Glycated haemoglobin and glycated protein and glucose concentrations in necropsy blood samples

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SUMMARY Glycated haemoglobin and glycated protein (fructosamine) and blood glucose concentrations were measured in blood samples collected from 75 patients at necropsy. Estimation of blood glucose was a poor indicator of glycaemia before death. Measurement of glycated haemoglobin by affinity chromatography distinguished non-diabetic patients from diabetic patients. The distinction was not as clear cut when HbA_{1c} was estimated using electroendosmosis. Seven patients, who at necropsy had no known history of diabetes, had glycated haemoglobin concentrations in the diabetic range. Two of these patients were found to be diabetic, and diabetes had been suspected at some time in another three patients.

It is concluded that measurement of glycated haemoglobin or HbA_{1c} in necropsy specimens is a valuable tool for assessing glycaemic control in known diabetic patients, and may be useful in diagnosing previously unsuspected diabetes.

Biochemical examination of necropsy material may be of value for determining the metabolic abnormalities responsible for death: results may establish a cause of death when necropsy fails to show clinically important anatomical disease, or may help evaluate the physiological effects of recognisable anatomic lesions. Hill suggested that blood glucose estimation after death was of no value.¹ He showed that blood glucose concentrations decreased by about 0.7 mmol/hour after death due to continued cell metabolism and bacterial degradation. Based on these findings a normal blood glucose concentration in life would be expected to have fallen to concentrations approaching zero in specimens collected six to 10 hours after death. In contrast, Tonge and Wannan showed that true glucose was detectable up to 60 hours after death.²

Glycated haemoglobin provides an assessment of long term carbohydrate control in diabetic patients.³ Interest in this began with the observation by Rahbar in 1968 that diabetic patients had raised concentrations of "fast-moving" haemoglobin (HbA_{1c}) when analysed by electrophoresis.⁴ Subsequent work in several laboratories led to the identification of HbA_{1c} as glycated haemoglobin⁵⁻⁶ with the Amadori product of glucose binding preferentially to the N-amino terminal valine of the β -chain. Glycation at other sites on the haemoglobin molecule does not result in an electrophoretically distinct fraction.

The methods available for the estimation of

glycated haemoglobin either measure total HbA_{1c} (electroendosmosis)⁷ or the main stable glycated fraction HbA_{1c} after isolation from the other fractions (isoelectric focusing).⁸ More recently methods using affinity chromatography separation have been described.⁹ This separates haemoglobins to which is bound a glucose molecule and therefore measures total glycated haemoglobin.

Several workers have investigated the possibility of using glycated haemoglobin as an indicator of glucose intolerance with methods based on charge separation.¹⁰⁻¹² They reported poor sensitivity with only patients with pronounced glucose intolerance showing high results. Workers using affinity chromatography have recently described more favourable sensitivity.¹³⁻¹⁴

In this study we used affinity chromatography and electroendosmosis to estimate total glycated haemoglobin and HbA_{1c} (respectively) in samples collected from 75 cadavers coming to necropsy. Glycated protein was estimated as fructosamine. The results were then compared with the known clinical state of the patients before death.

Patients and methods

A series of unselected patients who came to necropsy over one year were included in the study. Of the 75 patients studied, 42 were men (seven known diabetics)