Capillary electrophoresis for the screening and diagnosis of inherited hemoglobin disorders. Ready for prime time?

DOI 10.1515/cclm-2015-0545

Inherited hemoglobin (Hb) disorders, also known as hemoglobinopathies, are conventionally classified into two main categories, which entail structural Hb variants (i.e. qualitative or functional disorders) and thalassemias (i.e. quantitative disorders, characterized by defective globin production). According to recent statistics, approximately 7% of the worldwide population carries an inherited Hb disorder, and up to 500,000 babies are born each year with severe forms of these conditions [1]. Inherited Hb disorders are characteristic of tropics and subtropics, but their prevalence is now constantly increasing around the globe due to migration [2]. It is hence predictable that the diagnosis and management of inherited Hb disorders will grow exponentially around the globe, especially in some countries of the south Mediterranean area (e.g. Italy, Greece and Spain), due to the fact that civil wars and oppressive regimes in the Middle East and Africa have forced an ever increasing number of people on a perilous journey to Europe.

In agreement with the guidelines of the British Committee for Standards in Haematology, the choice of methodology and equipment for the diagnostics of inherited Hb disorders should be based on a balanced combination of workload, biological material (i.e. blood or dried blood spots), analytical performance, local availability of instrumentation and personnel, expertise and costs [3]. Although the current armamentarium for the screening and diagnosis of hemoglobinopathies includes many techniques, such as cellulose acetate electrophoresis (CAE), isoelectric focusing (IEF), low-pressure liquid chromatography (LPLC), high-performance liquid chromatography (HPLC), tandem mass spectrometry (MS/MS), capillary zone electrophoresis (CZE) and even genetic analysis, the Committee concluded that MS/MS and CE may be suitable alternative to HPLC provided that acceptable analytical and clinical performances can be fully demonstrated. Five years after the publication of these universally adopted recommendations, reliable evidence has accumulated that CZE may be an accurate tool for the screening and diagnosis of Hb disorders. In this issue of the journal we publish two studies that substantially support this assumption.

In the former article, You-Qiong et al. analyzed 15 samples (13 adult blood samples and 2 cord blood samples) of patients heterozygous for Hb New York by using both CZE and HPLC [4]. Interestingly, all cases could be diagnosed with CZE, whereas none of them could be detected by HPLC, as the variant could not be separated from HbA using the local equipment. Although the optimal performance of CZE for screening and diagnosis of Hb disorders has been recently confirmed in other studies [5], the potential advantages of this technique extend beyond the boundaries of the analytical domain. One of the major drawbacks of most commercial HPLC analyzers is represented by the challenge of accurately measuring HbA1c in patients with hemoglobinopathies, especially in the presence of common Hb variants, such as HbC, HbS or HbF values >10–15% [6]. Nevertheless, two recent studies published in an earlier issue of this journal convincingly showed that this shortcoming may be at least in part overcome by CZE. Ji et al. measured HbA1c in blood samples of patients with a variety of Hb disorders, and concluded that thalassemia, HbE, HbG Coushatta, HbG Taipei and Hb Kaohsiung complicated HbA1c detection, whereas glycated Hb could be accurately measured using CZE [7]. As regards other common Hb variants, in another study Weykamp et al. evaluated the analytical interference of HbS, HbC, HbD, HbE, HbJ and HbG on HbA1c detection, whereas glycated Hb could be accurately measured using CZE [8], and also concluded that glycated Hb can be reliably measured with CZE.

In the second article published in this issue of the journal, Pornprasert et al. developed specific quality control materials for the analysis of some forms of thalassemia and Hb variants that are commonly observed in South-East Asia [9]. Interestingly, the Hb typing control materials could be stored and then accurately analyzed by
many commercially available techniques, including HPLC and CZE, thus representing a valuable resource for internal and external quality assurance in the diagnostics of hemoglobinopathies.

The use of CZE is now commonplace in clinical laboratories, due to the versatility of this technique for performing protein electrophoresis [10, 11] and immunotyping [12], as well as for the measurement of HbA1c [13] or carbohydrate-deficient transferrin (CDT) [14]. Despite the use of CZE has several practical advantages, such as positive sample identification, cap piercing and on-board sample mixing capabilities, avoidance of some manual steps and reduced turn-around time, as well as high throughput and reproducibility [15], some technical issues still plague its accuracy, which typically include falsely elevated HbA2 values in patients with HbC or issues still plague its accuracy, which typically include high throughput and reproducibility [15], some technical manual steps and reduced turn-around time, as well as board sample mixing capabilities, avoidance of some positive sample identification, cap piercing and on-the-use of CZE has several practical advantages, such as positive sample identification, cap piercing and on

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: None declared.

Employment or leadership: None declared.

Honorarium: None declared.

Competing interests: The funding organization(s) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

References


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