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Commentary

Converting haemoglobin A1c and average glucose. Time to change?

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Conflicting results of estimated average glucose (eAG) calculated from HbA1c and average glucose (AG) values derived from continuous glucose monitoring (CGM) are very frequent sources of confusion and frustration in the dialogue with persons who have diabetes.

The translation of HbA1c into eAG is described in the A1c-Derived Average Glucose (ADAG) study from 2008 [1]. A total of 507 persons including 268 with type 1 diabetes, 159 with type 2 diabetes and 80 without diabetes, were monitored for 12 weeks. AG was calculated from 39 days of monitoring with a seven-point self-measured profile (a mean of 5.1 tests per day) of finger-stick capillary glucose (no night measurement) and from 13 days with CGM. Available data included ~2500 CGM and 230 fingerstick measurements per subject. A linear regression A was: HbA1c (%) = 0.6289 × eAG (mmol/l) + 1.63. This equation has been adopted universally to guide healthcare providers and patients.

CGM provides insight into AG calculated from measurements made every 5 min. Discrepancy between AG and eAG often raises the question if the CGM results in an individual differ systematically from capillary glucose or if an altered erythrocyte life span compromises the interpretation of HbA1c.

The term glucose management indicator (GMI) was introduced in 2018 to describe HbA1c estimated from CGM-derived AG [2]. The regression equation was B: GMI (%) = 0.4309 × AG (mmol/l) + 3.31. This equation was derived from a pooled group of 528 individuals with diabetes monitored with CGM for a mean of 48 days (range 13–89 days). This corresponds to ~13,500 measurements per subject or approximately five times as many as in the ADAG study. In both studies, the proportion of subjects with HbA1c > 9% was sparse, and the validity of the equation for very poor control must therefore be limited.

The two regression equations A and B plotted in the same diagram crosses at a point corresponding to a glucose value of 8.5 mmol/l and an HbA1c or GMI of 7.0% (53 mmol/mol) (Fig. 1). The ADAG equation has a steeper slope than the GMI equation. One reason may be that patients with a high HbA1c in the ADAG study had fewer high glucose values on the days dedicated to the study measurements than in the

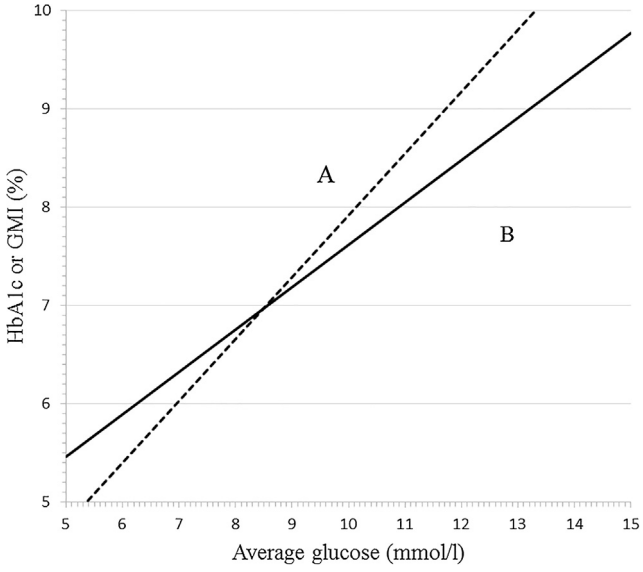

Fig. 1 – The relation between HbA1c, GMI and average glucose. (A) HbA1c (%) = 0.6289 × eAG (mmol/l) + 1.63 and (B) GMI (%) = 0.4309 × AG (mmol/l) + 3.31.

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approximately 32 days not reported. Another reason may be that nocturnal hypoglycaemia was underreported (only 13 CGM days) in persons with tight glycaemic control.

For a given individual, there is a wide range of possible differences between GMI and HbA1c [3]. It has been suggested that this difference (i.e., glycation index) is relatively constant, possibly reflecting individual erythrocyte life span [2]. Even if HbA1c and GMI are similar, the relation to eAG and AG strongly depends on the level of glycaemic control (Fig. 1). In populations with HbA1c and GMI values above 7.0%, it follows that eAG is progressively lower than the corresponding AG. The opposite is the case with very tight control.

HbA1c is a very well documented indicator of risk for diabetic complications, but its translation into AG and vice versa is problematic. Ideally, the two parameters should be evaluated separately. Nevertheless, their relation is a part of daily reflections in the clinical care. In a patient with HbA1c 8.5% (69 mmol/mol) and glycation index zero (i.e., GMI also 8.5%), the CGM report will show an AG of 12.1 mmol/l and estimate HbA1c at 9.2% (77 mmol/mol) according to the ADAG equation. The central lab will report an eAG of 10.9 mmol/l. This confusing discrepancy is an illusion created by the application of two different equations.

The technology for glucose monitoring has improved considerably since 2008. The time has therefore now come to suggest that the ADAG equation be replaced with an equation that takes advance of this evolution, if not universally then at least in reports from CGM [4].

Declaration of interests

None.

REFERENCES

[1] Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine JH. Translating the A1c assay into estimated average glucose value. Diabetes Care 2008;31:1473–8.

[2] Bergenstal RM, Beck RW, Close KL, Grunberger G, Sacks DB, Kowalski A, et al. Glucose management indicator (GMI): a new term for estimating A1c from continuous glucose monitoring. Diabetes Care 2018;41:2275–80.

[3] Beck RW, Connor CG, Mullen DM, Wesley DM, Bergenstal RM. The fallacy of average: how using HbA1c alone to assess glycemic control can be misleading. Diabetes Care 2017;40:994–9.

[4] Danne T, Nimri R, Battelino T, Bergenstal RM, Close KL, DeVries H, et al. International consensus on use of continuous glucose monitoring. Diabetes Care 2017;40:1631–40.