Association of British Clinical Diabetologists

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Does Liraglutide Therapy Affect the Metabolic Response in Patients with An Elevated Alanine Aminotransferase and Type 2 Diabetes Mellitus?: The Association of British Clinical Diabetologists (ABCD) Nationwide Liraglutide Audit

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Abstract

The aims were to evaluate the effect of 1) liraglutide on metabolic response in patients with an elevated ALT; 2) baseline ALT on metabolic response to liraglutide. Data were obtained from the UK ABCD audit of liraglutide in real-clinical use (2009–2013, n=5985). Inclusion criteria: patients with baseline and follow-up ALT (>6 weeks apart). Exclusion criteria: liraglutide cessation. Descriptive statistics were performed (expressed as %frequency, mean±SD, median (IQR)). Patients were categorised into normal or abnormal baseline ALT groups according to gender-based levels (normal ALT males ≤30.0, females ALT ≤19.0 U/L). Changes in ALT, weight and HbA_{1c} over time were calculated within and between ALT groups (ANCOVA, Wilcoxon tests). Spearman's correlation was used to assess the relationship between baseline variables including ALT and metabolic response. Of 1309 patients (age 55.5±11.3 years, 54.8% male, 66.6% Caucasian, diabetes duration 9.0 [6.0–13.0 years]), baseline ALT was 28 (21–42 U/L), weight 110.1±22.3 kg, BMI 38.7±7.3 kg/m^2 and HbA_{1c} 9.1±1.70%. Over 8.5 months (5.1–13.0), median ALT reduction was 1.0 U/L (–8.0–4.0), BMI 0.8 kg/m^2 (–1.7–0.0) and HbA_{1c} 0.7% (–1.7–0.1) (all p<0.0001). Comparing the normal baseline ALT group (n=524, 40.0%) to high ALT group (n=784, 59.9%), ALT changed from 19.0 (16.0–24.0) to 20.0 (15.0–26.0) (slight rise; p<0.001) and 38.0 (29.0–50.0) to 33.0 U/L (25.0–47.0) (p<0.0001), respectively. Baseline ALT did not correlate with weight or HbA_{1c} response but correlated with ALT change (correlation coefficient –0.40, p<0.0001). Baseline HbA_{1c} and weight did not correlate with ALT response. This analysis of serum ALT may have implications regarding non-alcoholic fatty liver disease, associated with T2D. We conclude that liraglutide in real clinical use has a clinically significant impact on ALT reduction in T2D patients with a high baseline ALT.

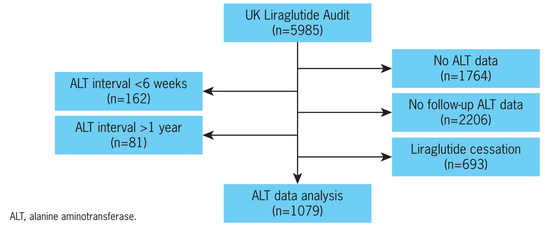
Introduction and aims

- The nationwide liraglutide audit is an initiative launched by the UK's Association of British Clinical Diabetologists (ABCD) to evaluate the real clinical use, efficacy and adverse effects of liraglutide.
- To date, anonymized data from 5985 patients with type 2 diabetes (T2D) treated with liraglutide has been collected (500 contributors, 89 centres, 2009–2013).
- In T2D patients, non-alcoholic fatty liver disease (NAFLD) is a commonly observed disorder[1] and serum alanine aminotransferase (ALT) levels are often used as a blood marker of liver injury.[2]
- Clinical trial data suggest that liraglutide may reduce ALT in patients with T2D, particularly when ALT is elevated at baseline.[3]
- The aim of the present sub-analysis of the ABCD liraglutide audit data was to determine whether 1) liraglutide treatment affected metabolic responses and elevated ALT levels, and 2) baseline ALT impacted upon the metabolic response to liraglutide.

Methods

- Data were obtained from the UK ABCD audit of liraglutide use in real clinical practice.
- Inclusion criteria: patients with ALT values at baseline and follow-up (>6 weeks apart).
  Exclusion criteria: liraglutide cessation.
- Median changes in HbA_{1c}, BMI and serum ALT were recorded for the study population after liraglutide therapy.
- Patients were stratified by normal or abnormal baseline ALT according to gender-based levels (males, normal ALT ≤30.0 U/L; females, normal ALT ≤19.0 U/L).
- Changes in ALT, HbA_{1c} and weight over time were calculated within and between ALT groups (analysis of covariance; ANCOVA, Wilcoxon tests).
- Spearman's correlation was used to assess the relationship between baseline variables including ALT and metabolic response.

Figure 1. Patient selection.

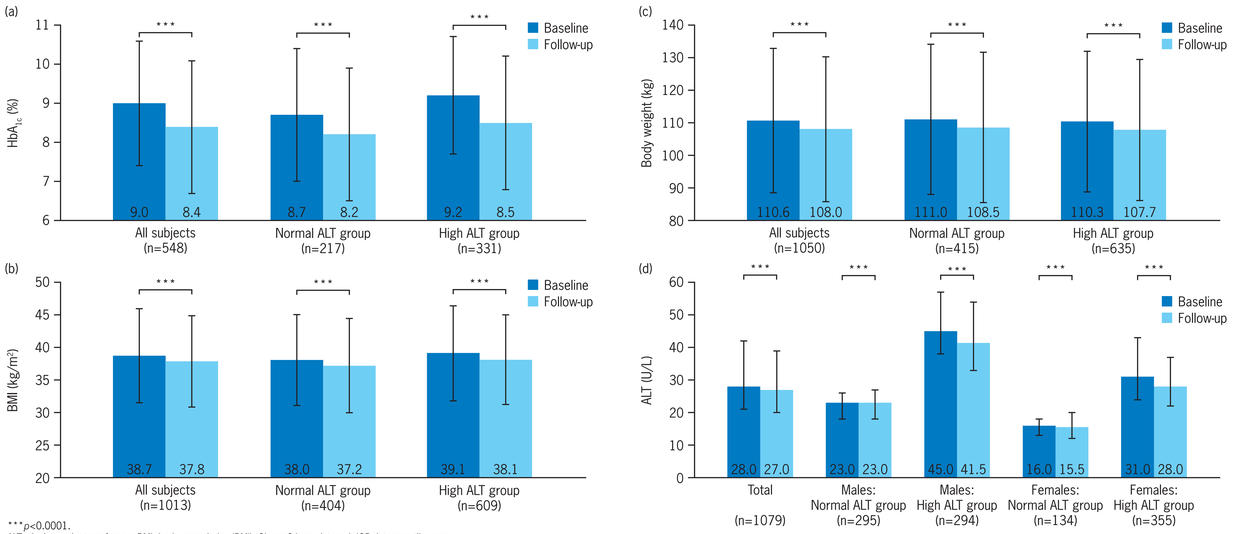


ALT, alanine aminotransferase.

Results

- Figure 1 shows how the 1079 out of 5985 patients selected for this analysis were chosen.
- Baseline characteristics of these 1079 patients are described in Table 1.
- Figure 2 (a–c) shows the HbA_{1c}, BMI and body weight values in normal and high ALT groups before and after liraglutide treatment (4.4 [3.0–6.2] months).
- Figure 2d shows the median ALT values at baseline and follow-up for male and female patients with normal and high ALT levels after liraglutide treatment (4.4 [3.0–6.2] months).
- Baseline ALT was inversely correlated with change in ALT (correlation coefficient 0.38, p<0.0001).
- Baseline ALT levels did not correlate with HbA_{1c} (correlation coefficient, –0.05, p=0.24), BMI (correlation coefficient, –0.38, p=0.73) or weight response (correlation coefficient, 0.00, p=0.99). HbA_{1c} and weight at baseline did not correlate with ALT response.

Figure 2. Mean values for metabolic parameters for all subjects and normal and high ALT groups before and after liraglutide therapy. The between normal and high ALT groups ANOVA values for a) HbA_{1c}, b) BMI and c) body weight were p=0.18, p=0.33 and p=0.56, respectively. Error bars represent standard deviation; (d) median change in ALT in all subjects and in males/females in normal and high ALT groups. Error bars represent 95% CI.



***p<0.0001.
ALT, alanine aminotransferase; BMI, body mass index (BMI); CI, confidence interval; IQR, interquartile range.

Table 1. Baseline characteristics of study participants

Characteristic	n=1079
Age, years ± SD	55 ± 11.0
Male, %	54.6
Median diabetes duration, years (IQR)	10 (6–14)
Caucasian, %	87.1
Mean HbA_{1c} ± SD	9.1 ± 1.7
Mean BMI, kg/m^2 ± SD	38.7 ± 7.2
Mean weight, kg ± SD	110.5 ± 22.2
Median ALT, U/L (IQR) Males Females	28 (21–42) 30 (23–45) 26 (19–37)
Median value for normal ALT at baseline, U/L (IQR) Males, n=295 (68.8%) Females, n=134 (31.2%)	 23 (18–26) 16 (13–18)
Median value for high ALT at baseline, U/L (IQR) Males, n=294 (45.3%) Females, n=355 (54.7%)	 45 (38–57) 31 (21–43)

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

Conclusions

- Liraglutide had a clinically significant impact on ALT reduction in patients with T2D with elevated ALT levels at baseline in routine clinical practice.
- This analysis utilising serum ALT may have implications regarding co-existing T2D and NAFLD. Future randomized control trials are required.

References

1. Day *et al. J Gastroen Hepatol* 2002;17:S377–84.
2. Schindhelm *et al. Diabetes Metab Res Rev* 2006; 22:437–43.
3. Armstrong *et al. Aliment Pharmacol Ther* 2013;37:234–42.

Acknowledgments

The ABCD nationwide GLP-1 receptor agonist audit program has received grants from Eli Lilly & Co and Novo Nordisk. The liraglutide audit was independently initiated and performed by ABCD, and the authors remained independent in the analysis and writing of this report. The authors take full responsibility for the content of the poster but are grateful to Watermeadow Medical (supported by Novo Nordisk) for writing assistance.

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Presented at the American Diabetes Association, 21–25 June 2013, Chicago, USA.