C-PEPTIDE AS A MEASURE OF INSULIN SECRETION

The physiology of C-peptide makes it appropriate for assessing insulin secretion. Insulin is produced in the pancreatic â-cells by enzymatic cleavage of the pro-hormone precursor proinsulin to produce insulin and C-peptide in equimolar amounts. C-peptide has negligible extraction by the liver and constant peripheral clearance. Its half-life is longer than insulin (20–30 min vs. 3–5 min) and it therefore circulates at concentrations approximately five times higher in the systemic circulation.7 C-peptide is commonly used in preference to insulin measurement when assessing â-cell function in clinical practice. In patients on insulin, C-peptide measurement must be used as exogenous insulin will be detected by insulin assays. 8 Insulin produced by the pancreas is extensively (approximately 50%) first-pass metabolized by the liver, both the extent of first-pass metabolism and peripheral clearance of insulin is variable, therefore peripheral insulin levels may not accurately reflect portal insulin secretion.[9,10] In non-insulin treated patients, peripheral C-peptide levels more accurately reflect portal insulin secretion than measurement of peripheral insulin.[11] C-peptide gives a measure of the patient's current status and has greater utility further from diagnosis and treatment of diabetes.12

UNITS FOR REPORTING C-PEPTIDE VALUES

The use of very different measurement units for reporting C-peptide values can lead to confusion in clinical care. C-peptide is commonly reported in nmol/L, pmol/L or ng/mL.

C- PEPTIDE IN TYPE 1 DIABETES

Type 1 diabetes accounts for approximately 5–10% of all cases of diabetes. Although the incidence peaks in puberty and early adult hood, new-onset type 1 diabetes occurs in all age-groups and people with type 1 diabetes live for many decades after onset of the disease, such that the overall prevalence of type 1 diabetes is higher in adults than in children.[13] The global prevalence of type 1 diabetes is 5.9 per 10,000 people, while the incidence has risen rapidly over the last 50 years and is currently estimated to be 15 per 100,000 people per year. [14]

Adults with new-onset type 1 diabetes can present with a short duration of illness of 1–4 weeks or a more slowly evolving process that can be mistaken for type 2 diabetes. Several other types of diabetes, for example monogenic diabetes, can be misdiagnosed as type 1 diabetes. In older adults, pancreatic cancer may present with diabetes and weight loss. A new and emerging issue is the development of profound insulin deficiency associated with the use of immune check-point inhibitors, which may present with hyperglycemia and diabetic ketoacidosis (DKA).[15,16]

Although profound insulin deficiency is the hallmark of type 1 diabetes, some adults with type 1 diabetes maintain some insulin secretion for years after diagnosis and may not require insulin treatment at diagnosis[17] , leading to diagnostic uncertainty about the type of diabetes and its management.

Fasting C-peptide is the expression of steady state, that is, static response of â cell to arterial plasma glucose concentration, whereas random (non-fasting) C-peptide is primarily affected by the incretin effect and elevation in plasma glucose following ingestion of the previous meal. A study conducted in children with type 1 diabetes showed that the C-peptide concentrations, whether measured fasting or 90 minutes after (90-CP) a mixed meal tolerance test (MMTT), were strongly related to the gold standard.[18] However, the 90-CP showed higher sensitivity and specificity than fasting C-peptide in identifying people with a peak C-peptide of 0.2 nmol/L or higher, which is a marker of clinically meaningful â-cell reserve.[19] Compared with stimulation tests, which are the current gold standard in the research setting, fasting and random measurements are easier to use in clinical practice because they are less time consuming to collect, less invasive and better tolerated by patients. [20,21]

The Diabetes Prevention Trial-Type 1 highlighted that the evaluation of C-peptide dynamics in response to oral challenges is crucial, specifically showing that a reduced early response can differentiate at-risk