.

Visual Inspection of Chromatograms Assists Interpretation of HbA_{1c}: A Case Report. Diabetes Care 2018;41:1829–1830

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We thank Li et al. (1) for their interest in our case report (2), which emphasized the value of visual inspection of chromatograms in clinical practice to assist interpretation of HbA_{1c}.

For consistency and comparability with the first and only available report, by Wajcman et al. in 1992 (3), we presented the identified mutation as c.242T>A, p.Leu81His (rs33936967), without including the translational initiation codon in variant sequence numbering. According to the latest nomenclature recommendations of the Human Genome Variation Society in 2007 (4), starting with number 1 at the A of the ATG for nucleotides and at the methionine encoded by the translational initiation codon for protein-level amino acids, this variant is named c.245T>A, p.Leu82His, but not c.245T>A, p.Leu81His.

We agree with Li et al. (1) that different assays and different kits of the same assay for HbA_{1c} measurement could have diverse interferences from different hemoglobin variants, as summarized by NGSP (5). However, the interference from rare hemoglobin variants should not be the sole criterion used to evaluate the clinical value of an assay or a kit, and the comparison of different measurement methods is beyond the scope of our case report. In the presence of rare variants, such as the Hb La Roche-sur-Yon variant in our reported patient, the HbA_{1c} assay interference is hardly predictable and a case-by-case interpretation of the results is necessary. If the measured HbA_{1c} level in our case had not been beyond the commonly observed range in clinical practice, this variant and the consequent interference would likely have been neglected. This fact raised our concern about the identification of cases with milder interference, and we thereby demonstrated the effectiveness and feasibility of visual inspection of the chromatogram for identifying some potential interferences. Nevertheless, it should be clarified that normal chromatograms do not guarantee the accuracy of HbA_{1c} measurements, while abnormal chromatograms indicate the possibility of interference with measurements, under which circumstances a repeat measurement using a different assay is warranted.

In summary, the diagnostic process of our case suggested the value of visual inspection of high-performance liquid chromatography chromatograms to help identify inaccurate HbA_{1c} measurements that were interfered with by hemoglobin variants, with no additional cost. However, our case provided little evidence regarding the selection of an assay or kit for HbA_{1c} measurement.

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References

1. Li J, Lei J, Xu A-p, Xia Y, Ji L. Comment on Li et al. Visual inspection of chromatograms assists interpretation of HbA_{1c}: a case report. Diabetes Care 2018;41:1829–1830 (Letter). Diabetes Care 2019;42:e9. DOI: 10.2337/dc18-1836
2. Li Q, Xiao Y, Shah AD, Li S. Visual inspection of chromatograms assists interpretation of HbA_{1c}: a case report. Diabetes Care 2018;41:1829–1830
3. Wajcman H, Kister J, Vasseur C, et al. Structure of the EF corner favors deamidation of asparaginyl residues in hemoglobin: the example of Hb La Roche-sur-Yon [β81 (EF5) Leu→His]. Biochim Biophys Acta 1992;1138:127–132
4. Ogino S, Gulley ML, den Dunnen JT, Wilson RB; Association for Molecular Pathology Training and Education Committtee. Standard mutation nomenclature in molecular diagnostics: practical and educational challenges. J Mol Diagn 2007;9:1–6
5. NGSP. HbA1c assay interferences [Internet], 2017. Available from http://www.ngsp.org/interf.asp. Accessed 14 September 2018

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