Safety and efficacy of liraglutide 1.2mg in patients with mild and moderate renal impairment: the ABCD nationwide liraglutide audit

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Abstract

Liraglutide is not predominantly eliminated by renal excretion. We assessed its safety and efficacy among patients with mild and moderate renal impairment.

Patients from a nationwide audit of liraglutide (1.2mg) use were divided according to pre-treatment renal function calculated by the Cockcroft-Gault formula. Adverse events, liraglutide discontinuation and changes in HbA_{1c}, weight, systolic blood pressure and serum creatinine were compared between groups of different pre-treatment renal function.

As compared with patients with normal renal function (n=1446), patients with mild renal impairment (n=288) and moderate renal impairment (n=57) were equally likely to report gastrointestinal side effects (adjusted OR 1.11 [95% CI 0.80–1.54] and 0.67 [95% CI 0.31–1.48]), respectively, but more frequently stopped liraglutide due to gastrointestinal side effects (adjusted OR 2.32 [95% CI 1.45–3.74] and 2.37 [95% CI 0.97–5.81]), respectively. Minor hypoglycaemia and acute renal failure were uncommonly reported and were not more frequent among patients with renal impairment. Patients remaining on treatment in all three groups achieved significant HbA_{1c} and weight reduction at six months (between -11 to -12mmol/mol [-1.0 to -1.1%] and -3.6 to -3.8kg). No effect of renal function was seen influencing the degree of HbA_{1c} and weight reduction. Liraglutide treatment was associated with a small reduction in serum creatinine among patients with renal impairment.

We concluded that liraglutide was safe, efficacious but more frequently discontinued among patients with mild renal impairment. More data are needed to establish its safety among patients with moderate or more significant renal impairment.
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Key words

liraglutide; GLP-1; incretin; renal impairment

Introduction

Liraglutide, an injectable glucagon-like peptide-1 receptor agonist (GLP-1RA), acts by mimicking the endogenous gut hormone, GLP-1. The physiological actions of GLP-1 in the body are diverse but include enhancing insulin secretion, inhibiting hyperglucagonaemia, delaying gastric emptying and suppressing appetite.[1] Clinical trials in type 2 diabetes have shown beneficial effects of liraglutide in reducing hyperglycaemia, body weight and systolic blood pressure (SBP), alongside a low treatment risk of hypoglycaemia.[2]

Unlike exenatide, the first GLP-1RA available for use, liraglutide is metabolised in the body much like a large peptide with minimal renal excretion.[3–6] In a pharmacokinetic study, administration of liraglutide to patients with varying degrees of renal impairment did not significantly increase a subject's exposure to the drug.[3] Nevertheless, due to limited experience in patients with renal impairment, as well as concerns with post-marketing reports of acute renal failure (ARF) being precipitated by GLP-1RAs, the prescribing information for liraglutide still advocates caution in initiating or escalating the dose of liraglutide in patients with (any degree of) renal impairment.[5–9]

The Association of British Clinical Diabetologists (ABCD) is the diabetes specialist society in the UK. ABCD conducted a nationwide audit on the use of liraglutide to ascertain its effectiveness and safety in real-life clinical practice. We used data from the audit to analyse the safety and efficacy of liraglutide 1.2mg among patients with mild and moderate renal impairment.

Subjects and methods

The ABCD nationwide liraglutide audit. From December 2009, ABCD invited diabetes centres across the UK to submit anonymised data of patients routinely treated with liraglutide. The

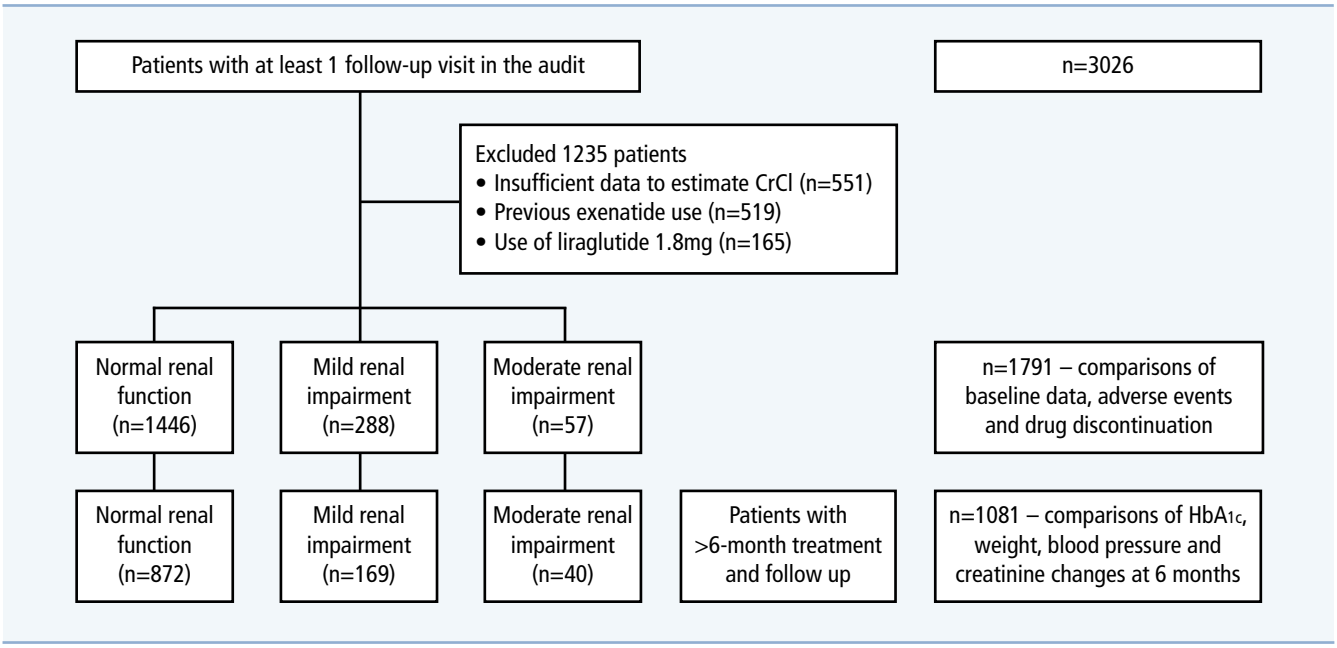

Figure 1. Patients in the ABCD nationwide liraglutide audit included for the analyses on safety and efficacy of liraglutide 1.2mg, stratified by pre-treatment renal function. (CrCl: creatinine clearance)

audit was opened for two years to all interested diabetes centres and the invitation was disseminated by electronic mail communication and conference presentations. Participation was voluntary and unfunded. Centres submitted varying degrees of data depending on the frequency of patients' health visits and duration of liraglutide treatment that had taken place. Data requested included patients' age, gender, ethnicity, pre- and post-liraglutide diabetes treatments, glycated haemoglobin (HbA_{1c}), body weight, body mass index (BMI), blood pressure, serum lipids and serum measures of renal and liver function, whenever these were available. Details on possible treatment related adverse events and discontinuation of liraglutide were also requested. Data entry and submission were performed using an audit software provided by ABCD.

Patients included for analyses. Patients in the audit were excluded from the current analyses if there was lack of baseline (pre-liraglutide treatment) data for the estimation of creatinine clearance, had prior exenatide treatment, or used the liraglutide 1.8mg dose (there were too few for meaningful comparisons). Remaining patients were divided into three groups based on estimated baseline creatinine clearance (eCrCl): those with normal renal function, (eCrCl ≥90ml/min), mild renal impairment, (eCrCl 60–89ml/min), and moderate renal impairment (eCrCl 30–59ml/min). CrCl was estimated using the Cockcroft-Gault formula: CrCL =

$$\frac{(140\text{-Age}) \times (\text{weight in kg}) \times 1.23 \times (0.85 \text{ if female})}{(\text{serum creatinine in } \mu\text{mol/L})}$$

Outcomes analysed. Safety outcomes compared between groups include the proportion of patients reporting gastrointestinal (GI) side effects, minor hypoglycaemia, ARF, and the proportion discontinuing liraglutide within six months of starting liraglutide. Mean changes in serum creatinine at six months were also compared. Nausea, vomiting or diarrhoea were grouped collectively as GI side effects. Minor hypoglycaemia was defined locally by individual contributing centres. We defined ARF as when there was an increase of serum creatinine by one and a half times that of the pre-liraglutide treatment level in line with local guidelines.[10]

The efficacy of liraglutide was assessed by comparing mean changes in HbA_{1c}, weight and SBP at six months between patient groups. Comparisons were restricted to among patients who completed at least six months of liraglutide treatment. The last available data for HbA_{1c}, SBP and serum creatinine at six months, but at least six weeks from starting liraglutide treatment, were used for analyses. Weight data were restricted to data at 26±6 weeks of treatment.

Statistical analyses. Inter-group baseline differences were compared using ANOVA, Kruskal-Wallis test or tabulated statistics for normally distributed, non-parametric and categorical data, respectively. Within patient groups, changes from baseline to six months for HbA_{1c}, weight, SBP and serum creatinine were compared using paired t-tests. Comparisons of mean HbA_{1c}, weight, SBP and serum creatinine changes between groups were performed using ANCOVA, using renal function group as a fixed effect and baseline values (HbA_{1c}, weight, SBP or serum creatinine) as covariates. Diabetes duration and insulin/non-insulin use status were also included as covariates in the analyses of HbA_{1c} and weight changes. Differences of adjusted means (least squares [LS] means) between renal function groups are reported using 95% confidence intervals (CIs) and adjusted p-values. The likelihood of patients with mild and moderate renal impairment, as compared with patients with normal renal function, reporting GI side effects, hypoglycaemia and discontinuing liraglutide

	n data	All	Normal renal function, eCrCl ≥90ml/min (n=1446)	Mild renal impairment, eCrCl 60–89ml/min (n=288)	Moderate renal impairment, eCrCl 30–59ml/min) (n=57)	P-value
eCrCl (ml/min)	1791	>90	>90	77±8	49±8	<0.01
Creatinine (µmol/L)	1791	85±26	78±17	109±25	151±52	<0.01
Male:female (% patients)	1791	55:45	56:44	51:49	33:67	<0.01
Ethnicity (% Caucasian)	1561	90.5	90.2	92.0	89.8	0.67
Age (years)	1791	56±11	53±10	65±8	70±11	<0.01
Diabetes duration (years)	1612	10 (5–13)	8 (5–12)	11 (8–15)	11 (8–16)	<0.01
HbA_{1c} (mmol/mol) HbA_{1c} (%)	1783 1783	78±19 9.3±1.7	79±19 9.4±1.7	77±17 9.2±1.6	78±21 9.3±1.9	0.23 0.23
Weight (kg)	1791	111.1±22.5	114.3±22.5	98.4±16.3	92.1±16.4	<0.01
BMI (kg/m^2)	1739	39.1±7.5	40.0±7.6	35.7±5.6	35.1±5.7	<0.01
SBP (mmHg)	1658	138±19	139±19	138±18	139±23	0.94
Insulin use (% patients)	1791	41.0	39.6	45.1	56.1	0.01

Continuous variables shown as mean ± SD; diabetes duration shown as median (inter-quartile range). eCrCl: estimated creatinine clearance; BMI: body mass index; SBP: systolic blood pressure.

Table 1. Baseline characteristics of 1791 patients in the ABCD nationwide liraglutide audit according to pre-treatment renal function

was assessed using binary logistic regression analyses. Additional variables entered for each analysis were: gender and metformin use (analysis on GI side effects); insulin use, sulphonylurea use and baseline HbA_{1c} (analysis on hypoglycaemia); and insulin use and gender (analysis on liraglutide discontinuation). Results are expressed as adjusted odds ratio (OR) with 95% CIs. P-values of <0.05 were deemed significant for all analyses. Statistical calculations were performed using Minitab® Release 14.11 (Minitab Ltd, Coventry, UK).

Results

Patients included for analyses. The audit received data on 3026 patients who had at least one clinic follow up after liraglutide initiation. Seventy-seven centres participated of which 72 centres were diabetes centres in hospitals and five were from primary care. A total of 1235 patients were excluded from the analyses (Figure 1). Data from the remaining 1791 patients were used to compare the rate of adverse events and drug discontinuation. In all, 1081 patients completed at least six months of liraglutide treatment and follow up; data from these patients were used to compare changes in HbA_{1c}, weight, SBP and serum creatinine.

Baseline characteristics of patients are shown in Table 1. Patients with mild or moderate renal impairment, as compared with patients with normal renal function, were more likely female, older, had longer duration of diabetes, were less overweight and were more likely to be on insulin treatment.

Adverse events and liraglutide discontinuation. Table 2 summarises the proportion of patients with normal renal function, mild renal impairment and moderate renal impairment who reported GI side effects, minor hypoglycaemia and liraglutide discontinuation. The proportions of patients reporting GI side effects were 17.8%, 19.8% and 14.0%, respectively. Patients with mild renal impairment or moderate renal impairment were not more likely to report GI side effects as compared with patients with normal renal function (adjusted OR 1.11 [95% CI 0.80–1.54, p=0.53] and adjusted OR 0.67 [95% CI 0.31–1.48, p=0.32], respectively). Female patients, rather than patients with poorer pre-treatment renal function, were more likely to report GI side effects (adjusted OR 1.82 [95% CI 1.42–2.34, p<0.01]).

The proportions of patients who reported minor hypoglycaemia were low at 1.3%, 1.4% and 0%, respectively. Patients with mild renal impairment were equally likely to report hypoglycaemia compared with patients with normal renal function (adjusted OR 0.79 [95% CI 0.26–2.39, p=0.67]). No cases of severe hypoglycaemia, as defined by the need for external assistance, were reported in any of the three groups.

Among patients with follow-up serum creatinine, ARF was reported among 4/592 (0.7%) patients with normal renal function and among 1/121 (0.8%) of those with mild renal impairment. No cases of ARF were reported among patients with moderate renal impairment. Two cases of ARF, one among a patient

	NRF (n=1446)	Mild RI (n=288)	Moderate RI (n=57)	Mild RI vs NRF OR [95% CI]	P-value	Moderate RI vs NRF OR [95% CI]	P-value
Gastrointestinal side effects	257 (17.8)	57 (19.8)	8 (14.0)	1.11 [0.80–1.54]	0.53	0.67 [0.31–1.48]	0.32
Hypoglycaemia	19 (1.3)	4 (1.4)	0 (0)	0.79 [0.26–2.39]	0.67	–	–
Liraglutide discontinuation – total	148 (10.2)	49 (17.0)	9 (15.8)	1.77 [1.25–2.52]	<0.01	1.73 [0.85–3.52]	0.13
Reason for discontinuation:							
Gastrointestinal side effects	53 (3.7)	26 (9.0)	5 (8.8)	2.32 [1.45–3.74]	<0.01	2.37 [0.97–5.81]	0.06
Lack of efficacy	36 (2.5)	9 (3.1)	1 (1.8)	1.24 [0.59–2.61]	0.57	0.68 [0.09–5.08]	0.71
Non-gastrointestinal side effects	10 (0.7)	4 (1.4)	0 (0)	NE	–	NE	–
Other reasons*	26 (1.8)	1 (0.3)	2 (3.5)	NE	–	NE	–
No reason specified	23 (1.6)	9 (3.1)	1 (1.8)	NE	–	NE	–

Values expressed as n (%) of patients. *Other reasons are varied but include intercurrent illness, difficulty obtaining prescriptions, planning pregnancy etc.
NRF: normal renal function; RI: renal impairment; OR: odds ratio; NE: not evaluated.

Table 2. Proportion of 1791 patients treated with liraglutide 1.2mg reporting gastrointestinal side effects, hypoglycaemia and liraglutide discontinuation: comparison between patients with mild and moderate renal impairment versus normal renal function

with normal renal function and one among a patient with mild renal impairment, were attributed to dehydration from the persistent side effect of diarrhoea. These occurred six months and one month, respectively, after liraglutide was initiated. Renal function improved vs baseline for both cases with the cessation of liraglutide. One case was due to diarrhoea thought to be more likely due to infectious gastroenteritis, with serum creatinine levels normalising and remaining normal after liraglutide was re-introduced. Two cases were asymptomatic elevations of serum creatinine at one and four months after liraglutide initiation, respectively. The first patient continued liraglutide treatment without any side effects and serum creatinine levels subsequently settled with cessation of an angiotensin-converting enzyme (ACE) inhibitor. The second patient was lost to the audit's follow up.

Assessment of mean serum creatinine changes at six months among patients with normal renal function, mild renal impairment and moderate renal impairment, showed a small but significant reduction of serum creatinine among patients with mild and moderate renal impairment (1µmol/L vs -3µmol/L vs -7µmol/L, p=0.02 for effect of renal function group). (Table 3.)

The proportions of patients who discontinued liraglutide before six months of treatment were 10.2%, 17.0% and 15.8% for patients with normal renal function, mild renal impairment and moderate renal impairment, respectively. Logistic regression showed that patients with mild renal impairment were more likely to discontinue liraglutide by six months compared with patients with normal renal function (adjusted OR 1.77 [95% CI 1.25–2.52, p<0.01]). This was due to more frequent discontinuation attributed to intolerable GI side effects (9.0% vs 3.7%, adjusted OR 2.32 [95% CI 1.45–3.74, p<0.01]), rather than more frequent discontinuation due to lack of drug efficacy (Table 2). Patients with moderate renal impairment were also more likely to discontinue liraglutide due to GI side effects but this did not reach statistical significance (8.8% vs 3.7%, adjusted OR 2.37 [95% CI 0.97–5.81, p=0.06]).

HbA1c results. Table 3 summarises the changes in HbA1c, weight, SBP and serum creatinine at six months among patients with normal renal function, mild renal impairment and moderate impairment.

Patients in all three groups of renal function achieved significant HbA1c reduction from baseline (all p<0.01) with liraglutide 1.2mg treatment. Adjusted mean ± SE HbA1c reductions for patients with normal renal function, mild and moderate renal impairment were -11±1mmol/mol (-1.0±0.1%), -12±1mmol/mol (-1.1±0.1%) and 12±3mmol/mol (-1.1±0.3%), respectively. No effect was seen for renal function group influencing HbA1c reduction (p>0.05).

Weight results. Patients in all three groups achieved significant weight reduction from baseline (normal renal function and mild renal impairment group [p<0.01], moderate renal impairment [p=0.01]). Adjusted mean ± SE weight reductions were -3.6±0.2kg, -3.8±0.6kg and -3.8±1.1kg, respectively. No effect was seen for renal function group influencing weight reduction (p>0.05).

Blood pressure results. Treatment with liraglutide was associated with a significant reduction in SBP for patients with normal renal function (-4±1mmHg [p<0.01]), but this did not reach significance in patients with mild renal impairment (-3±1mmHg [p=0.07]) or patients with moderate renal impairment (-5±3mmHg [p=0.09]). No effect of renal function group was seen influencing the degree of SBP reduction (p>0.05).

Discussion

Patients in the nationwide audit were characterised by being significantly obese (mean BMI 39.1kg/m^2), poorly controlled (mean HbA1c 78mmol/mol [9.3%]), and with many already on insulin treatment (41%). Most were started on liraglutide 1.2mg rather than the 1.8mg dose (after the usual dose escalation from 0.6mg). These characteristics stand in contrast to patients from a

	NRF	Mild RI	Moderate RI	Mild RI vs NRF LS mean difference [95% CI]	P-value	Moderate RI vs NRF LS mean difference [95% CI]	P-value
HbA_{1c} change (n=721, 132, 32)							
IFCC – mmol/mol	-11±1	-12±1	-12±3	-1 [-4.9 to 2.1]	0.62	-1 [-7 to 6]	0.97
DCCT – %	-1.0±0.1	-1.1±0.1	-1.1±0.3	-0.1 [-0.5 to 0.2]	0.62	0.0 [-0.6 to 0.7]	0.97
Weight change (kg) (n=553, 107, 27)	-3.6±0.2	-3.8±0.6	-3.8±1.1	-0.2 [-1.6 to 1.3]	0.96	-0.2 [-2.9 to 2.5]	0.98
SBP change (mmHg) (n=638, 117, 28)	-4±1	-3±1	-5±3	1 [-2 to 4]	0.78	-1 [-7 to 6]	0.95
Cr change (µmol/L) (n=592, 121, 28)	1±1	-3±1	-7±1	-4 [-8 to 0]	0.047	-8 [-16 to 0]	0.07

Values are adjusted (least squares [LS]) mean ± SE. NRF: normal renal function; RI: renal impairment; CI: confidence intervals; SBP: systolic blood pressure; Cr: creatinine.

Table 3. HbA_{1c}, weight, systolic blood pressure and serum creatinine changes at 6 months among patients treated with liraglutide 1.2mg: comparison between patients with mild and moderate renal impairment versus normal renal function

pooled analysis of the phase III clinical trial programme for liraglutide, which had a mean baseline BMI and HbA_{1c} of 31.9kg/m^2 and 68mmol/mol (8.4%), respectively.[11] There was likely an influence by national prescribing guidelines issued by the National Institute for Health and Clinical Excellence (NICE), which only recommend the use of liraglutide 1.2mg, and its use generally only among patients with BMI >35kg/m^2.[12] Nevertheless, the audit showed that the off-licence use of liraglutide with insulin, as well as the use of liraglutide in patients with BMI <35kg/m^2, was common in diabetes referral centres. The findings of the audit will be immediately relevant to specialist diabetes practice, but may not necessarily be able to be generalised to patients treated with the 1.8mg dose of liraglutide.

Findings from the audit provide important post-marketing safety data for the use of liraglutide in the 'real world'. Results from the audit showed equivalence in various outcome measures of safety and efficacy comparing patients with mild renal impairment with those with normal renal function, but more frequent discontinuation among the former group. Similar results were found for patients with moderate renal impairment, but the results will need to be interpreted with caution due to the small number of patients available for analyses.

Altered pharmacokinetics or pharmacodynamics of a drug in renal impairment may manifest by the occurrence of more frequent side effects. In our audit, the proportions of patients reporting GI side effects or hypoglycaemia with liraglutide treatment were not greater among patients with mild or moderate renal impairment. This supports findings from a pharmacokinetic study testing the 0.75mg dose of liraglutide, which showed no increase in drug exposure in patients with renal impairment. The prescribing information for liraglutide reported that after the administration of [3H]-liraglutide, the major component in plasma was intact liraglutide while no intact liraglutide was detected in urine or faeces. Only 6% and 5% of the administered radioactivity was excreted as liraglutide-related metabolites in urine and faeces, respectively. As opposed to native GLP-1 and its metabolites, liraglutide is metabolised endogenously much like large proteins rather than having a specific organ as a major route of elimination.[3,5]

The audit, however, found that patients with mild renal impairment more frequently discontinued liraglutide due to GI side effects as compared with patients with normal renal function. This was despite there being similar proportions of patients reporting GI side effects in both groups. This finding raises the possibility that the GI side effects experienced by patients with renal impairment treated with liraglutide may be more significant or persistent. A meta-analysis on the efficacy and safety of liraglutide in patients with renal impairment in the Liraglutide Effect and Action in Diabetes (LEAD) trials performed by Davidson *et al.* reported a related finding: they reported that patients with moderate or severe renal impairment had a slower rate of decline of nausea over time than patients with normal renal function or mild renal impairment.[13] Since our audit and the meta-analysis had relatively small numbers of patients with moderate renal impairment, there is a need for more studies to evaluate the safety of liraglutide at marketed doses of 1.2mg or 1.8mg among patients with more significant renal impairment. Nevertheless, in the absence of a substantial risk in precipitating acute renal dysfunction, we feel that a greater likelihood of needing to discontinue liraglutide due to GI side effects among patients with mild renal impairment may be clinically acceptable. This is as long as physicians and patients remain prudent regarding the risk of dehydration, and stop therapy when GI side effects persist.

Patients with type 2 diabetes treated with GLP-1RA may be at an increased risk of acute renal dysfunction due to dehydration as a result of the side effects of nausea, vomiting or diarrhoea. It is unclear whether patients with pre-existing renal impairment or concomitant use of drugs such as ACE inhibitors or diuretics are at an increased risk.[7–9] Reassuringly, we have found that ARF was uncommon with liraglutide treatment in clinical practice, and the risk not seemingly greater among patients with mild or moderate renal impairment. It is also worth noting that nausea was less persistent among patients treated with liraglutide 1.8mg as compared with exenatide 10µg twice daily in a previous head-to-head study.[14]

In contrast, we found a small but significant reduction of mean serum creatinine levels in association with liraglutide treatment among patients with mild and moderate renal impairment. The reason for this was not apparent; there were no differences in glycaemic or blood pressure improvements between the groups that could have helped explain this finding. If confirmed, it is also unclear whether the reduction in serum creatinine is beneficial or represents an improvement of underlying nephropathy, if this was present. Studies in diabetic rats have indicated the presence of GLP-1 receptors in kidneys, and the pharmacological activation of these receptors helped reverse indices of nephropathy in these rats.[15,16] More research is needed to determine whether liraglutide treatment is renoprotective in humans with renal impairment.

Finally, an important finding from the audit was that many patients achieved significant HbA_{1c} and weight reduction with liraglutide treatment. The magnitude of benefit appeared to be independent of patients' baseline renal function.

The pattern of results from the ABCD audit show remarkable similarity to those reported by Davidson *et al.*, who also assessed the efficacy and safety of liraglutide (both 1.2mg and 1.8mg) according to pre-treatment renal function as derived by the Cockcroft-Gault formula. As was found in our audit, patients in the meta-analysis with renal impairment were older, less overweight and were more likely female and had longer diabetes duration. The meta-analysis similarly reported no difference in efficacy or rates of adverse events among patients with mild or moderate renal impairment. The authors also similarly reported a trend of serum creatinine reduction among groups with greater degree of renal impairment. However, the meta-analysis did not report on the rates of liraglutide drug discontinuation among patient groups.

A limitation of the study relates to the potential inaccuracies in estimating glomerular filtration rates (GFRs) using currently available equations. The Cockcroft-Gault equation utilises variables of age, weight, gender and serum creatinine, and was chosen due to it being traditionally used for drug dosage adjustment. The pharmacokinetic studies and prescribing information for GLP-1RAs have also been reported using this method.[3–6] Alternative non-weight-based methods of estimating GFR include the Modification of Diet in Renal Disease (MDRD) equation and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[17] However, we chose not to use the MDRD equation due to reports of the equation being increasingly inaccurate in subjects with increasing obesity, and in view of the significant levels of obesity characterised in the audit.[18,19] It is possible that the choice of a different equation to estimate GFR would have yielded different results. Other limitations of our analysis include the unavoidable loss of data from patients being lost to follow up in real-life clinical practice and possible incomplete data recall of patients treated with liraglutide. This has the potential to introduce bias of the results in favour of patients attending clinics more frequently. This potential bias may or may not affect the results of one renal function group preferentially more than another. The audit, unlike a clinical trial, also did not possess a placebo control group of patients. Hence, we could not discount the possibility that the outcomes that were different between renal function groups were not due to other patient or treatment differences occurring between groups that were not quantified or fully adjusted by statistical analyses. For example, comparisons of blood pressure reduction among patient groups may have been confounded by possible differences in antihypertensive management between the patient groups. Nevertheless, the high concordance of our results with a clinical trial meta-analysis is a reassuring finding.

In conclusion, our data from real-life clinical practice showed that liraglutide 1.2mg was safe, efficacious but more frequently discontinued among patients with mild renal impairment as compared with patients with normal renal function. More data are needed to establish the safety of liraglutide among patients with moderate or more significant renal impairment.

Key points

- Liraglutide 1.2mg was equally effective in improving glycaemia and weight among patients with mild and moderate renal impairment as compared with patients with normal renal function
- Frequency of adverse events, including reported gastrointestinal side effects, was similar among patients with normal renal function and mild renal impairment. However, patients with mild renal impairment were more likely to discontinue liraglutide due to the gastrointestinal side effects
- Treatment with liraglutide may be associated with a small reduction of serum creatinine in patients with renal impairment

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Declaration of interests

KYT was employed as ABCD research fellow in the Nationwide ABCD audit programme (which includes audits of exenatide and liraglutide) by the Sandwell and West Birmingham Hospitals NHS Trust. This post is funded by ABCD from grants provided by Eli Lilly and Novo Nordisk. KYT has received speaker fees from Novo Nordisk, and educational sponsorship from Novo Nordisk, Eli Lilly, Sanofi-Aventis and Takeda.

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This audit was independently initiated and performed by ABCD, and the authors remained independent in the analysis and the writing of this report.

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