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SCIENTIFIC LETTERS

Interference of Hb D-Los Angeles on the measurement of glycated hemoglobin. A case report

Interferencia en la medida de la hemoglobina glicada en presencia de Hb D-Los Angeles. Presentación de un caso clínico

There are two techniques to assess the effectiveness of the management plan on glycaemic control: patient self-monitoring of blood glucose and glycated hemoglobin (HbA1c).[1] This last one reflects the average glycaemia along several months and it has a strong predictive value for diabetes complications.[2] However, the HbA1c test is subjected to certain limitations related to erythrocyte lifespan: hemolytic anemia, iron deficiency, blood transfusion, and hemoglobinopathies must be considered, particularly when the HbA1c result does not correlate with the patient's blood glucose levels.[1]

Mutations in genes encoding hemoglobin chains are present in about 7% of the worldwide population, and hemoglobinopathies are the more common single-gene genetic disorders in humans.[3] These genetic alterations can affect the production rate of globin chains and cause thalassemia, or they can modify the molecule structure and generate hemoglobin variants. Hemoglobin variants are usually the consequence of a single amino acid substitution caused by point mutations in genes encoding globin chains, resulting in a tetramer with different physicochemical characteristics. Most of the hemoglobin variants described do not cause symptomatic clinical manifestations.[3]

Hemoglobin D was first described in 1951. The most frequent denominations found in the literature for this mutant hemoglobin are hemoglobin D-Los Angeles or hemoglobin D-Punjab. Hb D-Los Angeles contains a substitution of glutamine for glutamic acid at position 121 of the beta globin chain [β121(GH4)Glu > Gln].[4] Hb D-Los Angeles is the fourth most often occurring hemoglobin variant worldwide. It is primarily found in the Punjab region of Pakistan and Northwestern India, with an estimated frequency of 2%, but is also common in persons from China, England, Holland, Australia, Greece, Yugoslavia, Turkey, etc. When Hb D-Los Angeles is inherited in heterozygous form does not present clinical or hematological alterations.[4]

A 77-year-old white man, native from San Pedro (Albacete, Spain), with a history of diabetes type 2 for over 25 years and treated with insulin for over 15 years, was attended in our outpatient department between 2004 and 2014. He also suffered from hypertension and hypercholesterolemia and he had history of myocardial infarction. His latest medications included byphasic insulin 30/70 three times a day, atorvastatin, olmesartan, amlodipine, hydrochlorothiazide, carvedilol and aspirin. Between 2007 and 2009, using the HA-8160 for the HbA1c assay, HbA1c levels were relatively low compared to those of serum glucose (Table 1). A further molecular study showed that the patient was heterozygous for Hb D-Los Angeles [β121 Glu > Gln; HBB: c.364 G > C].

The HbA1c measurement is highly method-dependent and it can be adversely affected by the presence of hemoglobin variants, which may be an incidental finding during the HbA1c analysis. An A1c deviation of 1% reflects a change of 1.4–1.9 mmol/L (25–34 mg/dL) in the average blood glucose concentration. Therefore, a falsely high or low HbA1c value caused by the presence of a clinically silent hemoglobin variant may lead to over- or under-treatment of diabetic patients. It has been reported a non-estimation or under-estimation of HbA1c fraction using the ADAMS A1c HA-8160 (Arkray, Kyoto, Japan) in the presence of Hb D-Los Angeles.[5–9] Nevertheless, the Variant II Turbo 2.0 (Bio-Rad Laboratories, Hercules, CA), our assay method for HbA1c since 2011, do not show any clinically significant interference in the presence of Hb D-Los Angeles trait.[10]

Table 1 HbA1c results and laboratory method.

Date	HbA1c (%/mmol/mol)	Glucose (mg/dL/mmol/L)	Laboratory method
October 2007	4.2/22.4	113/6.27	ADAMS A1c HA-8160
September 2008	4.5/22.7	140/7.77	ADAMS A1c HA-8160
April 2009	4.2/22.4	134/7.44	ADAMS A1c HA-8160
June 2012	7.7/60.7	136/7.55	Variant II Turbo 2.0
Jun 2014	6.1/43.2	91/5.05	Variant II Turbo 2.0

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In conclusion, to avoid reporting inaccurate results, laboratories should be aware of the limitations of their methods with respect to hemoglobin variants, and indicate this information in reports to physicians. On the other hand, physicians should consider the possibility of interference by an hemoglobin variant if a patient's HbA1c results is significantly different from what is expected on the basis of blood glucose self-monitoring.

References

1. American Diabetes Association. Glycemic targets. Diabetes Care. 2016;39 Suppl. 1:S39–46.
2. Stratton IM, Adler AI, Neil HAW, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000;321:405–12.
3. Giardine B, Borg J, Viennas E, Pavlidis C, Moradkhani K, Joly P, et al. Updates of the HbVar database of human hemoglobin variants and thalassemia mutations. Nuclear Acids Res. 2014;42. Database issue D1063–69.
4. De Souza L, Viviani J, da Silva DGH. Hemoglobin D-Punjab: origin, distribution and laboratory diagnosis. Rev Bras Hematol Hemoter. 2015;37:120–6.
5. Little RR, Roberts WL. A review of variant hemoglobins interfering with hemoglobin A1c measurement. J Diabetes Sci Technol. 2009;3:446–51.
6. Schnedl WJ, Lahousen T, Wallner SJ, Krause R, Lipp RW. Silent hemoglobin variants and determination of HbA1c with the high-resolution program of the HPLC HA-8160 hemoglobin analyser. Clin Biochem. 2005;38:88–91.
7. Little RR, Rohlfing CL, Hanson S, Connolly S, Higgins T, Weykamp CW, et al. Effects of hemoglobin E and D traits on measurements of glycated Hb (HbA1c) by 23 methods. Clin Chem. 2008;54:1277–82.
8. Lorenzo-Medina M, De La iglesia S, Ropero P, Martín-Alfaro R, Quintana-Hidalgo L. Interference of hemoglobin D on measurements of hemoglobin A1c by high-performace liquid chromatography HA-8160 in 27 patients. J Diabetes Sci Technol. 2012;6:1235–7.
9. Thevarajah M, Nadzimah MN, Chew YY. Interference of hemoglobin A1c detection using ion-exchange high performance liquid chromatography (HBPLC) method by clinically silent hemoglobin variant in University Malaya Medical Centre – A case report. Clin Biochem. 2009;42:430–4.
10. Rohlfing C, Hanson S, Weykamp C, Siebelder C, Higgins T, Molinaro R, et al. Effects of hemoglobin C, D, E and S traits on measurements of HbA1c by twelve methods. Clin Chim Acta. 2016;455:80–3.

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Catarata: una complicación precoz olvidada de la diabetes en la infancia y adolescencia

Cataract: A forgotten early complication of diabetes in children and adolescents

La catarata, definida como la opacificación del cristalino, es una de las afecciones más frecuentes en el individuo conforme va avanzando la edad. Según su localización se describen 2 tipos, nuclear y subcortical o capsular. La diabetes mellitus es la responsable de la quinta parte de todas las cataratas, aumentando la prevalencia de la subcortical de 2 a 5 veces en el paciente de cualquier edad, y hasta 20 veces si nos limitamos a los menores de 40 años[1]. La opacificación es resultado del efecto osmótico del exceso de sorbitol generado por la hiperglucemia y a mayor duración e intensidad de la misma antes se produce[1].

Nuestro objetivo es presentar 2 casos de catarata en niños con diabetes tipo 1 y recordar la existencia de esta importante complicación incluso en las edades pediátricas para hacer un diagnóstico y tratamiento precoz.

El primer caso es un varón prepúber de 12 años de edad y 10 de evolución de la diabetes con un pésimo control metabólico. Acudía muy irregularmente al hospital, casi exclusivamente en los episodios de cetoacidosis provocados por abandono del tratamiento insulínico, y sus niveles de hemoglobina glicada estaban en torno al 14% (el criterio de buen control de la diabetes en la infancia y la adolescencia es una glicada menor o igual al 7,5%)[2,3]. El segundo es una mujer de 13 años de edad y 6 meses de evolución de la diabetes, con desarrollo puberal completo y menarquia a los 11 años. En el momento del diagnóstico de la catarata la paciente se encontraba en fase de «luna de miel» (requerimiento de insulina de 0,2 U/kg/día) con un control metabólico óptimo (hemoglobinas glicadas 5,7 y 5,9%). El único periodo de hiperglucemia en su historia era el previo al diagnóstico, pues refería alrededor de 6 meses de clínica cardinal antes de recibir tratamiento insulínico y la glicada al inicio era del 14,5%.

El primer paciente fue remitido a oftalmología por la mala evolución de la diabetes, aprovechando un ingreso por cetoacidosis, mientras que la segunda acudió por propia iniciativa a un oftalmólogo privado, sin presentar ningún síntoma visual. En los 2 casos la exploración oftalmológica