

CASE REPORT

LOW HbA1c; IS IT DAPSONE?

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A 51-year-old male was referred to the diabetes clinic by the GP with low HbA1c (13 mmol/mol). His complaints were dizziness and intermittent palpitations for the last two years. No precipitating cause could be identified. He denied any chest pain, shortness of breath or syncope. He had a background of schizophrenia, epilepsy, coeliac disease, depression and dermatitis herpetiformis. He was on dapsone, venlafaxine, procyclidine, furosemide, diazepam, omeprazole, meloxicam and folic acid. On examination, his pulse was 82 beats per minute, blood pressure 131/74 mm of Hg, respiratory rate was 14/minute and his saturations on room air were 94%. Neurologic, cardiovascular, respiratory and abdominal examination was unremarkable. His investigations showed Hb of 121g/L (130–180) WCC 7.8×10^9 g/L (4–11), platelets 182×10^9 (150–400), MCV 83 fl (80–100), TSH 2.53 mU/L (0.4–4.0 mU/L), anti TTG 14.9 (normal). Renal, liver function, serum folate, vitamin B12 and complement levels were within normal limits with a negative ANCA and ANA. His oral glucose tolerance test was negative for diabetes with fasting and two-hour post prandial blood sugar of 4.8mmol/L and 6.9 mmol/L respectively. Because of the history of chronic Dapsone use and possibility of drug induced low HbA1c, patient was investigated along those lines. The low HbA1c was attributed to haemolysis secondary to dapsone. HbA1c improved to 42 mmol/mol within three months following discontinuation of dapsone. His haemoglobin level also normalized (142 g/L). Clinicians should consider haemolysis as a possible factor falsely reducing HbA1c while interpreting results in these patients. This is of particular importance in patients with diabetes.

Keywords: Dapsone; HbA1c

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INTRODUCTION

HbA1c (Glycatedhaemoglobin) is used as an indicator of long term glycaemic levels in patients with diabetes. The normal life of red blood cells is one hundred and twenty days and HbA1c reflects the blood glucose levels to which the red blood cells have been exposed. There are quite a few causes in which the HbA1c levels may be falsely low or high. This can lead to a false interpretation of the patient's long term glycaemic control which can pose challenges in diagnosis and management

Here we discuss a case of a non-diabetic patient who was referred from the GP to the diabetes clinic due to a low HbA1c

CASE REPORT

A 51-year-old male was referred to the diabetes clinic by the GP due to a low HbA1c (13 mmol/mol). He was complaining of symptoms of dizziness and intermittent palpitations for the last couple of years. The symptoms were present at rest and on exertion. There were no particular precipitating factors which he could recognize as a cause for his symptoms. He denied any chest pain, shortness of breath or syncope. He had a 24-hour holter monitor to look for any cardiac arrhythmia as a causative factor. The results of the test were unremarkable

He had a background of Schizophrenia, Epilepsy, Coeliac Disease, Depression and Dermatitis Herpetiformis

He was on Dapsone, Venlafaxine, Procyclidine, Furosemide, Diazepam, Omeprazole, Meloxicam and Folic Acid

He was a non-smoker and did not take any alcohol. He was independent in all activities of daily living and lived alone.

On examination, his pulse was 82 beats per minute, blood pressure 131/74 mm of Hg, respiratory rate was 14/minute and his saturations on room air were 94%. He had mild peripheral cyanosis on general physical examination. The rest of the cardiovascular, abdominal, respiratory of abdominal examination was normal.

His investigations showed Hb of 121g/L (130–180) WCC 7.8×10^9 g/L (4–11), platelets 182×10^9 (150–400), MCV 83fl (80–100), reticulocyte count was raised at 2.1% (0.5–1.5%), TSH 2.53mU/L (0.4–4.0 mU/L), anti TTG 14.9 (normal). Renal, liver function, serum folate, vitamin B12 and complement levels were within normal limits with a negative ANCA and ANA. His oral glucose tolerance test was negative for diabetes with fasting and two-hour post prandial blood sugar of 4.8 mmol/L and 6.9 mmol/L respectively (Reference: fasting <6.1mmol/L, 2 hours <7.8 mmol/L)

The low HbA1c was suspected to be low due to rapid cell turnover and chronic haemolysis due to Dapsone which he had been taking due to his dermaantitisherpetiformis. His Dapsone was stopped after discussion with dermatology.

He was followed up in clinic two months later and an HbA1c done at the time was 42 mmol/mol. Another level taken two months after that was 39mmol/mol.

Hence the low HbA1c normalized after stopping Dapsone. His symptoms improved and this was attributed to methaemoglobinemia secondary to Dapsone intake. This was confirmed on an arterial blood gas that he had when he presented to clinic. He was subsequently discharged from the outpatient clinic. His haemoglobin had also normalized to 142 g/L (130–180g/L)

DISCUSSION

HbA1c was first described by Rahbar *et al.* in 1969.¹ Later studies showed HbA1c levels correlating with glycaemic control over two to three months. This resulted in it being used in the management of patients with diabetes in the 80's.² It became essential in diabetes practice as a result of the Diabetes Control and Complications Trial (DCCT).³ and the United Kingdom Prospective Diabetes Study (UKPDS).⁴

The HbA1c target for patients with diabetes is 48 mmol/mol (6.5%). The UKPDS and DCCT demonstrated a reduction in microvascular complications by twenty five percent when HbA1c levels fall by 11 mmol/mol (1%).^{3,4} A recent study has recommended HbA1c as a diagnostic tool for diabetes.⁵ Pharmaceutical companies market the efficacy of their anti-diabetic drugs based on their reduction in HbA1c levels.

However, HbA1c can be falsely low or high in a number of conditions which can pose a diagnostic challenge to clinicians and can over or under-estimate long term glycaemic levels. They are summarized in table-1.

Table-1: Causes of altered HbA1c

LOW HbA1c	HIGH HbA1C
Blood transfusion	Iron deficiency
Haemoglobinopathies	Vitamin B12 deficiency
Acute/chronic blood loss	Uraemia
Chronic Liver Disease	Heavy alcohol intake
Drugs	Elevated bilirubin
High triglyceride levels	Drugs

Dapsone is used in the management of dermatitis herpetiformis, leprosy and various other skin disorders. It belongs to the 'sulfones' group of drugs. It is also used as prophylaxis against toxoplasmosis and pneumocystis in immunocompromised individuals. It inhibits bacterial synthesis of dihydrofolic acid. It competes with para-

aminobenzoate for the active site of dihydropteroate synthase. Its anti-inflammatory action is mediated by inhibition of the enzyme myeloperoxidase. Jollow *et al*⁶ demonstrated that N-hydroxy metabolites of dapsone are hemotoxic and induce premature sequestration of red blood cells in the spleen in rats. Common side effects include haemolysis, hepatitis, cholestatic jaundice, headache, nausea and rash amongst others.

One of the first reports of reduction in HbA1c secondary to dapsone was in the United Kingdom. The patient was taking dapsone for dermatitis herpetiformis. His HbA1c declined to 3.7% (17mmol/mol) despite high blood glucose levels. He had a raised reticulocyte count suggestive of haemolysis similar to our patient.

Serratrice J *et al.*⁸ noticed an interference in HbA1c in a patient who was on dapsone for polychondritis. Albright *et al*⁹ observed a return of HbA1c to normal levels following reduction in the dose of dapsone who had been put on it as a treatment for necrobiosis lipoidica diabetorum. In our patient, the HbA1c levels also normalized following discontinuation of dapsone

We demonstrated from our case that dapsone was the likely etiologic agent for the falsely low HbA1c levels. The HbA1c levels normalized within three months of discontinuing the drug. There are many other drugs and clinical conditions which can have a similar effect on HbA1c. Clinicians should consider haemolysis as a possible factor falsely reducing HbA1c while interpreting results in these patients. This is of particular importance in patients with diabetes as it could result in sub-optimal management and lead to long term complications.

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