The inappropriate use of HbA1c testing to monitor glycemia: is there evidence in laboratory data?

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Abstract

Rationale, aims and objectives Diabetes is a chronic illness and have relatively high prevalence. Glycemic control is fundamental to the management of diabetes. Hemoglobin A1c (HbA1c) is a commonly used laboratory test to monitor glycemia and to manage diabetes. This study aimed to assess the appropriateness of the frequency of HbA1c test order with respect to the commonly approved guidelines for monitoring glycaemia of patients. **Methods** To assess the rate of inappropriate test orders, laboratory records of HbA1c tests ordered between 2002 and 2004 were evaluated. Inappropriate orders were defined as any order for a given patient that takes place within a 29- or 89-day-period following the previous HbA1c order. The effects of various parameters, like ordering clinics, the first HbA1c level, or the on-line availability of test results on test ordering were evaluated. **Results** Evaluation of test intervals showed that 10.3% of all orders and 33.8% of the inpatients' orders were performed within 29 days, 35.5% of all orders and 55% of the inpatients' orders were within 89 days. **Conclusions** Inappropriate laboratory utilization of HbA1c testing is very common especially in the inpatient clinics. We think that the application of the guidelines may decrease unnecessary health expenditure.

Introduction

Glycohemoglobin (GHb) is a general term for hemoglobin nonenzymatically glycated by glucose. It is used in clinical practice to monitor glycaemia in diabetic patients and it serves as a predictor of the risk of developing diabetic complications (Krishnamurti & Steffes 2001; Sacks *et al*. 2002; Schellhase *et al*. 2005). GHb is often reported as Hemoglobin A1c (HbA1c) (Goldstein *et al*. 2004). The HbA1c concentration represents the integrated values for plasma glucose in the preceding 6–8 weeks and is not meaningfully affected by glycemic instability (Sacks 1999; Derr *et al*. 2003). The plasma glucose in the preceding month makes up 50% of the HbA1c, whereas that in days 60–120 determines only 25% (Tahara & Shima 1995).

There are many different HbA1c assay methods in current use. The standardization of these assays is required to compare reported results between labo-

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ratories. In 1996, the National Glycohemoglobin Standardization Program (NGSP) was initiated to standardize GHb test results among laboratories to Diabetes Care Complication Trial (DCCT) – equivalent values (Sacks *et al*. 2002). To evaluate the differences of HbA1c results during diabetes management, the maximum allowable inter-assay coefficient variation (CV) of analysis method must be 5% (Westgard & Darcy 2004).

There is controversy on the optimal frequency of GHb testing (Sacks *et al*. 2002). In the absence of evidence-based guidelines, expert opinion recommends HbA1c testing at least twice a year in patients who have stable glycemic control and more frequently (quarterly assessment) in those whose therapy has changed or who are not meeting glycemic goals (Goldstein *et al*. 2004; American Diabetes Association 2005). On the other hand, National Commission for Quality Assurance do not recommend the use of HbA1c more than two times a year (National Committee for Quality Assurance 1999). There are also other reports suggesting more frequent monitoring (every 4 or 8 weeks) of patients with major change in therapy and of diabetic pregnancy (McIntosh *et al*. 2001; Medicare National Coverage Decisions 2002; Sacks 1999; American Diabetes Association 2004).

Considering the relatively high prevalence of diabetes (Amos *et al*. 1997), inappropriate use of HbA1c test frequent repetition of HbA1c test can be expected. Redundant laboratory tests are an important component of repeat laboratory testing (Van Walraven & Raymond 2003). The appropriateness of laboratory utilization is especially important for a developing country with limited financial resources. To the best of our knowledge, the appropriateness of laboratory utilization for HbA1c testing has not been addressed in the medical literature.

In this study we aimed to assess the appropriateness of the frequency of HbA1c test order with respect to the commonly approved guidelines for monitoring glycaemia of patients and we evaluated the factors that may effect test ordering.

Methods

Our institution is a 770-bed university hospital with registered 145 231 inpatient and 1 507 202 outpatient between 2002 and 2004. A total of 10 496 HbA1c test orders from 6128 patients in a 2-year period (10 July 2002 to 10 July 2004) were examined initially. The data from laboratory information system (LIS) were analysed using computer programme utilizing Microsoft® Excel's macro programming capability (available from authors) to calculate the order intervals and test frequency for each patient.

Only the data from patients whose initial HbA1c assays were performed between 10 July 2002 and 10 July 2003 and having at least two separate test results were included for further analysis. Those with a missing or invalid patient identifier, with missing sex or age information or with a missing test result were excluded from the analysis. To assess appropriateness of HbA1c repeat testing, fist order of each patient was not included in the analysis. Finally, 3452 total repeating orders (for 1429 patients) were evaluated.

The minimum time interval required between two consecutive HbA1c tests is controversial. While the American Diabetes Association (ADA) recommends quarterly assessment, common knowledge dictates that the minimum time interval between two consecutive HbA1c tests should not be less than 30 or 90 days (Sacks *et al*. 2002; Goldstein *et al*. 2004; American Diabetes Association 2005). Therefore, an inappropriate order is defined as any order for a given patient that takes place within a 29- or 89-day-period following the previous HbA1c order.

Various parameters, including the level of the first HbA1c measurement or the on-line availability of test results through hospital information system were evaluated to assess their effect on HbA1c ordering. We also sought to determine the effect of time interval between two consecutive orders on HbA1c level. Only first and second orders were used to determine the magnitude of change on HbA1c level for each patient. The tests, which were ordered on the same day, were excluded. The orders were separated five groups for the initial HbA1c results: orders with initial HbA1c level less than 5.7%, 7%, 9%, 11% and more than 11.01%. To calculate the magnitude of change on HbA1c level, the following formula was used: Average Change percentage = [(Result of second order – Result of first order)/Result of first order] × 100.

All statistical analysis was performed using SPSS 11.0 program. We examined the relation of monitoring frequency and the variables, which may affect

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HbA1c monitoring, by using 'Chi-square and ANOVA tests'.

GHb analysis was performed as HbA1c with immuno-turbidimetric method (Roche Integra 400, USA) certified by NEQAS external quality control system and calibrated to DCCT reference method. CV percentage of our method was 3%. The reference range of our method was 4.5–5.7%.

Results

Hemoglobin A1c orders for inpatient clinics were 11% and for outpatient clinics were 89% of total orders. Majority of HbA1c test (46.4%) was ordered from the diabetic outpatient clinic. Only 1.8% of the orders were from the obstetric clinic. A total of 204 HbA1c orders (10.3% total repeating orders), which were performed within 29-day interval, were accepted as certainly inappropriate tests orders. This corresponds to 33.8% of the repeating orders for inpatient clinics, most of which (21.5%) were reordered within a week period. When we evaluated the test orders by ADA recommendations, 35.5% of total repeating orders, which were performed before 90 days, might be evaluated as inappropriate. It was 55% of total repeating orders for inpatient clinics. The frequencies of HbA1c orders were shown at Table 1.

Table 1 The order intervals in all repeating HbA1c orders by inpatient and outpatient clinics

	Orders location n *(% of total repeating orders) (*n = 3452)		
Order interval (day)*	*Inpatient clinic*	*Outpatient clinic*	*All clinics combined*
<7	21.5	1.7	4.4
8–29	12.3	5.4	5.9
30–59	11.1	11.7	10.8
60–89	10.1	16.6	14.4
90–119	12.1	19.9	17.26
120–179	10.1	19.20	16.2
>180	22.8	25.5	31.0
Total	100	100	100

*Order interval was defined as the time interval between two consecutive orders.
HbA1c, Hemoglobin A1c.

After 1 April when laboratory information system was improved, there was no difference in monitoring frequency in all patients. Although there was no statistical significance we have seen that the rates of HbA1c tests ordered within 0–29 days were decreased from 35.7% to 32.4% in inpatient clinics.

Monitoring frequency was associated with first HbA1c levels in outpatients ($P = 0.001$), but there was no association in inpatients (Fig. 1). The percentage value of second HbA1c tests of outpatient clinics, which were ordered within 89 days, was 31.8%. The majority of initial HbA1c test results (50.7%) in outpatient clinics were below 7.00% HbA1c level.

Differences in the reduction of HbA1c levels according to the order intervals are shown in Table 2. Test results, which were ordered with different time period, were changed regarding to duration time. Especially, average change of test results, which were

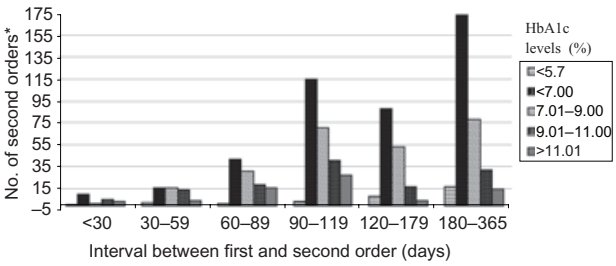


Figure 1 The distribution of first HbA1c levels with respect to monitoring frequency in outpatient clinics. *The number of second orders in outpatient clinics is 934.

Table 2 Association of duration between first and second order with change of HbA1c level

Order interval (days)	*Second orders (*n = *1214)*	*Average change†* *(%)*	*Standarts deviation (SD)*
<30	152	–1.84*	12.5
30–59	141	–5.98	13
60–89	136	–8.09	16.1
90–119	177	–6.28	16.9
120–179	204	–4.19	17.7
180–365	404	–0.51*	19.7

*Statistically different ($P = 0.001$).
†Change is expressed as the difference between the second and first assay divided by the value of the formula [(second–first)/first] × 100 Tests, which ordered on the same day, were excluded ($n = 215$).
HbA1c, Hemoglobin A1c.

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ordered <30-day and 180–365-day interval, was significantly lower than the other's ($P = 0.001$). Also there was no statistically difference between the other groups with 30–59 days, 60–89 days, 90–119 days and 120–179 days.

Discussion

Because of its absence of well-controlled studies that suggest a definite testing protocol, there is no consensus of optimal frequency of HbA1c testing. Although there has been an association of monitoring frequency with reduction of HbA1c level, the high rate of test orders is especially important for a developing country with limited financial resources. It has not always been clear that more frequent testing, as a result of doctors managing patients more aggressively, can reduce the end organ complications of diabetes. Aggressive glycemic control cannot reduce GHb levels and also increases the risk of treatment complications such as hypoglycemia (Turner 1998; UK Prospective Diabetes Study Group 1998).

Apart from the differences in guidelines' recommendations, the conditions like patient's literacy, cooperation or emotional status and doctor's willingness to follow guidelines or knowledge status and economic factors may effect diabetic patient management and laboratory test utilization (Valenstein *et al*. 1988; Valenstein *et al*. 2001; Taylor 2005).

Even if all patients were considered to have a major change in therapy or as diabetic pregnancy, 10.3% all repeating orders and 33.8% of the inpatient's orders, which were performed within 29-day interval, were accepted as certainly inappropriate tests orders.

The ADA recommends GHb testing at least twice a year in patients who have stable glycemic control and more frequently (quarterly assessment) in patients whose therapy has changed or who are not meeting glycemic goals. When we evaluated the test orders by ADA recommendations (35.5%), 1226 tests of total repeating orders that were performed before 90 days might be evaluated as inappropriate. Considering that the cost of one HbA1c testing was 10.00 Euros, 12 260 Euros (for 1226 tests) is an unnecessary expenditure for the health system.

In our study the rate of inappropriate tests in all clinics was lower than the some studies (Durand *et al*. 1993; Ozbek *et al*. 2004). For the reason of this situation, we observed that majority of orders were from specialized diabetic outpatient clinic. The previous studies showed that, inappropriate testing was very common during hospitalization (Valenstein *et al*. 1988; Van Walraven & Naylor 1998). For our analysis, the rate of inappropriate tests that ordered from inpatient clinics was significantly higher than the outpatient clinics.

In our study, monitoring frequency was not significantly associated with initial HbA1c level and the HbA1c testing, which were reordered within 7 days, was very common in the inpatient population. Following the improvement of LIS, although not statistically significant, the rates of inappropriate HbA1c tests were decreased. But, 4-month period might be short to evaluate the effect of laboratory information technology. Frequency of unnecessary laboratory tests can be decreased providing price information, educational interventions, redesigning of requisition form and introducing diagnostic algorithms (Pilon *et al*. 1997; Hampers *et al*. 1999; Emerson & Emerson 2001). Using a reminder program especially for the inpatient clinics, may aid to decrease inappropriate HbA1c tests.

In our study, test results, which were ordered with different duration time, were changed regarding to duration time. The average change of test results, which were ordered <30-day and 180–365-day interval, was significantly lower than the other's ($P = 0.001$). But there was no statistically difference between other groups with 30–59 days, 60–89 days, 90–119 days and 120–179 days. It seems to be that the effects of monthly, semi-annually or quarterly assessment on the average change of HbA1c level were not different. On the other hand, when the initial HbA1c level was 9,01% and over, there was statistically difference between the average change of HbA1c tests, which were ordered within 30–89-day interval ($P < 0.05$) (data not shown). But this issue needs to be tested by further studies on larger population. To determine optimal interval between two consecutive HbA1c orders, there seems to be a need for well-controlled and defined studies in terms of patient management.

A total of 1438 orders (for 1438 patients) were not repeated. 26% of these orders that have 8% and over HbA1c result (data not shown). The ADA recom-

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mends that the goal of therapy should be a GHb concentration <7% and that treatment regimens should be re-evaluated if GHb values are >8% (These values are applicable only if the assay method is certified as traceable to the diabetes control and complications trial (DCCT) reference method (Sacks *et al*. 2002). The ADA also recommends more frequent assessment in patients who have not meeting glycemic goals. We assume that these patients followed in different hospitals or not controlled again. We are planning to learn the explanation of this situation by reaching the patients by mail or telephone.

Finally, our study has shown that inappropriate laboratory utilization of HbA1c test for monitoring diabetes is common in our hospital. We think that the application of recommendations in practical guidelines and a warning system of the inpatients may eliminate inappropriate utilization and decrease unnecessary health expenditure.

References

American Diabetes Association (2004) Preconception care of women with diabetes. *Diabetes Care* **27**, 76–78.

American Diabetes Association (2005) Standarts of Medical Care in Diabetes. *Diabetes Care* **28**, 4–36.

Amos A.F., McVarty D.J. & Zimmot P. (1997) The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabetic Medicine* **14**, 7–55.

Derr R., Garrett E., Stacy G.A. & Saudek C.D. (2003) Is HbA (1c) affected by glycemic instability? *Diabetes Care* **26**, 2728–2733.

Durand-Zaleski I., Rymer J.C., Roudot-Thoraval F., Revuz J. & Rosa J. (1993) Reducing unnecessary laboratory use with new test request form: example of tumour markers. *Lancet* **17**, 150–153.

Emerson J.F. & Emerson S.S. (2001) The impact of requisition design on laboratory utilization. *American Journal of Clinical Pathology* **116**, 879–884.

Goldstein D.E., Little R.R., Lorenz R.A., Malone J.I., Nathan D.M. & Peterson C.M. (2004) American diabetes association. Tests of glycemia in diabetes. *Diabetes Care* **27**, 91–93.

Hampers L.C., Cha S., Gutglass D.J., Krug S.E. & Binns H.J. (1999) The effect of price information on test ordering behavior and patient outcomes in a pediatric emergency department. *Pediatrics* **103**, 877–882.

Krishnamurti U. & Steffes M.W. (2001) Glycohemoglobin: a primary predictor of the development or reversal of complications of diabetes mellitus. *Clinical Chemistry* **47**, 1157–1165.

McIntosh A., Hutchinson A., Home P.D., *et al.* (2001) *Clinical Guidelines and Evidence Review for Type 2 Diabetes: Management of Blood Glucose.* Scharr, University of Sheffield, Sheffield, UK.

Medicare National Coverage Decisions (2002) Effective November 25, Nebraska.

National Committee for Quality Assurance (1999) *HEDIS 2000: Technical Specifications.* National commission for quality assurance, Washington DC.

Ozbek O.A., Oktem M.A., Dogan G. & Abacioglu Y.H. (2004) Application of hepatitis serology testing algorithms to assess inappropriate laboratory utilization. *Journal of Evaluation in Clinical Practice* **10**, 519–523.

Pilon C.S., Leathley M., London R., McLean S., Phang P.T., Priestly R., Rosenberg F.M., Singer J., Anis A.H. & Dodek P.M. (1997) Practice guideline for arterial blood gas measurement in the intensive care unit decreases numbers and increases appropriateness of tests. *Critical Care Medicine* **25**, 1308–1313.

Sacks D.B. (1999) Carbohydrates. In *Tietz Textbook of Clinical Chemistry*, 3rd edn (eds C.A. Burtis, E.R. Ashwood & N.W. Tietz), pp. 790–794. W.B. Saunders, Philadelphia, USA.

Sacks D.B., Bruns D.E., Goldstein D.E., Maclaren N.K., McDonald J.M. & Parrott M. (2002) Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clinical Chemistry* **48**, 436–472.

Schellhase K.G., Koepsell T.D. & Weiss N.S. (2005) Glycemic control and the risk of multiple microvascular diabetic complications. *Family Medicine* **37**, 125–130.

Tahara Y. & Shima K. (1995) Kinetics of HbA1c, glycated albumin, and fructosamine and analysis of their weight functions against preceding plasma glucose level. *Diabetes Care* **18**, 440–447.

Taylor J.B. (2005) Relationships among patient age, diagnosis, hospital type, and clinical laboratory utilization. *Clinical Laboratory Science* **18**, 8–15.

Turner R.C. (1998) The UK prospective diabetes study-a review. *Diabetes Care* **21**, C35–C38.

UK Prospective Diabetes Study Group (1998) Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* **352**, 837–853.

Valenstein P., Leiken A. & Lehmann C. (1988) Test-ordering by multiple physicians increases unnecessary laboratory examinations. *Archives of Pathology and Laboratory Medicine* **112**, 238–241.

Valenstein P.N., Walsh M.K., Pappas A.A. & Howanitz P.J. (2001) Interinstitutional variation in glycohemoglobin monitoring and glycemic control of diabetic patients. *Archives of Pathology and Laboratory Medicine* **125**, 191–197.

Van Walraven C. & Naylor C.D. (1998) Do we know what inappropriate laboratory utilization is? *Journal of the American Medical Association* **6**, 550–559.

Van Walraven C. & Raymond M. (2003) Population-based study of repeat laboratory testing. *Clinical Chemistry* **49**, 1997–2005.

Westgard J.O. & Darcy T. (2004) The truth about quality: medical usefulness and analytical reliability of laboratory tests. *Clinica Chimica Acta* **346**, 3–11.

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