CASE REPORT

A discrepancy between plasma glycated albumin and HbA1c levels in a patient with steroid-induced diabetes mellitus

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SUMMARY

A 57-year-old man was admitted for the treatment of steroid-induced diabetes mellitus (DM). He also had interstitial pneumonia and, to treat it, 20 mg prednisolone had been started in April 2014. Although glycated haemoglobin (HbA1c) level was 7.8% (62 mmol/mol), his glycated albumin (GA) level was normal (13.9%) and the ratio of GA to HbA1c (GA:HbA1c) was lower than that of normal participants and patients with type 2 DM. Plasma GA and GA:HbA1c levels became persistently lower. In September 2015, HbA1c levels measured by HPLC and immunoprecipitation methods were almost the same (6.8% (51 mmol/mol) and 6.7% (50 mmol/mol), respectively), but GA (10.2%) and GA:HbA1c (1.6) were much lower. We report the case of a patient with DM where steroid administration may have caused a decrease in plasma GA and GA:HbA1c levels via increased albumin turnover.

BACKGROUND

Glycated albumin (GA) and glycated haemoglobin (HbA1c) are markers that are often used in the treatment of patients with diabetes mellitus (DM). GA and HbA1c reflect short-term and long-term blood glycaemic control, respectively.^{1–3} GA and HbA1c are influenced by conditions that affect albumin and haemoglobin turnover, respectively. GA measurement might be affected by nephrotic syndrome, hypothyroidism and liver cirrhosis.^{4–7} Considering that steroid administration increases albumin turnover,⁸ plasma GA levels would be decreased compared with plasma HbA1c levels. However, there were some reports of discrepancies between HbA1c and GA in patients with steroid-induced DM.

We report a discrepancy between plasma GA and HbA1c in a patient with steroid-induced DM. In this case, the patient's plasma GA levels were lower than his HbA1c values. The factors influencing HbA1c values, such as anaemia and haemoglobinopathy, are well known to general physicians,⁹ but the factors influencing plasma GA levels are rarely taken into consideration. This case reminds us that steroid administration can influence plasma GA levels via increased albumin turnover.

CASE PRESENTATION

A 57-year-old man had interstitial pneumonia associated with polymyositis and dermatomyositis. To treat the interstitial pneumonia, 20 mg prednisolone

had been started in April 2014. His HbA1c levels gradually increased from 6.0% (42 mmol/mol) to 7.6% (60 mmol/mol) and his postprandial 2 h glucose levels were above 200 mg/dL. Thus, he was diagnosed with steroid-induced DM. In July 2014, he was admitted to our department and 500 mg metformin was started. In August 2014, HbA1c and GA levels were tested at the same time. GA (13.9%) was lower than HbA1c (7.8% (62 mmol/mol)). After the introduction of metformin, the patient's HbA1c levels decreased to 7% (53 mmol/mol). We then measured GA and HbA1c over time, but a discrepancy between GA and HbA1c continued (table 1). In December 2014, the metformin dose was increased to 1500 mg, and, in June 2015, 0.9 mg liraglutide was added to 1500 mg metformin. Although liraglutide was administered, HbA1c levels were still 7% (53 mmol/mol), and we considered that an estimation of monitoring blood glucose levels would be needed. In September 2015, we measured HbA1c values at the same time using two different methods (HPLC and immune-precipitation method) and 1,5-anhydroglucitol (AG) levels, which reflect postprandial hyperglycaemia. The HbA1c value measured using the HPLC method (6.8% (51 mmol/mol)) was almost the same as that measured using the immune-precipitation method (6.7% (50 mmol/mol)). Comparable with these results, 1,5-AG was as low as 6.4 ng/mL, and postprandial 2 h plasma glucose levels were 140–180 mg/day. In contrast, GA (10.2%) was lower than actual glycaemic levels. Similarly, GA:HbA1c was lower (1.60) than the previously-reported values of GA:HbA1c (2.5) in normal participants and patients with type 2 DM (T2DM).¹⁰

OUTCOME AND FOLLOW-UP

To more tightly control postprandial glycaemic levels, we added liraglutide and metformin to 50 mg miglitol. In December 2015, the patient's HbA1c levels had improved from 6.8% (51 mmol/mol) to 6.1% (43 mmol/mol) and 1,5-AG was also improved from 6.4 to 13.4 ng/mL. Plasma GA levels were also decreased from 10.2% to 9.1%. Throughout his treatment for steroid-induced DM, the patient had no hypoglycaemic episodes and plasma albumin and haemoglobin levels remained normal (table 1).

DISCUSSION

HbA1c reflects fasting plasma glucose levels and GA reflects postprandial glucose levels.^{11 12} Some

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Table 1 A discrepancy between glycated albumin and HbA1c

	April 2014	June 2014	July 2014	August 2014	October 2014	November 2014	December 2014	May 2015	August 2015	September 2015	December 2015
Prednisolone (mg)		30	30	20	20	20	20	20	20	20	17.5
Metformin (mg)			500	1000	1000	1000	1500	1500	1500	1500	1500
Liraglutide (mg)									0.9	0.9	0.9
Migliitol (mg)										50	50
Glycated haemoglobin (HbA1c) % (mmol/mol IFCC)	6.0 (42)	6.9 (52)	7.6 (60)	7.8 (62)	6.7 (50)	6.5 (48)	7.0 (53)	6.6 (49)	7.2 (55)	6.8 (51)	6.1 (43)
Haemoglobin (mg/dL)	16	16.5	15.6	15.8	14.6	16.4	16	13.7	14.4	13.5	14
Glycated albumin % (GA)	ND	ND	ND	13.9	11.6	11.7	11.2	10.6	10.9	10.2	9.1
Albumin (mg/dL)	4.9	4.1	ND	4.4	4.2	ND	4.3	4.2	4.2	4	4.3
GA:HbA1c	ND	ND	ND	1.78	1.73	1.80	1.60	1.60	1.51	1.50	1.49

IFCC, International Federation of Clinical Chemistry; HPLC, High performance liquid chromatography; ND, not determined.

studies have shown that the ratios of GA to HbA1c (GA:HbA1c) reflect postprandial glucose excursion.^{13–15} Considering that steroid administration can cause remarkable postprandial hyperglycaemia,¹⁶ GA appears to be a good marker for the estimation of blood glycaemic levels in patients with steroid-induced DM. However, GA is not a good marker for glycaemic control in patients with steroid-induced DM. Cushing syndrome involves adrenal tumours that secrete excess glucocorticoid. Some reported that plasma GA:HbA1c levels in patients with Cushing syndrome are lower than those in patients with T2DM (2.5).¹⁰ Similarly, our patient's plasma GA levels were persistently lower (1.49–1.80). Steroids cause protein synthesis and degradation to simultaneously increase and this increases protein turnover.⁸ Moreover, considering that chronic inflammation also might promote albumin turnover,¹⁷ the existence of interstitial pneumonia in this patient also might have caused lower plasma GA and GA:HbA1c levels. Therefore, steroid administration and interstitial pneumonia might lower plasma GA and GA:HbA1c levels.

In conclusion, we report the case of a discrepancy between GA and HbA1c levels seen in a patient with steroid-induced DM. It is possible that steroid administration could lower GA levels compared with HbA1c levels.

Learning points

- Glycated albumin (GA) rather than glycated haemoglobin (HbA1c) is suitable for estimating postprandial hyperglycaemia and glucose variability.
- Steroid-induced diabetes mellitus is characterised by postprandial hyperglycaemia resulting from insulin resistance.
- Steroid administration can cause albumin turnover to increase.
- Steroid administration can lower plasma GA levels compared with actual plasma glycaemic levels.

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REFERENCES

- Guthrow CE, Morris MA, Day JF, et al. Enhanced nonenzymatic glucosylation of human serum albumin in diabetes mellitus. *Proc Natl Acad Sci USA* 1979;76:4258–61.
- Day JF, Thorpe SR, Baynes JW. Nonenzymatically glucosylated albumin. In vitro preparation and isolation from normal human serum. *J Biol Chem* 1979;254:595–7.
- Dolhofer R, Wieland OH. Glycosylation of serum albumin: elevated glycosyl-albumin in diabetic patients. *FEBS Lett* 1979;103:282–6.
- Schleicher ED, Olgemöller B, Wiedenmann E, et al. Specific glycation of albumin depends on its half-life. *Clin Chem* 1993;39:625–8.
- Moriyama K, Kanamoto N, Hataya Y, et al. A case of type 2 diabetes mellitus developing hypothyroidism discovered as a result of a discrepancy between glycated hemoglobin and glycated albumin values. *Diabetes Res Clin Pract* 2006;71:227–32.
- Bando Y, Kanehara H, Toya D, et al. Association of serum glycated albumin to haemoglobin A1C ratio with hepatic function tests in patients with chronic liver disease. *Ann Clin Biochem* 2009;46:368–72.
- Lee JE. Alternative biomarkers for assessing glycemic control in diabetes: fructosamine, glycated albumin, and 1,5-anhydroglucitol. *Ann Pediatr Endocrinol Metab* 2015;20:74–8.
- Rothschild MA, Schreiber SS, Oratz M, et al. The effects of adrenocortical hormones on albumin metabolism studied with albumin-I 131. *J Clin Invest* 1958;37:1229–35.
- Iizuka K, Mizuno M, Niwa H, et al. A rare case of variant hemoglobin (Hb Yahata) suspected based on inconsistent plasma glucose and HbA1c levels. *Intern Med* 2015;54:1771–5.
- Kitamura T, Otsuki M, Tamada D, et al. Glycated albumin is set lower in relation to plasma glucose levels in patients with Cushing's syndrome. *Clin Chim Acta* 2013;424:164–7.
- Monnier L, Lapinski H, Colette C. Contributions of fasting and postprandial plasma glucose increments to the overall diurnal hyperglycemia of type 2 diabetic patients: variations with increasing levels of HbA1c. *Diabetes Care* 2003;26:881–5.
- Sakuma N, Omura M, Oda E, et al. Converse contributions of fasting and postprandial glucose to HbA1c and glycated albumin. *Diabetol Int* 2011;2:162–71.
- Matsumoto H, Murase-Mishiba Y, Yamamoto N, et al. Glycated albumin to glycated hemoglobin ratio is a sensitive indicator of blood glucose variability in patients with fulminant type 1 diabetes. *Intern Med* 2012;51:1315–21.
- Saisho Y, Tanaka K, Abe T, et al. Glycated albumin to glycated hemoglobin ratio reflects postprandial glucose excursion and relates to beta cell function in both type 1 and type 2 diabetes. *Diabetol Int* 2011;2:146–53.
- Ogawa A, Hayashi A, Kishihara E, et al. New indices for predicting glycaemic variability. *PLoS ONE* 2012;7:e46517.
- Yates CJ, Fourlanos S, Colman PG, et al. Divided dosing reduces prednisolone-induced hyperglycaemia and glycaemic variability: a randomized trial after kidney transplantation. *Nephrol Dial Transplant* 2014;29:698–705.
- Don BR, Kaysen G. Serum albumin: relationship to inflammation and nutrition. *Semin Dial* 2004;17:432–7.

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