Does dapagliflozin affect the metabolic response in patients with elevated alanine aminotransferase (ALT) and Type 2 diabetes?: the Association of British Clinical Diabetologists (ABCD) nationwide dapagliflozin audit

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To evaluate the effect of:
(1) Dapagliflozin on metabolic response in type 2 diabetes patients with elevated alanine aminotransferase (ALT)
(2) Baseline ALT on metabolic response to dapagliflozin.

Background
Liver disease is common in type 2 diabetes, mainly due to the high prevalence of non-alcoholic fatty liver disease (NAFLD). ALT levels tend to be elevated in those with more fatty liver and tends to fall when liver fat reduces.

Methods
Anonymised patient data was collected by an online password protected questionnaire contributed by practicing clinicians from both acute hospitals and GP surgeries in UK.

Only those with both baseline and follow up ALT values within a median of 6-0 (4-0) months were included and excluded those who had bariatric surgery. Depending on baseline ALT, they were categorized into three groups: ALT<30U/L, ALT 30-50U/L, and ALT>50U/L.

Descriptive statistical analysis was performed. Changes in ALT, weight, and HbA1c over time were calculated within and between ALT groups with Wilcoxon signed rank test. And spearman’s correlation was used to derive the relationship between baseline variables including ALT and the metabolic response.

In this ABCD nationwide audit of dapagliflozin in real clinical use, 147 contributors from 57 centres all over UK submitted data on 1725 patients. Of these, we have included 558 into this analysis with both a baseline and at least one ALT follow up measurement and categorized these into three groups.

Baseline characteristics [expressed as mean ± SD and median (interquartile range)] shows that in higher ALT groups, there were more males who were much younger with a lower duration of type 2 diabetes.

In real clinical use, patients are more heavier and with much more poorer glycaemic control than in combined clinical trials of dapagliflozin.

Discussion
Apart from a positive impact on glycemic control and weight, dapagliflozin has a clinically and statistically significant response on ALT reduction in type 2 diabetes patients with a high baseline ALT>30U/L. As discussed earlier, it may well be that those with higher ALT’s are those with more fatty livers. It is possible that this is indicating some reduction in liver fat in those with higher liver fat. Baseline ALT correlated with ALT fall, weakly with HbA1c fall and did not correlate with weight fall. This result may have implications regarding the insulin resistance associated with fatty liver and non-alcoholic fatty liver disease.

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