

## Is it time to ditch HbA1c on dialysis? Results of an observational study using continuous glucose monitoring (CGM) in patients with Type 2 diabetes and chronic kidney disease (CKD) stage 3-5, and patients with Type 2 diabetes on haemodialysis.

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**INTRODUCTION:** Renal impairment affects endogenous and exogenous insulin metabolism, contributing to an overall decline in blood glucose levels as kidney failure progresses<sup>1</sup>. The situation in haemodialysis is complicated further by poor diet and irregular meals, with haemodialysis itself altering insulin secretion, resistance and clearance<sup>2</sup>. Current guidelines<sup>3</sup> advise HbA1c levels of 58 to 68 mmol/mol in the haemodialysis population to reduce incident hypoglycaemia, however HbA1c measurement underestimates true glycaemic control in haemodialysis patients<sup>4</sup>.

**METHODS:** Fifty patients with Type 2 diabetes and CKD stage 3-5 (pre-dialysis), and fifty patients with Type 2 diabetes and on haemodialysis underwent CGM for 1 week. Patients continued their usual anti-diabetic medications throughout the study. Serum HbA1c and baseline measurements were obtained. A hypoglycaemic episode was noted if CGM readings were below 3.9 mmol/L for 15 consecutive minutes. Negative binomial regression analysed whether number of hypoglycaemic episodes were influenced by severity of kidney failure; first by CKD vs haemodialysis, then by CKD stage (3B, 4, or haemodialysis). Mean CGM glucose, estimated CGM HbA1c, percentage of time spent in normoglycaemia (3.9 to 10.0 mmol/L) and hyperglycaemia (above 10.0 mmol/L) were calculated, and robust bootstrapped ANOVA evaluated whether being in CKD stage 3-5 or haemodialysis influenced overall glycaemic control.

**RESULTS:** Mean age and weight were 69.6 years and 89.6kg in CKD patients, compared to 63.5 years and 83.7kg in haemodialysis patients. Mean serum HbA1c between CKD (58mmol/mol) and haemodialysis patients (59mmol/mol) was not significantly different ( $p=0.649$ ). Haemodialysis patients had significantly fewer hypoglycaemic episodes compared to CKD stage 3-5 patients (1.5 vs 3.3 episodes,  $p=0.025$ ). CKD stage 3-5 patients were 3.6 times more likely to have a hypoglycaemic episode compared to haemodialysis patients ( $p=0.016$ ). The effect of CKD stage on the number of hypoglycaemic episodes was also significant ( $p=0.030$ ). CKD stage 4 patients had the most number of hypoglycaemic episodes (4.5), followed by CKD stage 3B patients (2.6) and haemodialysis patients (1.5). We expected that hypoglycaemic episodes would be more frequent as kidney function declines. However post-hoc comparisons between each successive CKD stage was non-significant (CKD stage 3B vs CKD stage 4,  $p=0.232$ ; CKD stage 4 vs haemodialysis,  $p=0.09$ ). Mean estimated CGM HbA1c and mean CGM sensor glucose for haemodialysis patients (69mmol/mol, 10.8mmol/L) was significantly higher than that for CKD patients (56mmol/mol, 9.04mmol/L) ( $p<0.001$ ). Haemodialysis patients spent significantly less time in normoglycaemia (47% vs 65%,  $p<0.001$ ) and significantly more time in hyperglycaemia (52% vs 32%,  $p<0.001$ ), when compared to CKD patients.

**DISCUSSION:** CKD stage 3-5 patients had significantly more hypoglycaemic episodes than haemodialysis patients at an equivalent HbA1c, however, this was in the context of haemodialysis patients spending more time in hyperglycaemia. Although the haemodialysis patients in our study had a serum HbA1c level at the lower end of the recommended range, CGM showed poorer glycaemic control than expected with a lower hypoglycaemic incidence than feared, suggesting current guidelines aimed at avoiding extremes of

hypoglycaemia results in significant hyperglycaemia. Utility of HbA1c targeting in haemodialysis patients needs reviewing, and CGM to monitor diabetes control should be considered in these patients.