Haemoglobin Hope and glycated haemoglobin: One peak may or may not hide the other, depending on the assay

Hémoglobine Hope et hémoglobine glyquée : un pic peut en cacher un autre selon la méthode de dosage utilisée

Keywords: Glycated haemoglobin; Haemoglobin variant; Capillary electrophoresis; High-performance liquid chromatography

Mots clés : Hémoglobine glyquée ; Variant de l’hémoglobine ; Électrophorèse capillaire ; Chromatographie liquide à haute performance

Haemoglobin A1c (HbA1c), or glycated haemoglobin, is the product of a non-enzymatic reaction of glycation and an important biochemical marker that is widely used to estimate long-term glycaemic control in diabetic patients. Given the average lifespan of red blood cells, this marker allows the evaluation of glycaemic control over the past 2–3 months as well as the future risk of developing diabetes-related complications.

Four methods — ion-exchange high-performance liquid chromatography (HPLC), boronate affinity HPLC, and immuno- and enzymatic assays — are currently classically used to measure HbA1c [1]. Recently, however, capillary electrophoresis was developed for the assessment of HbA1c and compared with the boronate affinity HPLC method, previously shown to be unaffected by the presence of haemoglobin variants [2]. The results revealed that the CAPILLARYS 2 Flex Piercing system (SEBIA, Lisses, France) did not interfere with any of the common haemoglobin variants tested [3].

Currently, in our biochemistry department, we use the ion-exchange HPLC method (VARIANT II A1c, BIO-RAD, Marnes-la-Coquette, France), which separates haemoglobin species based on the charge differences between HbA1c and other variants. Recently, we received a blood sample for measurement of HbA1c that was from a 35-year-old female patient, a native of Senegal, and found a peak of HbA1c that measured 46% on the chromatogram (Fig. 1). We therefore suspected the presence of an unusual haemoglobin variant migrating with HbA1c, as previously reported [4]. Information from the patient’s medical records indicated the presence of haemoglobin Hope in the heterozygous state (mutant beta globin: 136 Gly > Asp). Although the frequency of haemoglobin Hope is not clearly established, its presence has been described in several black, Japanese, Thai, Laotian and Cuban families. Although VARIANT II is known to use a method subject to little interference from other heterozygote common variants of haemoglobin [1], interference with haemoglobin Hope when using this assay has been described and can lead to misinterpretation of HbA1c [4,5].

![Fig. 1. HbA1c and haemoglobin Hope remain indistinguishable when using BIO-RAD VARIANT II A1c (left). In contrast, HbA1c and haemoglobin HOPE display separate, distinct peaks on capillary electrophoresis using the SEBIA CAPILLARYS 2 Flex Piercing analyzer (right).](image-url)
For this reason, we re-assayed the patient’s blood sample using a new capillary electrophoresis method (CAPILLARYS 2 Flex Piercing) for HbA1c. As shown in Fig. 1, despite being unable to measure HbA1c using this method (as was the case with VARIANT II), the peak corresponding to the haemoglobin variant was detectable on electrophoresis and, above all, differed from that corresponding to HbA1c.

In conclusion, we present here a case of haemoglobin Hope migrating at the level of the HbA1c peak when using a classical ion-exchange HPLC method, leading to an erroneous HbA1c value. In contrast, capillary electrophoresis was able to distinguish HbA1c from haemoglobin Hope. To the best of our knowledge, this is the first report of capillary electrophoresis measurement of HbA1c in a patient displaying haemoglobin Hope in the heterozygous state. While capillary electrophoresis was able to detect the unusual haemoglobin Hope variant, it did not permit assessment of HbA1c. However, other methods have been reported to be unaffected by the presence of haemoglobin Hope and could be used as alternatives in this context [4,5]. Finally, this case serves as a reminder that biologists and physicians need to be aware of the limitations of available techniques that measure HbA1c, especially in the presence of haemoglobin variants.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Acknowledgments

We thank SEBIA for giving us the opportunity to use the CAPILLARYS 2 Flex Piercing HbA1c analyzer.

References


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