C-peptide: Stepping Out of Insulin's Shadow and into the Spotlight

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Dear Editor,

We have read with interest the paper of Majaliwa et al[1] published by Global Pediatrics Health on the correlation between C-peptide and retinopathy and nephropathy in diabetic patients. We agree with them that there is a correlation between C-peptide levels and complications.

There is evidence on the cascade of interconnected physiological events:

Reduced C-peptide levels are indicative of insufficient insulin secretion by pancreatic beta cells; this deficiency in insulin secretion leads to inadequate glycemic control, despite more complex and intensive treatment regimens. This chronic state of metabolic imbalance significantly elevates the risk of developing long-term diabetic complications, such as nephropathy and retinopathy.

However, C-peptide, a peptide co-released with insulin from pancreatic beta cells which was initially considered merely a byproduct of proinsulin processing, is not just a marker of insulin secretion but acts as a biologically active molecule itself by preventing complications. This concept was already hypothesized in 2010.[2]

C-peptide mitigates renal damage through several mechanisms, including reducing glomerular hyperfiltration, lowering proteinuria, exhibiting vasoprotective properties, inhibiting renal fibrosis, and promoting cell survival by preventing apoptosis. These beneficial effects stem from C-peptide's ability to activate multiple signaling pathways, including the PI3K/Akt, PKC, MAPK, and NF-kB pathways, ultimately leading to improved renal blood flow, reduced inflammation, and enhanced cell survival.[2]

Recent research has even significantly advanced the exploration of C-peptide as a potential therapy for preventing diabetes complications, moving beyond its initial consideration as a simple adjuvant treatment. Current investigations are focusing on 2 primary areas. First, recognizing the inherent limitations of C-peptide's short half-life, scientists are developing novel formulations designed to increase its pharmacokinetic stability, thereby improving its efficacy and practicality.[3] Second, researchers are investigating the potential of Sertoli cells, which are "immune-privileged" and not typically targeted by the immune system, as delivery vehicles for C-peptide. By engineering these cells to secrete C-peptide, this approach aims to provide a continuous and long-term treatment option while minimizing the risk of immune rejection.[4]

While challenges remain in developing stable C-peptide analogs and determining optimal administration routes and dosages, its potential as a therapeutic tool for diabetic nephropathy holds promise. Further research is crucial to fully elucidate C-peptide's mechanisms of action and translate its therapeutic potential into clinical practice.

In our opinion, a Journal as influential as Global Pediatrics Health, in such innovative and interesting articles as "Correlation of C-Peptide With Complications Observed in Children and Adolescents With Type 1 Diabetes in Tanzania: A Cross-Sectional Survey," cannot ignore this crucial aspect.

Author Contributions

All authors reviewed and provided feedback on manuscript drafts. In addition, the authors had the following responsibilities: G.M. and D.I. conceived the letter, A.Z, and A.S.C wrote the manuscript and contributed to the discussion. G.M. and D.I. are the guarantors of this work and take responsibility for the integrity of the data. All authors have approved the final article.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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