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# Analysis on difference in gastrointestinal hormone levels of patients with the history of diabetes and concurrent nephropathy and study on the role of liraglutide

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**Abstract. – OBJECTIVE: To compare the difference in the gastrointestinal hormone levels of the patients with the history of diabetes and concurrent nephropathy and investigate the clinical effect of liraglutide in the treatment of diabetic nephropathy (DN).**

**PATIENTS AND METHODS: 42 cases of patients with DN admitted in our hospital from April 2010-May 2015 were selected and divided into phase I-II group (group A, n = 22) and phase III-IV group (group B, n = 20) according to DN phases and 20 cases of patients with diabetes rather than nephropathy admitted in our hospital during the same period were selected as the control group, all of whom underwent the routine biochemical test and gastrointestinal hormone test, the differences in gastrin (GAS), motilin (MTL) and glucagon (GLC) of DN patients were compared at different phases, the gastric emptying test was carried out on them and the gastric emptying time was recorded. All patients were treated with liraglutide and the changes in fasting blood glucose (FBG), glycosylated hemoglobin (HbAlc), serum creatinine (Cr), blood urea nitrogen (BUN), insulin (FINS) and insulin resistance level (HOMA-IR) were tested before treatment and after 10 weeks' treatment, the changes in the tumor necrosis factor (TNF-α), interleukin -6 (IL-6) and transforming growth factor (TGF-β1) were determined, and the change in the gastrointestinal hormone levels of patients was recorded after treatment.**

**RESULTS: (1) the GAS, MTL, GLC and gastric emptying time in group B were higher than those in group A and the control group ($p < 0.05$), and the above indicators in group A were higher ($p < 0.05$); (2) after 10 weeks' treatment, the gastrointestinal hormone levels in the three groups were reduced and the gastric emptying time was shortened, the difference was statistically significant ($p < 0.05$) compared with those before treatment, after 10 weeks' treatment, the GAS, MTL, GLC and gastric emptying time in group B were higher than group A and the control group, those in group A were higher than control group ($p < 0.05$); (3) before treatment, the comparative differences in FBG, HbAlc, FINS and HOMA-IR among the three groups were not statistically significant ($p > 0.05$), and after 10 weeks' treatment, the differences in FBG, HbAlc and HOMA-IR among three groups were reduced and FINS was increased, the difference in those between before treatment and after treatment was statistically significant ($p < 0.05$) and the comparative difference among the three groups was not statistically significant ($p > 0.05$); (4) before treatment, Cr and BUN levels in group A and group B were higher than the control group ($p < 0.05$), after 10 weeks' treatment, the Cr and BUN levels among three groups were significantly decreased ($p < 0.05$), Cr and BUN in group A and group B were higher than the control group, cr and BUN levels in group B were higher than group A ($p < 0.05$); (5) before treatment, the difference by comparing IL-6, TNF-α and TGF-β1 among three groups were not statistically significant ($p > 0.05$), after 10 weeks' treatment, the indicators in the three groups were decreased significantly ($p < 0.05$), but the comparative difference among the three groups were not statistically significant ($p > 0.05$); (6) the difference by comparing the efficiencies among the three treatment was not statistically significant ($p > 0.05$).**

**CONCLUSIONS: There are some correlations between the gastrointestinal hormone levels and the degree of renal impairment of DN patients. Good results will be achieved by applying liraglutide in intervention with different phases of DN and DM patients, which cannot only regulate the gastrointestinal hormone levels and lower the blood sugar levels of patients, but can also reduce the insulin resistance and delay the process of renal damage.**

*Key Words:*

Diabetes, Diabetic nephropathy, Gastrointestinal hormone, Liraglutide.

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## Introduction

Diabetic nephropathy (DN) is a kind of common chronic complication of diabetes mellitus (DM), most patients are accompanied with gastrointestinal tract tension alleviation, reduced gastric motility, reduced contractility, extended gastric emptying time and other gastrointestinal problems[1]. But the pathogenesis of gastrointestinal disorders in the diabetic patients has been not clear. Some studies[2] show that the autonomic neuropathy, blood glucose level change, and gastrointestinal hormone imbalance may be related to DM patient's gastrointestinal disorders. Meanwhile, Werner U[3] show that the difference in renal function levels is related to the change in gastrointestinal motility. Liraglutide, as a kind of glucagon-like peptide-1 (GLP-1) long-acting analog, has a higher homology with native GLP-1, which can increase satiety, improve gastrointestinal emptying disorder, regulate blood glucose, stimulate β cell proliferation and regeneration and regulate β-cell dysfunction by regulating the secretion of glucagon and glucagon, thus it has a significant effect on insulin regulation and gastrointestinal hormone regulation of DM and nephrotic patients[4]. Moreover, some clinical tests[5] have demonstrated that liraglutide had higher tolerability and safety and the occurrence of hypoglycemia in patients was lower, although the gastrointestinal reactions are common, they were often transient without affecting the treatment. Based on the above situation, in order to further investigate the difference in gastrointestinal hormone levels of patients with diabetic nephropathy and intervention mechanism of liraglutide, we carried out the study and analysis on 42 cases of DN patients, and 20 cases of DM patients admitted in our hospital.

## Patients and Methods

### General Information

42 cases of diabetic patients admitted to our hospital from April 2010-May 2015 were selected, all of whom were in line with diabetes mellitus and DN standards approved by the endocrine and metabolic disease academic conference[6], and the patients with a history of gastric ulcer, gastritis, cholelithiasis, pancreatic inflammation, cholecystitis, irritable colon syndrome and abdominal surgery were excluded. Those enrolled within three months were forbidden to take drugs affecting gastrointestinal hormone. Among them, there were 25 males and 17 females, aged from 41-84 years old, mean: (64.9 ± 5.6) years old, with a history of 4-24 years' diabetes, mean: (10.6 ± 7.6) years old; fasting blood glucose (FBG) (8.7 ± 3.3) mmol/L. The patients were divided into group A (phase I-II, n = 22) and group B (phase III-IV, n = 20) according to DN phases, while 20 cases of patients with diabetes rather than nephropathy admitted during the same period were selected as the control group, the comparative difference in sex, age, duration and FBG level in the three groups were not statistically significant ($p > 0.05$), shown in Table I.

### Methods

(1) 3 ml elbow venous blood of all patients on the next day after admission to the hospital were extracted under empty stomach, centrifuged at a speed of 3000 r/min and stored at -80°C for testing and the automatic biochemical analyzer was used to detect and test HbAlc, FBG, gastrin (GAS), motilin (MTL) and glucagon (GLC) levels. (2) The gastric emptying test was carried out, the barium meal method was used to determine the gastric emptying time, before the test, the patients fasted for 10h, ate a normal standard meal at 7:30 in the morning (400 ml water + 80 g cooked pasta + 50 g poached egg + 20 g peanut kernel), were required to finish eating within 15 min, then take a small barium capsule and underwent chest radiography after 1h, 2h, 4h, and 6h's eating, the number of all barium within the stomach of patients at different time points was recorded, if there were still small barium within the stomach after 6h, the observation time would be extended to 8h and the gastric emptying time was recorded. All the patients did not eat any food and water

**Table I.** Comparison of baseline information in the three groups (n, $\bar{x} \pm s$).

| Group category | Sex (male/female) | Duration (years) | Age (years old) | FBG (mmol/L) |
|---|---|---|---|---|
| Group A | 13/9 | 10.51 ± 7.55 | 63.28 ± 8.95 | 8.72 ± 3.42 |
| Group B | 12/8 | 11.51 ± 6.97 | 67.31 ± 7.98 | 9.23 ± 2.45 |
| Control group | 11/9 | 10.16 ± 5.34 | 62.18 ± 8.59 | 8.99 ± 2.74 |

*Note*: The comparative difference in sex, age, duration and FBG level were statistically significant, $p > 0.05$.

during the observation period when the gastric emptying time was more than 6h; it would be considered as emptying abnormalities. (3) Treatment method: DN patients and patients with diabetes rather than nephropathy were treated with liraglutide, since examination, the application was started on the next day, subcutaneous injection was carried out before going to bed every day, the initial dose in the first week was 0.6 mg/times, 1 times/d; it was increased to 1.2 mg/times from the second week, 1 time/d, a total of 10 weeks' treatment. This study was approved by the Ethics Committee of Shanxian Central Hospital No. 1.

### Observation Indicators

(1) 3 ml elbow venous blood was collected under empty stomach before treatment and after 10 weeks' treatment. The automatic biochemical analyzer was used to determine FBG, and the colorimetric method was applied to determine Cr and BUN levels. The glycosylated hemoglobin detector and ion chromatography were used to determinate HbAlc. The ELISA kits were used to determine the blood IL-6, TNF-α and TGF-β1 levels strictly according to the reagent using instruction. 75 g glucose was orally taken for insulin test. The fully automatic chemiluminescence immunoassay was used to determine FINS level and the HOMA-IR was calculated with stabile model method. (2) After 10 weeks' treatment, the changes in GAS, MTL and GLC levels were tested, the gastric emptying test was carried out, and the gastric emptying time was recorded. (3) After 10 weeks' treatment, the therapeutic effect was evaluated, according to the literature[7], cure: the symptoms and signs were basically disappeared, the gastric motility was returned to normal condition, the gastric emptying was normal, and the gastric barium emptying rate ≥ 90%; significant effect: the symptoms and signs were improved significantly, the gastric motility was enhanced, the gastric emptying time was significantly shortened, and the gastric barium emptying rate was between 50% and 89%; improvement: the symptoms and signs were improved, the gastric motility was also improved, the gastric emptying time was shortened, and the gastric emptying barium rate was between 30% and 49%; invalid: the symptoms and signs were not improved, there was no change in gastric emptying time and the gastric motility was not improved; (4) electrocardiogram, stool routine examination, blood and urine routine examination, liver and kidney function and other tests were carried out before treatment and after 10 weeks' treatment, and the treatment safety was monitored.

### Statistical Analysis

SPSS19.0 software (SPSS Inc., Chicago, IL, USA) was used for processing the study data, the count data was tested with $\chi^2$-test, the measurement data was expressed as ($\bar{x} \pm s$), the normality and homogeneity variance tests were carried out, the transformation of variables not in line with the normal distribution showed a normal or near-normal distribution. The comparison between the two groups was tested with *t*-test method, and the comparison among the three groups and above was carried out with the analysis of variance. Furthermore, the comparison among groups was carried out with LSD analysis. The Pearson linear correlation analysis was used for correlation analysis. $p < 0.05$: the difference was statistically significant

## Results

### Comparison of Gastrointestinal Hormones and Gastric Emptying Times of Patients at Different Phases of DN and Patients with DM Rather than Nephropathy

The GAS, MTL, GLC and gastric emptying time in group B were higher than group A and the control group; the comparative difference was statistically significant ($p < 0.05$). The above indicators in group A were higher that the control group, and the comparative difference was statistically significant ($p < 0.05$), as shown in Table II.

**Table II.** Comparison of gastrointestinal hormone levels of patients at different phases of DN and patients with DM rather than nephropathy ($\bar{x} \pm s$).

| Group category | GAS (pg/ml) | MTL (pg/ml) | GLC (pg/ml) | Gastric emptying time (h) |
|---|---|---|---|---|
| Group A | 72.33 ± 38.51 | 239.16 ± 38.52 | 111.22 ± 44.28 | 4.42 ± 1.22 |
| Group B | 133.36 ± 47.92[a] | 433.31 ± 192.84[a] | 212.03 ± 61.28[a] | 6.96 ± 1.08[a] |
| Control group | 56.73 ± 22.04[b] | 135.41 ± 22.66[b] | 94.13 ± 33.11[b] | 3.50 ± 0.66[b] |

*Note*: Comparing with group A and control group, [a]$p < 0.05$; Comparing with group A and B, [b]$p < 0.05$.

### Comparison of Gastrointestinal Hormone Levels and Gastric Emptying Times in the Three Groups after 10 Weeks' Treatment

After 10 weeks' treatment, the gastrointestinal hormone levels in the three groups were decreased, the gastric emptying time was shortened, and by comparing those before treatment, the difference was statistically significant ($p < 0.05$). After 10 weeks' treatment, the GAS, MTL, GLC and gastric emptying time in group B were higher than group A and the control group, and those in group A were higher that the control group ($p < 0.05$), as shown in Table III.

### Comparison of FBG, HbAlc, FINS, and HOMA-IR in the Three Groups before Treatment and after 10 Weeks' Treatment

Before the treatment, the difference by comparing FBG, HbAlc, fasting insulin (FINS) and HOMA-IR in the three groups was not statistically significant ($p > 0.05$). After 10 weeks' treatment, the FBG, HbAlc, and HOMA-IR in the three groups had been reduced, FINS was increased, by comparing those in the same group before treatment, the difference was statistically significant ($p < 0.05$). However, the comparative difference among the three groups was not statistically significant ($p > 0.05$), as shown in Table IV.

### Comparison of Cr, BUN, and Microalbuminuria Levels in the Three Groups Before Treatment and After 10 Weeks' Treatment

Before the treatment, the levels of creatinine (Cr), blood urea nitrogen (BUN) and microalbuminuria in group A and group B were higher that the control group ($p < 0.05$), after 10 weeks' treatment, the levels of Cr, BUN, and microalbuminuria in the three groups were significantly decreased, and the difference by comparing those before the treatment was statistically significant ($p < 0.05$), the levels of Cr, BUN, and microalbuminuria in group A and group B two groups were higher the control group and the levels of Cr, BUN, and microalbuminuria in group B were higher than group A ($p < 0.05$), as shown in Table V.

### Comparison of IL-6, TNF-α, and TGF-β1 Levels in the Three Groups before Treatment and after 10 Weeks' Treatment

Before the treatment, by comparing IL-6, TNF-α, and TGF-β1 in the three groups, the difference was not statistically significant ($p > 0.05$). After 10 weeks' treatment, the indicators in the three groups were significantly decreased, and the difference by comparing those in the same group before treatment was statistically significant ($p < 0.05$), but the difference by comparing those among the three groups was statistically significant ($p > 0.05$), as shown in Table VI.

### Comparison of Therapeutic Effects Among the Three Groups

The difference by comparing the therapeutic effects among the three groups was not statistically significant ($p > 0.05$), as shown in Table VII. And there were no serious adverse reactions during the treatment period among the three groups.

## Discussion

DM is a common disease, which can cause disability and has a high death rate[8]. DN is a kind of its common chronic complication. There are recent studies[9,10] finding that most DN patients are with lesions in the gastrointestinal tract and the gastrointestinal lesion degree of the patients with advanced DN is higher than those with early DN. Gilbey et al[11] believe that the peripheral autonomic neuropathy, smooth muscle degeneration, high blood sugar, kidney gastrointestinal peptide hormone degradation and removal can participate in DN gastrointestinal lesions. The long history of diabetes mellitus and long-term higher blood sugar can lead to an increase in the intracellular

**Table III.** Comparison of gastrointestinal hormone levels and gastric emptying times in the three groups after 10 weeks' treatment ($\bar{x} \pm s$).

| Group category | GAS (pg/ml) | MTL (pg/ml) | GLC (pg/ml) | Gastric emptying time (h) |
|---|---|---|---|---|
| Group A | 55.72 ± 26.67 | 168.45 ± 26.47 | 90.23 ± 20.44 | 3.48 ± 0.54 |
| Group B | 83.66 ± 38.44[a] | 310.02 ± 166.34[a] | 166.33 ± 58.62[a] | 5.26 ± 0.98[a] |
| Control group | 45.22 ± 18.06[b] | 86.33 ± 12.65[b] | 78.33 ± 26.23[b] | 2.76 ± 0.33[b] |

*Note*: Comparing with group A and the control group, [a]$p < 0.05$; comparing with group A and group B, [b]$p < 0.05$.

**Table IV.** Comparison of FBG, HbAlc, FINS and HOMA-IR in the three group before treatment and after 10 weeks' treatment ($\bar{x} \pm s$).

| Group category | Group category | FBG (mmol/L) | HbAlc (%) | FINS (μu/ml) | HOMA-IR (%) |
|---|---|---|---|---|---|
| Group A | Before treatment | 8.72 ± 3.42 | 7.78 ± 0.41 | 22.16 ± 1.26 | 11.44 ± 4.41 |
| | After 10 weeks' treatment | 7.24 ±0.26[a] | 7.02 ± 0.26[a] | 36.42 ± 5.78[a] | 5.62 ± 0.46[a] |
| Group B | Before treatment | 9.23 ± 2.45 | 7.98 ± 0.61 | 22.21 ± 0.97 | 9.79 ± 4.89 |
| | After 10 weeks' treatment | 7.28 ± 0.44[a] | 7.04 ± 0.24[a] | 35.16 ± 6.01[a] | 5.68 ± 0.54[a] |
| Control group | Before treatment | 8.99 ± 2.74 | 7.82 ± 0.66 | 22.76 ± 1.11 | 10.16 ± 4.39 |
| | After 10 weeks' treatment | 7.31 ± 0.27[a] | 7.05 ± 0.21[a] | 37.68 ± 5.68[a] | 5.61 ± 0.45[a] |

*Note*: Comparing those in the same group before treatment, [a]$p < 0.05$.

**Table V.** Comparison of Cr, BUN and microalbuminuria levels in the three groups before treatment and after 10 weeks' treatment ($\bar{x} \pm s$).

| Group category | Group category | Cr (μmol/L) | BUN (μmol/L) | Microalbuminuria (mg/24h) |
|---|---|---|---|---|
| Group A | Before treatment | 86.54 ± 20.11 | 287.42 ± 43.88 | 257.84 ± 31.85 |
| | After 10 weeks' treatment | 51.26 ± 16.33[b,c,e] | 172.64 ± 37.28[b,c,e] | 163.58 ± 23.92 [b,c,e] |
| Group B | Before treatment | 97.54 ± 18.36 | 316.41 ± 51.26 | 564.13 ± 51.74 |
| | After 10 weeks' treatment | 67.44 ± 15.68[b,c] | 240.36 ± 28.94[a,b] | 391.42 ± 39.05[b,c] |
| Control group | Before treatment | 75.26 ± 14.26[a] | 243.65 ± 42.78[a] | 21.64 ± 4.26 |
| | After 10 weeks' treatment | 40.11 ± 14.42[b] | 216.67 ± 38.46[b] | 19.31 ± 3.47[b] |

*Note*: Comparing with those in the control group before treatment, [a]$p < 0.05$; comparing with those in the same group before treatment, [b]$p < 0.05$; comparing with those in the control group after 10 weeks' treatment, [c]$p < 0.05$; comparing with those in group B group after 10 weeks' treatment, [e]$p < 0.05$.

**Table VI.** Comparison of IL-6, TNF-α and TGF-β1 levels in the three groups before treatment and after 10 weeks' treatment ($\bar{x} \pm s$).

| Group category | Group category | IL-6 (pg/mL) | TNF-α (pg/mL) | TGF-β1 (μg/L) |
|---|---|---|---|---|
| Group A | Before treatment | 33.15 ± 7.32 | 53.22 ± 15.83 | 80.13 ± 16.75 |
| | After 10 weeks' treatment | 15.41 ± 4.26[a] | 27.61 ± 9.42[a] | 40.69 ± 10.26[a] |
| Group B | Before treatment | 33.18 ± 7.28 | 53.26 ± 15.79 | 80.14 ± 17.03 |
| | After 10 weeks' treatment | 17.95 ± 5.26[a] | 29.26 ± 10.16[a] | 43.64 ± 12.69[a] |
| Control group | Before treatment | 33.21 ± 7.36 | 53.25 ± 15.85 | 80.16 ± 16.97 |
| | After 10 weeks' treatment | 14.26 ± 4.56[a] | 26.55 ± 10.27[a] | 38.47 ± 12.26[a] |

*Note*: Comparing those in the same group before treatment, [a]$p < 0.05$.

**Table VII.** Comparison of therapeutic effects among the three groups [n (%)].

| Group category | Cure | Significant effect | Valid | Improvement | Invalid | Total effective rate |
|---|---|---|---|---|---|---|
| Group A | 5 (22.73) | 7 (31.82) | 5 (22.73) | 1 (4.55) | 2 (9.09) | 20 (90.91) |
| Group B | 4 (20.00) | 5 (25.00) | 5 (25.00) | 0 (0) | 2 (10.00) | 18 (90.00) |
| Control group | 5 (25.00) | 5 (25.00) | 4 (20.00) | 0 (0) | 1 (5.00) | 19 (95.00) |

sorbitol levels and a decrease in inositol levels, which result in the nerve cell degeneration reaction so that the nerve axon will show segmental demyelination changes. Simultaneously, long-term higher blood sugar can inhibit the gastrointestinal motion in the body, cause an increase in gastrin, abnormal secondary motilin secretion, inhibit gastric motility, cause gastric dysrhythmia and prolong gastric emptying time[12]. The diabetic microvascular disease can cause ischemia, neurotrophic weakening and losing which can aggravate smooth muscle disease and cause abnormal

gastrointestinal activity of patients with DM. In addition, the kidney is the key place for human gastrointestinal peptide hormone degradation and removal, DN patients are often accompanied with renal failure, the impaired kidney function can lead to internal environment disturbance and abnormal gastrointestinal peptide hormone. The present work found that the GAS, MTL, and GLC of patients during phase III-IV according to DN phases were higher than those of the patients with pure diabetes during phase I-II according to DN phases and the gastric emptying time was extended. These results suggest that the kidney function decrease degree was significantly related to the decrease in the gastrointestinal function, speculating that the degree of renal function damage could be forecast by detecting the gastrointestinal hormone changes of the patients with DN.

DN is the key cause of end-stage renal disease, the prevention progression of DN has become the key subject in the research field of diabetes[13]. Diabetes and concurrent kidney disease are currently treated with an insulin secretagogue, insulin, biguanide, α-glucosidase inhibitor, GLP-1 and other analogue therapies[14]. In recent years, GLP-1 has become a hotspot of diabetes research with its unique mechanism of action. GLP-1 is composed of a plurality of amino acids, belonging to incretin, which can promote glucose-dependent insulin secretion, limit glucagon loss, suppress appetite and increase satiety, which can not only reduce blood sugar, control weight, but can also have an important role in the cardiovascular, kidney, gastrointestinal tract, central nervous system and other pancreatic tissues simultaneously[15]. Under normal physiological conditions, after a meal, the secretion of human plasma insulin will be rapidly increased, the glucagon levels will be decreased, and both of them will manually adjust and control postprandial blood glucose. But the patients with type 2 diabetes will be with inadequate or delayed postprandial insulin secretion and glucagon rise. While GLP-1 has a role in glucose-dependent insulinotropic hormone, which can inhibit glucagon secretion, promote β cell proliferation and decrease blood glucose. Simultaneously, Guang[16] found that GLP-1 could act on the hypothalamus, inhibit food intake, control appetite and inhibit gastric secretion.

Liraglutide is a kind of GLP-1 analog, and the likeness with GLP is up to 95%[17], which is mainly caused by the secretion of intestinal epithelial L-cells. Feeding can directly trigger liraglutide secretion; it may also be impacted by nervous and endocrine secretion simultaneously. Liraglutide mainly plays a role through its combination with GLP-1 receptors, which stimulate the secretion of pancreatic β-cell, inhibit α-cell in order to secret glucagon and lower blood sugar levels. At present, the relationship between GLP-1 and its analogs, and the associated riles in the gastrointestinal tract are controversial. Some researchers[18] show that GLP-1 can inhibit gastric emptying, cause abdominal swelling, activate the vagus nerve, transmit the satiety signals to the brain, issue a directive and reduce food intake. There are also studies[19] finding that, the peripheral injection of GLP-1 can simultaneously be combined with GLP-1R, play an effect and mediate gastrointestinal hormone regulation. The present study found that after administration of liraglutide intervention, the gastrointestinal hormone levels in the three groups were reduced, the gastric emptying time was shortened and the difference by comparing those before treatment was statistically significant ($p < 0.05$). Taken together, these results confirmed the regulation of liraglutide on gastrointestinal hormone which indicates that it had a positive effect on the patients with DN at different phases. Secondly, after 10 weeks' liraglutide intervention, the FBG, HbAlc and HOMA-IR levels in the three groups were reduced, and FINS was increased, confirming the liraglutide has a regulation role in glucose and insulin, which were consistent with the results reported by Calanna et al[20]. In addition, after 10 weeks' treatment, various inflammatory mediators such as IL-6, TNF-α and TGF-β1 in the three groups were decreased significantly, and the difference by comparing those in the same group before treatment was statistically significant ($p < 0.05$) but the difference by comparing those among the three groups was not statistically significant ($p > 0.05$); these results indicate that liraglutide can adjust the level of diabetes inflammatory mediators and delay the progression of the disease. Meanwhile, after treatment, the serum creatinine and uric acid were decreased in the three groups, confirming that it could reduce kidney damage degree of the diabetic patients, delay renal interstitial fibrosis and glomerular sclerosis and promote kidney drainage natriuresis. Additionally, the difference by comparing the treatment effects in the three groups was not statistically significant ($p > 0.05$), indicating liraglutide had better intervention effect on patients at different DN phases and patients with diabetes.

## Conclusions

The gastrointestinal hormone levels of the patients with advanced DN are higher than the patients with early DN and DM. Also, gastric emptying time is longer than the early DN and DM patients, and the gastrointestinal hormone secretion levels of patients with DN is related to the degree of renal impairment. The application of liraglutide intervention has a better treatment effect on the early and advanced DN and DM patients, which can adjust the gastrointestinal hormone levels, lower blood sugar, reduce insulin resistance and correct the renal damage.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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