The effect of semaglutide on alanine aminotransferase (ALT) levels: results from the Association of British Clinical Diabetologists (ABCD) nationwide audit

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Introduction

The ABCD semaglutide audit programme launched in 2020 with the aim of collecting routine clinical data from users of this medication. Previous work from the ABCD audits has demonstrated reductions in weight and HbA1c on commencement of semaglutide, including in those switched from alternative glucagon-like peptide 1 receptor agonist (GLP1RA) drugs

Previous trials and real-world evidence examining the effects of liraglutide on non-alcoholic fatty liver disease (NAFLD) have demonstrated favorable outcomes[1-3].

The aim of this analysis was to assess the impact of semaglutide on alanine aminotransferase (ALT) which may be used a surrogate marker of NAFLD.

Methods

Data were extracted from the ABCD audit tool and included providing at least one follow-up visit had occurred. Missing data were multiply imputed. Multivariate linear regression analysis was performed in Stata 16 to correct for change in co-variates. Stratified analysis by baseline ALT was also performed as follows: normal ALT (ALT<30U/L); raised ALT (ALT 3—60U/L) and significantly raised ALT (twice male reference limit, ALT>60U/L).

Results

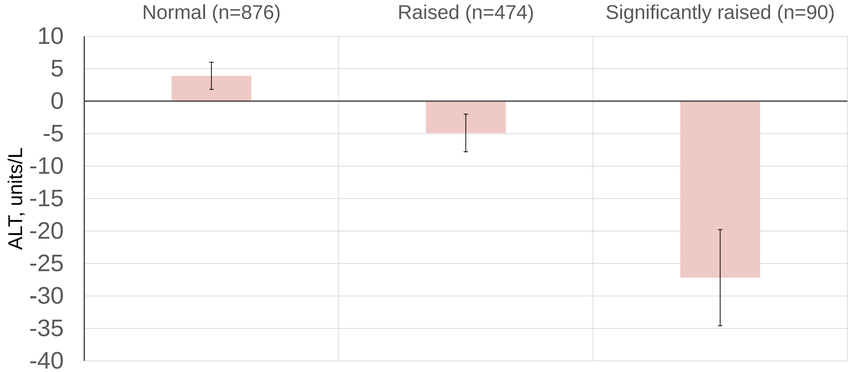
Baseline characteristics are summarized in table 1, median follow-up was 0.7 years. HbA1c reduced by 1.17% (95% CI 1.15-1.20, P<0.001) and weight reduced by 2.4kg (95% CI 1.7-3.1, P<0.001). HbA1c change predicted reductions in ALT but change in weight did not.

Across the whole population, no change in ALT was noted (P=0.19).

Characteristic		n=1,440
Age, years ± SD		58.9 ± 11.0
Male, %		50.2
Median diabetes duration, year (IQR)		10.9 (6-15.4)
Mean Hba1C,	% ± SD	9.4 ± 1.7
	mmol/mol ± SD	79.5 ± 18.5
Mean BMI, kg/m2 ± SD		37.1 ± 7.4
Mean weight, kg ± SD		104.6 ± 22.7
Median ALT at baseline, U/L (IQR)		
Normal ALT		20 (16-25)
Raised ALT		38 (33-45)
Significantly raised ALT		75 (67-91)

ALT, alanine aminotransferase; BMI, body mass index
IQR, interquartile range; SD, standard deviation

Table 1. (above) Baseline characteristic of included individuals
Figure 1. (below) Change in ALT from baseline, corrected for change in HbA1c. Error bars=95% CI. All results significant to p<0.01



Results

ALT fell by 4.9U/L (95% CI 2-7.8,P<0.001) in the raised ALT group and by 27.2U/L (95%CI 19.8-34.6, P<0.001) in the significantly raised subgroup. A slight but statistically significant increase in ALT was noted in those with normal levels at baseline.

Conclusions

Semaglutide use is associated with reductions in ALT from baseline in individuals with raised or very raised levels at baseline. In those with normal ALT a slight increase in ALT was observed. Changes in ALT in this analysis appear to be independent of weight change but are associated with change in HbA1c.

Given the established efficacy of liraglutide in the management of NAFLD it might be prudent for further work to utilize established scoring systems such as a Fib4 scores or to focus on hard end-points such as liver fat content (as assessed by MRI) or biopsy outcomes in a small randomized control trial .

We will continue to monitor and report real world outcomes with semaglutide including in its oral form, moving forward

References

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COI: TSJC has received speaker fees and/or support to attending meetings from NovoNordisk, Abbott Diabetes Care and Sanofi