Liraglutide is Safe and Effective in Mild or Moderate Renal Impairment: the Association of British Clinical Diabetologists (ABCD) Nationwide Liraglutide Audit

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Abstract

We evaluated the safety and efficacy of liraglutide among patients with mild or moderate renal impairment. Data was obtained from a nationwide audit of liraglutide use in UK. Among 4129 patients, we excluded patients with follow-up <6 months, previously on exenatide, used liraglutide 1.8 mg (too few to analyze), or lacked baseline data to estimate creatinine clearance (CrCl) using the Cockcroft–Gault formula. Remaining 1081 patients were divided into CKD group 1 (normal, eCrCl>90 mL/min) (n=872), CKD group 2 (mild renal impairment, eCrCl 60–90 mL/min) (n=169) and CKD group 3 (moderate renal impairment, eCrCl 30–59 mL/min) (n=40). Effect of CKD group on changes of A1c, weight, systolic blood pressure (SBP) and creatinine (Cr) at 6 months were analyzed using ANCOVA using baseline values as covariates, while proportion of patients reaching A1c ≤7%, suffering gastrointestinal (GI) side effects (adjusted for gender), or hypoglycemia (adjusted for insulin and sulfonylurea use) using logistic regression. A1c and weight reduction for all three groups were significantly reduced from baseline; CKD group 1, −1.0% (0.1) and −3.6 kg (0.2), CKD group 2, −0.9% (0.1) and −3.3 kg (0.4), and group 3, −0.8% (0.2) and 2.5 kg (0.9). There were no influences of CKD group on A1c reduction (p=0.46) or weight reduction (p=0.95). Similarly, no effect of CKD group was seen on SBP reduction (−4 mmHg vs. −3 mmHg vs. −6 mmHg, p=0.74), rates of GI side effects (15.3% vs. 12.4% vs. 17.5%, CKD 2 vs. 1 OR [95%CI] 0.8 [0.5,1.2], p=0.26) or rates of reported hypoglycemia (1.7% vs. 1.2% vs. 0%, CKD 2 vs. 1 OR 0.5 [0.1,2.2] (p=0.36). A small but significant reduction of Cr was observed with advancing CKD group (+1 µmol/L vs. −3 µmol/L vs. −7 µmol/L, p=0.02). 1 case of acute renal failure attributed to dehydration from prolonged vomiting was reported in CKD group 2. We conclude that liraglutide 1.2 mg is safe and effective in real-life clinical practice among patients with mild or moderate renal impairment.

Introduction

- Many patients with type 2 diabetes (T2D) develop renal impairment (RI) as disease progresses.[1]
- Unlike many antidiabetic treatments, liraglutide, a once-daily human glucagon-like peptide-1 (GLP-1) analog, is metabolized in a similar manner to large proteins and not excreted via the kidneys.[2] Liraglutide may, therefore, be of particular value in T2D patients with RI.

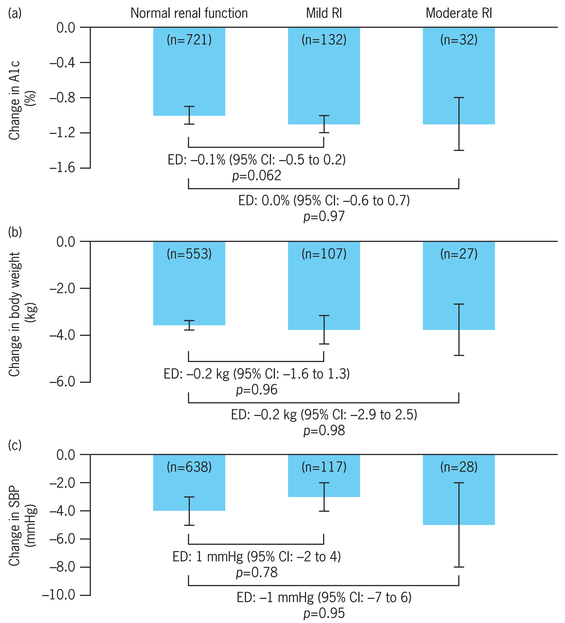
Aim

- To evaluate the safety and efficacy of liraglutide treatment among patients with mild or moderate RI using data from a nationwide UK clinical audit.

Methods

- Data were obtained from the ABCD nationwide clinical audit of liraglutide use in the UK. Among 4129 patients, 3048 were excluded due to: <6 months follow-up, previously on exenatide, used liraglutide 1.8 mg (too few to analyze) or lacked baseline data to estimate creatinine clearance (eCrCl) using the Cockcroft–Gault formula.
- The remaining 1081 patients were divided into three groups: normal renal function (NRF) (eCrCl >90 mL/min) (n=872), mild RI (eCrCl 60–90 mL/min) (n=169) and moderate RI (eCrCl 30–59 mL/min) (n=40).
- Effect of RI on changes in A1c, weight, systolic blood pressure (SBP) and serum creatinine (Cr) at 6 months were analyzed using analysis of covariance (ANCOVA). Baseline values (all analyses) and insulin use and disease duration (A1c and weight only) were used as covariates.
- Logistic regression was used to analyze the proportion of patients reaching A1c ≤7%, or suffering gastrointestinal (GI) side effects or hypoglycemia.

Figure 1. Comparisons of the change in (a) A1c, (b) body weight and (c) SBP from baseline following 6 months of liraglutide 1.2 mg treatment in T2D patients with normal renal function and mild or moderate RI.



Data are adjusted least-squares means (±SE). Estimated differences (ED) between patient groups were analyzed by ANCOVA using baseline values (all analyses) and insulin use and disease duration (A1c and weight only) as covariates.
CI, confidence interval.

Results

Efficacy

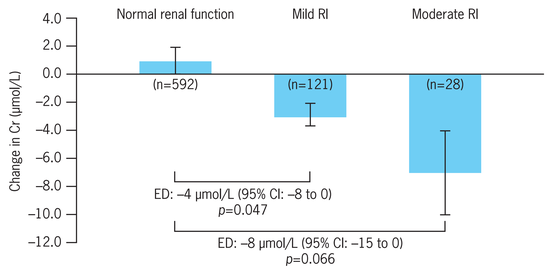
- Following 6 months of liraglutide 1.2 mg treatment, unadjusted mean (SE) reductions in A1c and weight from baseline for patients with NRF, mild RI and moderate RI were: −1.0% (0.1) and −3.6 kg (0.2), −0.9% (0.1) and −3.3 kg (0.4), and −0.8% (0.2) and −2.5 kg (0.9), respectively (p<0.05 for all).
- Unadjusted mean (SE) reductions from baseline in SBP were also observed for all three groups following liraglutide treatment: −4 mmHg (1), p<0.001; −3 mmHg (1), p=0.07 and −6 mmHg (3), p=0.09, respectively.

Table 1. Odds ratio of achieving glycemic target or experiencing GI side effects or hypoglycemia in patients with mild or moderate RI compared with patients with NRF.

	NRF	Mild RI	Moderate RI	Mild RI vs. NRF OR (95% CI); p-value	Moderate RI vs. NRF OR (95% CI); p-value
Achieving A1c ≤7% (%)	25.0	25.8	18.8	1.21 (0.73 to 2.00); 0.46	0.57 (0.19 to 1.69); 0.31
GI side effects (%)	15.3	12.4	17.5	0.76 (0.46 to 1.25); 0.28	1.06 (0.46 to 2.47); 0.89
Hypoglycemia (%)	1.7	1.2	0.0	0.49 (0.11 to 2.22); 0.36	N/A

Odds ratios (ORs) for differences between patient groups were calculated by logistic regression.
N/A, not applicable.

Figure 2. Comparison of the change in Cr from baseline following 6 months of liraglutide 1.2 mg treatment in T2D patients with normal renal function and mild or moderate RI.



Data are adjusted least-sqaures means (±SE). Estimated differences (ED) between patient groups were analyzed by ANCOVA using baseline values as covariates.

- Estimated differences between adjusted mean changes in A1c, weight and SBP from baseline and the proportion of patients achieving the glycemic target (A1c ≤7%) were not statistically different between patients with NRF, mild RI or moderate RI (Figure 1 and Table 1).

Safety

- Proportions of patients experiencing GI side effects and hypoglycemia were similar for patients with NRF, mild RI or moderate RI, respectively.
  - RI had no effect on the proportion of patients who experienced GI side effects or reported hypoglycemia (Table 1).
- A small reduction of Cr was observed with increasing severity of RI following liraglutide treatment, with the difference between normal renal function and mild RI achieving statistical significance (Figure 2).
- One patient with mild RI treated with liraglutide experienced acute renal failure, attributed to dehydration from prolonged vomiting.

Conclusions

- These data suggest that liraglutide 1.2 mg is well tolerated and effective in real-life clinical practice among patients with mild or moderate RI.
- Due to the small numbers of patients with moderate RI in these analyses, further study in a larger population is required to fully characterize the safety and efficacy of liraglutide in T2D patients with moderate RI.

References

1. Retnakaran *et al. Diabetes*. 2006;55:1832–9.
2. Novo Nordisk. Liraglutide Summary of Product Characteristics. 2012. http://www.medicines.org.uk/emc/medicine/21986/SPC/

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