Original Article

Analytical performance of point-of-care device QuikRead go in HbA1c analysis

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Background: Point-of-care (POC) analysers are crucial in acute care diagnostics. Due to easy access, they are also used in monitoring chronic diseases. However, use of POC devises in measurement of glycated haemoglobin (HbA1c) and monitoring diabetes mellitus is controversial.

Methods: We compared QuikRead go analyser's HbA1c measurement performance to cobas c513 in a clinical laboratory with leftover venous K2-ethylenediaminetetraacetic acid (K2-EDTA) samples (n=151).

Results: The methods correlated well (r=0.984), but differed statistically significantly (P<0.0001) with an average negative bias of 2 mmol/mol for QuikRead go. The method deviation compared to cobas c513 was high, −20 to 11 mmol/mol (min–max), in HbA1c above 48 mmol/mol (n=98), and less, −5.5 to 1.4 mmol/mol, below HbA1c 48 mmol/mol (n=51).

Conclusions: This deviation in high level HbA1c should not be considered clinically acceptable. Deviating results can cause erroneous decisions regarding diabetes mellitus diagnosis and treatment. In lower HbA1c, the device showed relatively good performance. Concluding from this, the deviation is method-dependent and not related solely on preanalytical issues. These findings demonstrate the importance of understanding analytical variation when laboratory results and various methods are used in monitoring chronic diseases. Further studies with venous and finger-prick samples on QuikRead go analyser are needed to confirm the findings presented here.

Keywords: Haemoglobin (HbA1c); point-of-care (POC); QuikRead go

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Introduction

Background

Diabetes mellitus (DM) is affecting people worldwide with an estimated global prevalence of 9.3% in 2019, and rising (1). As glycated haemoglobin (HbA1c) reflects blood glucose levels over the past 2–3 months (2,3), it is widely used as a diagnostic and treatment monitoring laboratory test of DM. One of the American Diabetes Association (ADA) criteria for DM diagnosis is HbA1c ≥48 mmol/mol, with a remark of using a National Glycohemoglobin Standardization Program (NGSP) certified laboratory method standardised to the Diabetes Control and Complications Trial (DCCT) assay (4). The central goal in DM treatment is to maintain good or adequate blood glucose levels, and thereafter reduce the risk for secondary diseases, complications and overall

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mortality. American Diabetes Association Professional Practice Committee recommends HbA1c target below 53 mmol/mol for majority of nonpregnant adult DM patients (5). Certain trials such as ACCORD and ADVANCE set more stringent HbA1c targets, 42 and 48 mmol/mol, respectively (6,7).

HbA1c point-of-care (POC) testing is suggested to provide higher patient treatment compliance and flexible and timely DM treatment adjustment. Various studies describe lower HbA1c levels for patients followed with POC measurements (8-11). POC devices may also serve as diagnostic tools in remote health care units with no access to full laboratory services. However, method evaluation and comparison studies show variable, even unacceptable, performance for various HbA1c POC devices (12,13). Some studies claim certain POC devices to perform well compared to reference laboratory method (14), while others show bias, most often negative (15-17). The data depends on the analyser and the study setting, and should not be generalised. Adequate performance of HbA1c measurement under various clinical settings and reliability of the results are crucial in the era of POC testing (18). Ideally, new devices are tested with patient blood samples in a clinical setting (12,18).

Rationale and knowledge gap

QuikRead go is a small-scale single test POC analyser. Quantitative measurement of C-reactive protein and detection of Streptococcus A bacteria with QuikRead go correlates well or adequately to laboratory reference method (19-22). In this study, we examined the performance of QuikRead go in quantitative HbA1c analysis compared to a quantitative immunoturbidimetric HbA1c method.

Objective

The aim was to gain knowledge of the applicability of QuikRead go in diagnostics and management of DM. To our knowledge, there is no previously published HbA1c data for QuikRead go. We present this article in accordance with the MDAR reporting checklist (available at https://jlpm.amegroups.com/article/view/10.21037/jlpm-23-21/rc).

Highlight box

Key findings

- QuikRead go and cobas c513 HbA1c methods correlated well (r=0.984).
- QuikRead go HbA1c showed bias of –2 mmol/mol compared to cobas c513.
- QuikRead go HbA1c concentrations above 48 mmol/mol deviated significantly compared to cobas c513 (–20 to 11 mmol/mol).

What is known and what is new?

- QuikRead go POC analyser performs well with various analytes.
- No data of QuikRead go HbA1c analysis compared to an automated laboratory method is previously published.
- We compared QuikRead go to cobas c513 HbA1c with 151 samples.

What is the implication, and what should change now?

- Analytical variation should be minimal in monitoring chronic diseases.
- Clinician should be aware of a possible bias between different measurement methods.
- Further studies are needed to confirm these findings.

Methods

The samples (n=151, with 74 female; median age 60 years; range, 14–97 years) were anonymised leftover K2-EDTA whole blood patient samples drawn on the day of analysis. They were routinely tested with cobas c513 (Roche Diagnostics, Mannheim, Germany) for HbA1c, stored in +4 ℃ for maximum of 6 hours and analysed with QuikRead go (Aidian Oy, Espoo, Finland) the same day in a clinical laboratory (Clinical Chemistry, Tyks Laboratories, Turku University Hospital, Turku, Finland).

The samples for QuikRead go HbA1c analysis were selected to cover a wide range of HbA1c concentrations. Clotted samples and samples with insufficient amount of blood were excluded from the study. One person performed all QuikRead go analyses. We evaluated QuikRead go method reliability with two-level controls (target 46–60 or 40–52 mmol/mol and 77–104 or 66–90 mmol/mol, with two different lot series) measured in every analytical batch (n=11). A single lot of QuikRead go test cuvettes was used in the study.

Cobas c513 HbA1c, utilizing turbidimetric inhibition immunoassay (Tina-Quant Gen. 3), is standardised against the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) reference method and is transferrable to DCCT/NGSP. The analysis was performed under ISO 15189 accreditation. The performance of comparison method (Roche cobas c513 and Tina-quant haemoglobin A1cDx Gen 3) was verified earlier following procedures meeting the needs of ISO 15189. QuikRead go HbA1c turbidimetric immunoassay is also traceable to

Table 1 Bias for the samples (total n=149) below and above HbA1c 48 mmol/mol measured with QuikRead go point-of-care analyser (Aidian Oy, Espoo, Finland) and cobas c513 with Tina-Quant gen 3 (Roche Diagnostics, Mannheim, Germany). In addition, the number of samples exceeding bias ±5 mmol/mol is presented

Parameter	HbA1c <48 mmol/mol	HbA1c ≥48 mmol/mol
Mean bias ± SD (95 % CI) (mmol/mol)	−1.9±1.6 (−2.3 to −1.4)	−2.1±5.8 (−3.2 to −0.9)
Min bias (mmol/mol)	−5.5	−20
Max bias (mmol/mol)	1.4	11
Number	51	98
Number with bias >5 mmol/mol	0	6
Number with bias >−5 mmol/mol	1	24

HbA1c, haemoglobin; SD, standard deviation; CI, confidence interval.

IFCC reference method.

Statistical analysis

MedCalc 20.218 with Shapiro-Wilk test, Wilcoxon Signed Rank Test and Bland Altman analysis, were applied for statistical analysis.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Turku Clinical Research Centre (No. T14/2022). No patient permission or evaluation from the ethics committee were needed for this method-comparison study with anonymised samples.

Results

Between-day repeatability coefficient of variation (CV, %) was 2.2 and 0.67 with lower and higher control, respectively. For two samples, QuikRead go gave no result with repeated measurements (HbA1c 30 and 86 mmol/mol with cobas c513). For six samples QuikRead go gave error messages, and the measurements were repeated twice or thrice to get a result. Certain (n=6), but not all, samples with high result deviation were repeated with QuikRead go (cobas c513 *vs.* QuikRead go: 90 *vs.* 78/77, 73 *vs.* 62/65, 95 *vs.* 77/80, 92 *vs.* 83/85, 98 *vs.* 78/77 and 78 *vs.* 63/64 mmol/mol). In the repeated QuikRead go measurements the deviation was 1–5%.

The results of cobas c513 and QuikRead go HbA1c correlated well (r=0.984), but differed statistically significantly (P<0.0001). Cobas c513 gave slightly higher HbA1c results [median 62 mmol/mol (25^{th}–75^{th} interquartile range: 38–89 mmol/mol)] compared to QuikRead go [61 (37–84 mmol/mol)], with an overall negative bias 2 mmol/mol for QuikRead go. With HbA1c below 48 mmol/mol (n=51), the result deviation varied from −5.5 to 1.4 mmol/mol (min-max), and with HbA1c equal and above 48 mmol/mol (n=98) from −20 to 11 mmol/mol. Mean proportional difference was −1.9 [95% confidence interval (CI): −2.3 to −1.4] and −2.1 (95% CI: −3.2 to −0.9) in these groups, respectively (*Table 1*, *Figure 1*). Altogether, the bias between QuikRead go and cobas c513 were more than ±5 mmol/mol in 31 (21%) out of 149 samples. None of the samples had blood HbA1c below 60 g/L (lower measurement range for QuikRead go).

Discussion

Key findings

POC device QuikRead go gave excellent control repeatability with low and high controls, provided by the manufacturer. Due to limited resources, we did not systematically evaluate method repeatability with blood samples, but the samples (n=6) with deviating results compared to cobas c513 gave 1–5% (1–3 mmol/mol) difference in reanalysis. Lack of duplicate QuikRead go measurements is a weakness of this study, and comprehensive repeatability for the device cannot be calculated from these data. Despite of very low difference observed in the reanalysis performed, the possibility of random error cannot be excluded due to lack of comprehensive duplicate measurements.

QuikRead go HbA1c correlated well with cobas c513 data. However, there was overall negative bias of

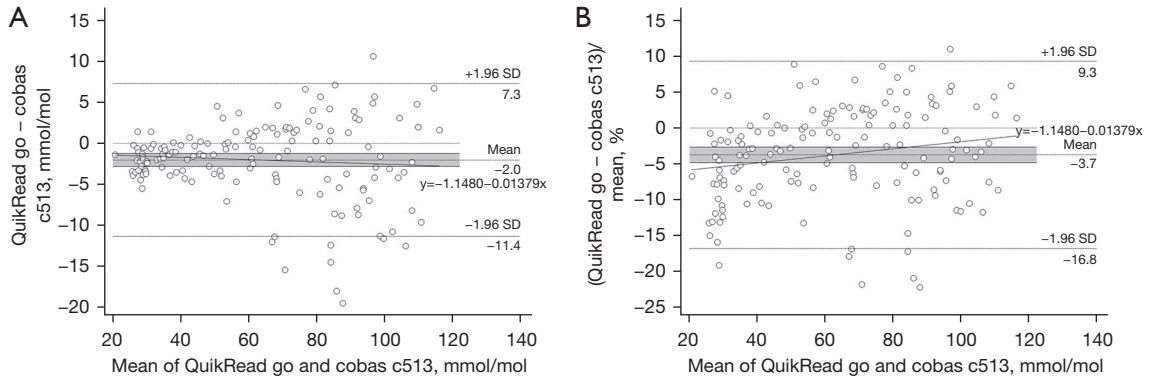

Figure 1 HbA1c (mmol/mol) measured with QuikRead go point-of-care analyser (Aidian Oy, Espoo, Finland) compared to cobas c513 with Tina-Quant gen 3 (Roche Diagnostics, Mannheim, Germany) (n=149). (A) Bias as absolute values (mmol/mol); (B) bias as percentage. The line of regression is solid. Mean bias is dashed with 95% confidence interval in solid and shade grey. Lower and upper limit of agreements ±1.96 SD are fine dashed. SD, standard deviation.

2 mmol/mol for QuikRead go. Below the diagnostic cut-off 48 mmol/mol, the device performed well when absolute HbA1c concentrations are considered, although proportional bias was even bigger than above 48 mmol/mol. All the samples with HbA1c below 48 mmol/mol measured with cobas c513 were below this cut-off also when measured with QuikRead go, but two samples measured above the cut-off with cobas c513 (48 and 52 mmol/mol) were below the cut-off with QuikRead go (46 and 47 mmol/mol, respectively). In comparison, HbA1c biological variation is 1.6% (CV) causing only ±0.77 mmol/mol variation at the diagnostic cut-off (23). A total acceptable error of 5 mmol/mol has been used as a quality target by International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Committee on Education and Use of Biomarkers in Diabetes and the EurA1c Trial Group (24,25). In a clinical context, a tighter limit, such as 3.3 mmol/mol suggested by the EurA1c Trial Group (24,25), may be reasonable. It is worth noting that in 21% of these study samples the bias exceeded 5 mmol/mol. Thereafter, the bias observed here can be considered clinically relevant.

Strengths and limitations

A sample collector was used with each sample according to manufacturer's written instructions with no excess blood outside the collector. The analysis is validated on only 1 µL of blood in the collector and any excess blood can cause result deviation. This was acknowledged in this study. User friendliness was not widely evaluated, as a single person performed all the analysis. This should be tested in a separate study with an emphasis on the possible effect of misuse of sample collector and imprecise amount of blood collected.

Although the QuikRead go method repeatability was not studied thoroughly, the strength of this study is that it was performed in a clinical laboratory with fresh patient samples with a wide range of HbA1c concentrations, and that several factors possibly affecting measurement deviation were eliminated.

Comparison with similar researches

Previously published data has shown similar negative bias for other HbA1c POC devices (26). Measured HbA1c concentration varies between analysers and laboratories. A large European HbA1c assay performance trial showed −0.9 mmol/mol bias with 4.4% between laboratory variation for Roche analysers, and their overall performance was borderline (25). Comparison method cobas c513 used in this study is routinely assessed and compared against target values assigned by a reference laboratory using a standardised IFCC reference method. The performance has constantly been acceptable. In relation to this, the bias between QuikRead go and cobas c513 is high, specifically in HbA1c concentrations above diagnostic cut-off 48 mmol/mol with significant and clinically relevant deviations.

Explanations of findings

Although QuikRead go is standardised against IFCC method, it is possible that incomplete erythrocyte haemolysis or factors affecting sample turbidity caused

result variation. HbA1c variants are extremely rare in Finnish population. Thereafter, it is highly unlikely that these explain the deviation seen in this study, although this could not be definitely confirmed. All samples had HbA1c above the measurement range for QuikRead go, eliminating severe anaemia as an interfering factor.

All samples in this study were single tube venous samples. Thereafter, possible bias from capillary sampling was eliminated. Finger capillary sample could bring further imprecision to POC HbA1c measurement due to preanalytical challenges. QuikRead go measurement failure in analysing two samples remained unclear, as there was no clotting or abnormalities with the reference method. In addition, the error messages followed by successful measurements in six samples remained unclear. No further analysis of assay interference was done. As the same person performed all QuikRead go analyses, inter-individual variation in sample handling cannot explain the deviation.

Implications and actions needed

While the use of POC devices is not generally recommended in DM diagnosis (27), they are commonly used in DM monitoring in various health care units. A negative analytical bias might lead to inadequate DM treatment and cause diagnostic error when compared to laboratory measurement. POC devices are valuable tools in health care units outside clinical diagnostic laboratories for, e.g., detecting critically low HbA1c, major infections and evaluating the severity of infection. However, in most of these clinical settings, the result is confirmed or the analyte trend followed with laboratory tests. HbA1c is one of the rare tests guiding long-term medical treatment based solely on POC data.

Some studies support POC use in DM treatment monitoring and have showed better DM glucose balance monitored with POC measurements and fast feedback (10,28,29). To make correct DM treatment adjustments, the HbA1c measurement should thereafter be accurate at all levels. Further studies with a larger amount of samples and ideally various POC devices, in addition to QuikRead go, compared to an IFCC/DCCT standardised method are crucial for any definitive conclusions.

Conclusions

Both methods compared in this study are standardised against an IFCC reference methods. In spite of this, QuikRead go POC-analyser showed negative bias, and more importantly, high variation in HbA1c concentrations compared to cobas c513. With higher HbA1c concentrations, the bias and result variation are clinically unacceptable. These findings highlight that QuikRead go POC device should be used with consideration, specifically if used in an interchangeable manner with cobas c513 automated analyser, in monitoring chronic diseases where analytical variability should be minimal.

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Footnote

Reporting Checklist: The authors have completed the MDAR reporting checklist. Available at https://jlpm.amegroups.com/article/view/10.21037/jlpm-23-21/rc

Data Sharing Statement: Available at https://jlpm.amegroups.com/article/view/10.21037/jlpm-23-21/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jlpm.amegroups.com/article/view/10.21037/jlpm-23-21/coif). ALP reports that the analyser and the reagents were provided by the manufacturer (Aidian Oy, Espoo, Finland). The profit was solely for the institution (Turku University Hospital). HMP reports receiving payment for a short scientific lecture on EuroMedLab 2023 (topic is related to digital solutions) and other support for attending EuroMedLab 2023. JD has no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Turku Clinical

Research Centre (No. T14/2022). No patient permission or evaluation from the ethics committee were needed for this method-comparison study with anonymised samples.

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