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18 November 2019

Swindon GPs and Practice Diabetes Nurses

Re: Use of serum fructosamine in general clinical practice

HbA1c reflects prevailing glycaemia over the preceding 2 – 4 months however may not be reliable in conditions where there is abnormal haemoglobin metabolism. Therefore clinicians need to be aware of certain clinical situations where HbA1c may not be suitable for monitoring overall diabetes control.

In these cases self-glucose monitoring must be undertaken with the help of fructosamine measurements. Rare haemoglobinopathies including homozygous sickle cell and complex thalassaemia/haemoglobinopathy heterozygotes, haemolytic anaemia, severe blood loss, anaemia with haemoglobin below 100g/L, splenomegaly, renal dialysis (especially treated with erythropoietin), antiretroviral therapy and chronic liver disease may decrease HbA1c. Iron deficiency anaemia, end stage renal failure (carbamyated haemoglobin), hypertriglyceridaemia, hyperbilirubinaemia and alcoholism may increase HbA1c levels. Iron and vitamin B12 anaemia and their treatment may raise or lower HbA1c but the effect is small.

Serum fructosamine is formed by non-enzymatic glycosylation of serum proteins, predominately albumin. The degree of protein glycation is proportional to the concentration of plasma glucose over the lifetime of the protein. Albumin, the most common serum protein, typically accounts for 80% of all fructosamine. Because a half-life of serum albumin is 14 – 21 days serum fructosamine generally reflects the state of glycaemia control over the preceding 2 – 3 weeks.

What is the relationship between HbA1c and fructosamine? The half-life of HbA1c is much longer than that of albumin (half-life of a red blood cell is 120 days) and HbA1c reflects average glycaemic control over 3 – 4 months. HbA1c and fructosamine are highly correlated. The relationship between the fructosamine level and the HbA1c level can be presented as a line degradation analysis, as follows;

- **HbA1c = 0.017 x fructosamine level (mmol/L) + 1.61**

In practice, fructosamine testing refers to a laboratory test for diabetes management which is rarely used in clinical practice however the main advantage of the test is that it can detect overall changes in blood glucose control within a few weeks rather than months. Fructosamine is considered to be useful when the HbA1c measured may be unreliable as mentioned above.

Testing of serum fructosamine is indicated for monitoring of glycaemic control in the following circumstances:

- conditions in which HbA1c may be unreliable ie haemoglobinopathy, haemolytic anaemia, recent blood loss, anaemia with Hb < 100g/L, renal dialysis patients especially treated with erythropoietin, splenomegaly.
- Effect of changes in (less than 6 weeks) in diet, exercise or medication
- When a narrow time frame is required such as ascertaining glycaemic control at the time of conception

Which factors may affect the reliability of fructosamine test results? All conditions that affect serum albumin production (increased or decreased turnover) may affect the ability of fructosamine assay such as the following:

- Hepatic diseases (cirrhosis), nephrotic syndrome, thyroid disease, paraproteinaemia
- High levels of ascorbic acid interfere with fructosamine assay. Patients should refrain from ascorbic acid supplements for a minimum of 24 hours prior to a sample collection

Therefore serum fructosamine (glycated protein level) enables assessment of long-term glycaemic control (2-3 weeks) in patients with diabetes mellitus. Normal values vary in relation to serum albumin concentration and are 200-285mmol/L when serum albumin concentration level is 5g/dl (50g/L). Reduction in serum albumin lowers the serum fructosamine value.

What is the clinical interpretation of fructosamine?

Fructosamine levels indicate the average level of blood glucose control over the past 2 – 3 weeks. In individuals with diabetes mellitus, an increased level of serum fructosamine is associated with prolonged hyperglycaemia for 2 – 3 weeks prior to testing. The higher the fructosamine value, the poorer the degree of glycaemic control. A trend from high to normal fructosamine may indicate that changes to a treatment regime are effective.

Seeing fructosamine concentrations in patients with well controlled diabetes may overlap with those of patients who are not diabetic. The fructosamine test is not used as a screening test for diabetes diagnosis.

I hope the above information will help you to identify patients with diabetes and conditions where HbA1c may not be reliable as a test to monitor their overall diabetes control. In such cases mainly blood glucose monitoring with individualised glucose targets prior to meals mainly between 5 and 7mmol/L and two hours after meals, lower than 8.5 – 9mmol/L to be used along with measurements of fructosamine.

Fructosamine blood test may be requested via ICE, and is listed within the *Other Chemistry Tests* tab.

With kind regards

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