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LETTER

Factors to Consider When Determining Whether Lipotoxicity Solely Causes B-Cell Decompensation in KPT2D [Letter]

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Dear editor

I read with great interest the paper by Ye et al,[1] which identified the significance of raised triglycerides in the treatment of ketosis-prone type 2 diabetes (KPT2D). The study concluded the need to implement lifestyle changes and administration of lipid-lowering medication for paediatric, hyperglycaemic KPT2D patients. As a - 5th year medical student, who completed an intercalated BSc focusing on lipidology in diabetes mellitus, I would like to discuss further factors which should be considered when evaluating the conclusion.

I commend the paper on importantly highlighting the significant difference in triglyceride levels and obesity between KPT2D and type 2 diabetes mellitus (T2DM) patients. The paper interestingly identified that both glucotoxicity and lipotoxicity lead to β-cell decompensation. However, the study chose patients in tertiary care who were highly hyperglycaemic; this would make it difficult to determine whether it is exclusively the poor glycaemic control or the hypertriglyceridemia contributing to pancreatic cell destruction and therefore it is unknown whether lipid-lowering medications would in fact help.

Furthermore, the medication regiment of patients was not accounted for in this paper. Lipid-lowering medications such as statins both have affect on triglyceride levels as well as glycaemic control. Triglyceride levels may have been underestimated for patients currently on statins. A meta-analysis found that statins generally cause a higher HbA1c, particularly atorvastatin, where as pitavastatin improves it; this could have affected their conclusion.[2] Moreover, certain T2DM medications, such as sulfonylureas, can cause a rise in a patients lipid profile, with raised total cholesterol, LDL and triglycerides.[3]

The study did not stratify patients based on gender or ethnicity which could be confounding factors. Research has shown that patients of black ethnicity have a less atherogenic lipid profile than those of white ethnicity. Patients of Asian ethnicity have higher triglyceride levels overall.[4] Moreover, the exclusion criteria stated that all the patients in the study were autoantibody negative; however, there is an increasing understanding in the pathology of T2D and the autoimmune component of the disease.[5]

Lipid profiles change over time and oscillate day to day, therefore using a one-off measurement of triglyceride levels is not representative of the patients general

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lipid profile. It would be useful to do a longitudinal study and identify the average triglyceride levels over a longer period of time for each patient.

In conclusion, the research findings are useful in identifying KPT2D patients who may require treatment earlier on to avoid atherogenic lipid profiles and develop better glycaemic control. However, this needs to be done in all sectors of care and in an ethnically diverse community in order to make the data more representative and useful to extrapolate. It is also imperative to understand the exact mechanisms behind how triglycerides and other lipoproteins lead to β-cell decompensation and whether results differ in patients with well-controlled glucose levels.

Disclosure

The author reports no conflicts of interest in this communication.

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