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

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

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 immunoenzymatic 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).
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.

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References


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Severe hypertriglyceridaemia in patients treated with lipid-modifying agents

Hypertriglycéridémie sévère chez des patients sous traitement hypolipémiant

Keywords: Hypertriglyceridaemia; Cardiovascular disease; Antilipaemic agents; Europe

Mots clés : Hypertriglycéridémie ; Maladies cardiovasculaires ; Hypolipémiants ; Europe

1. Background

Few studies have been conducted among patients with severe hypertriglyceridaemia (shTG), and real-life management of this lipid disorder is not well established and remains poorly documented [1].

2. Objective

The demographic and medical characteristics of patients with treated but uncontrolled shTG, supervised by general practitioners from five European countries, were identified, and the therapies prescribed for their lipid disorders were analyzed.

3. Methods and findings

Data were extracted from the Cegedim Strategic Data Longitudinal Patient Databases (LPDs) from Belgium, France, Germany and Italy, and from The Health Improvement Network (THIN) database in the United Kingdom. LPD and THIN databases are electronic medical records. Currently, 2.9 million patients are registered with practices in THIN, 1.6 million in LPD France, 0.8 million in LPD Italy, 0.7 million in LPD Germany and 0.3 million in LPD Belgium. The study population comprised 303,290 patients, aged 18 years and over, with at