Research Article

Efficacy and Safety of Dapagliflozin versus Liraglutide in Patients with Overweight or Obesity and Type 2 Diabetes Mellitus: A Randomised Controlled Clinical Trial in Tianjin, China

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Objective. We aimed to clarify the efficacy of dapagliflozin versus liraglutide in patients with overweight or obesity and type 2 diabetes mellitus (T2DM) at the beginning of the coronavirus disease 2019 (COVID-19) pandemic. Methods. T2DM patients with overweight or obesity who visited the Metabolic Disease Management Center at Tianjin Fourth Central Hospital from October 2019 to January 2020 were recruited and randomised to receive dapagliflozin or liraglutide for 24 weeks. Changes in blood glucose and lipid levels, blood pressure, and body weight, as well as the occurrence of hypoglycaemia and other adverse events, were compared. Results. 309 patients completed the study (143 in liraglutide group and 166 in dapagliflozin group). After 24 weeks, HbA1c, fasting blood glucose (FPG), and 2 h postprandial blood glucose (2hPG) levels significantly decreased from 8.80% ± 1.41% to 7.02% ± 1.05%, 10.41 ± 3.13 to 7.59 ± 2.16 mmol/L, and 17.90 ± 4.39 to 10.12 ± 2.47 mmol/L, respectively, in the dapagliflozin group, and from 8.92% ± 1.49% to 6.78% ± 1.00%, 10.04 ± 2.99 to 7.20 ± 1.63 mmol/L, and 17.30 ± 4.39 to 10.13 ± 4.15 mmol/L, respectively, in the liraglutide group. Changes in HbA1c, FPG, and 2hPG levels between groups were not significantly different. Systolic blood pressure (SBP) and low-density lipoprotein cholesterol (LDL-C) level significantly decreased from 144.1 ± 19.1 to 139.7 ± 16.2 mmHg (p = 0.001) and from 3.21 ± 0.94 to 2.98 ± 0.89 mmol/L (p = 0.014), respectively, in the dapagliflozin group. After COVID-19 outbreak, the number of patients taking sleep-promoting drugs increased from 4.9% to 9.4% (p = 0.029). Conclusions. Liraglutide and dapagliflozin had strong hypoglycaemic effects in patients with overweight or obesity and T2DM at the beginning of the COVID-19 pandemic. Dapagliflozin may be beneficial in improving SBP and LDL-C levels; however, further research is warranted.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a common chronic metabolic disease with an increasing global prevalence. According to WHO criteria, the number of patients with diabetes mellitus (DM) in China has rapidly increased to 11.2%, and the number of patients with T2DM is the highest in the world [1]. The number of global deaths due to diabetes in 2000 was estimated at 2.9 million, accounting for 5.2% of all deaths [2]. T2DM increases all-cause mortality, including cardiovascular, stroke-associated, and ischemic heart disease mortalities [3, 4]. Obesity is one of the major risk factors for developing T2DM, and its high global incidence promotes increases in cardiovascular morbidity and mortality rates [5]. There is low compliance with blood glucose monitoring and subsequent control in China, and data from the China National HbA1c Surveillance System showed that the HbA1c (<7%) compliance rate in China is only 27.7% [6].
Metformin is a safe, low-cost, widely used, hypoglycaemic drug that has an outstanding ability to decrease plasma glucose levels and has been employed for over 60 years to treat early stages of T2DM [7]. Additionally, metformin has other beneficial effects; for example, it is a candidate drug for reducing the risk of amiodarone-induced hyperthyroidism and interstitial lung disease [8]. However, fewer patients than expected receive metformin as first-line monotherapy because of secondary failure [9]. Therefore, it is important to select hypoglycaemic drugs that can be used in combination with metformin to benefit patients with T2DM. T2DM is associated with a substantially increased risk of death in Chinese adults, especially relating to cardiovascular disease, and almost 50% of such deaths are caused by stroke [10].

Sodium-glucose transporter-2 inhibitors (SGLT2is) [11] and glucagon-like peptide-1 receptor agonists (GLP-1RAs) [12] have been shown to have multiple cardiovascular and renal benefits in patients with diabetes. Current studies also suggest that these benefits apply to T2DM patients with multiple comorbidities, including chronic kidney disease [13] and heart failure with reduced ejection fraction [14].

Coronavirus disease 2019 (COVID-19) threatened the world as a new public health crisis following its emergence in Wuhan, Hubei Province, China, in December 2019 [15]. Cities in China, including Tianjin, took strict epidemic prevention measures. Few studies focused on the efficacy and safety of prescribing a combination of SGLT2i and GLP-1RA to patients with overweight or obesity and T2DM with poor blood glucose control who are using metformin in China during the COVID-19 pandemic. This study was aimed at comparing the efficacy and safety of dapagliflozin and liraglutide in patients with overweight or obesity and T2DM during this period.

2. Materials and Methods

2.1. Participants. Patients with T2DM who visited the Metabolic Disease Management Center (MMC) at Tianjin Fourth Central Hospital from October 2019 to January 2020 were recruited for the study. The study inclusion criteria were as follows: (a) age ≥ 18 years, (b) body mass index (BMI) ≥ 24 kg/m² [16], (c) stable dose of metformin (≥1500 mg/d) alone or in combination with premixed insulin for ≥8 weeks, and (d) HbA1c level ≥ 7.0%.

The exclusion criteria were as follows: (a) type 1 and other special types of diabetes such as gestational diabetes, (b) severe mental illness and unclear consciousness, (c) active tuberculosis and other infectious diseases, and (d) high risk for volume depletion, hypotension, and/or electrolyte imbalances (in the opinion of the investigator). Laboratory exclusion criteria included haemoglobin < 120 g/L (male), <110 g/L (female), or thyroid-stimulating hormone levels outside the central laboratory normal range.

Enrolled patients voluntarily withdrew from the study during the observation period. Written informed consent was obtained from all participants.

2.2. Study Design. This was a single-centre, randomised, parallel, controlled clinical observational study that lasted for 24 weeks. According to the random number table and time sequence of patient enrolment, the researchers divided the patients meeting enrolment conditions into dapagliflozin and liraglutide treatment groups at a ratio of 1:1. Dapagliflozin was initiated at 5 mg and titrated up to 10 mg by the second week unless (in the opinion of the investigator) the patient was unable to tolerate titration to 10 mg, in which case the dose was maintained at 5 mg. The liraglutide group patients were subcutaneously injected 0.6 mg/d at the beginning, and this dose increased to 1.2 mg/d by the second week. If intolerance occurred during the process, the dose was adjusted to 0.6 mg/d.

According to the MMC system, we collected the following information: name, sex, age, contact information, smoking/drinking history, family history of diabetes, history of hypertension, coronary heart disease (CHD), and diabetes course. Blood glucose, lipid, and HbA1c levels; body weight; and blood pressure were monitored and recorded during the observation period. The body weight of patients and systolic and diastolic blood pressure levels were recorded at baseline, week 12, and week 24. The blood index monitoring plan was as follows: (1) at baseline: fasting peripheral blood glucose (FPG), 2 h postprandial peripheral blood glucose (2hPG), HbA1c, alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, serum creatinine, haemoglobin, triglyceride (Tg), low-density lipoprotein cholesterol (LDL-C), fasting venous blood glucose, and serum insulin levels; (2) week 12: FPG, 2hPG, and HbA1c levels; and (3) week 24: FPG, 2hPG, HbA1c, Tg, and LDL-C levels. Nurses provided education regarding diet and exercise, blood glucose and blood pressure monitoring, and liraglutide injection techniques, as well as the identification and treatment of adverse events (AEs), including hypoglycaemia. AEs were recorded and treated throughout the study.

The outbreak of COVID-19 in December 2019 caused enormous disruption to the daily routines of the global community [17]. Various measures [18] were applied to prevent and control disease progression and minimise the impact of the pandemic in China. Tianjin reported its first case of COVID-19 in January 2020, and strict measures were taken to limit the outdoor activities of the residents from January to April 2020. Such measures altered implementation of the usual follow-up procedures. Tianjin Fourth Central Hospital provided door-to-door drug delivery services for patients to avoid drug disconnection. The researchers contacted the patients by phone and WeChat every two weeks to determine any difficulties and provide the patients with home exercise programs. The lives of Tianjin residents gradually returned to normal in April 2020, but COVID-19 became a global pandemic that affected the health and well-being of most people. In addition to the physical, economic, and social impacts, the psychological impacts of this pandemic have been increasingly reported in scientific literature [19]. Therefore, changes in sleep quality before and after the epidemic were also assessed using questionnaires in this study.

The clinical study protocol was approved by the Institutional Review Board (IRB) of Tianjin 4th Central Hospital, and all steps were conducted in accordance with the
180 patients assigned dapagliflozin.

2 stopped taking dapagliflozin for severe urinary tract infection, and 12 did not complete follow up.

166 patients completed follow-up in dapagliflozin group at week 24.

180 patients assigned liraglutide.

1 patient was isolated outside Tianjin and could not get in touch, and 36 did not complete follow up.

143 patients completed follow-up in liraglutide group at week 24.

Figure 1: The study flow chart.

principles of the World Medical Association Declaration of Helsinki (trial registration code: ChiCTR1800019864). The IRB approved the collection and use of patient records according to the regulations for clinical trials in humans (IRB approval No. 2018-SZXLL066).

2.3. Study Evaluations. The primary objectives of this study were as follows: (a) after 24 weeks, to assess the effect of the addition of dapagliflozin compared to the addition of liraglutide on HbA1c level, and (b) over 24 weeks, to assess the overall safety and tolerability of dapagliflozin compared to liraglutide.

The secondary objectives were as follows: to assess 2 h incremental postprandial glucose excursion (PPGE), FPG, 2hPG, and the proportion of subjects with an HbA1c level lower than 7.0% after 24 weeks of treatment. Changes in Tg and LDL-C levels, body weight, and blood pressure from baseline were compared between the two groups. Venous blood samples were collected in EDTA tubes from fasting patients in the morning. BMI was calculated as body weight (kg)/height squared (m²). Patients with BMI (≥ 24 and < 28 kg/m²) were considered overweight, and those with BMI ≥ 28 kg/m² were considered obese [16].

2.4. Indicators and Evaluation Criteria. The following evaluation criteria were employed: (1) T2DM: the diagnosis of T2DM was based on the 2020 Chinese diabetes treatment guidelines: FPG level ≥ 7.0 mmol/L (fasting was defined as no caloric intake for at least 8 h) or 2 h plasma glucose level ≥ 11.1 mmol/L [20]. (2) BMI: an Omron infrared height and weight meter was used to automatically measure the height and weight. Body weight was measured using the same scale on an empty stomach at the MMC clinic in the morning. BMI was calculated as body weight (kg)/height squared (m²). Patients with BMI (≥ 24 and < 28 kg/m²) were considered obese [16]. (3) Homeostatic Model Assessment Insulin Resistance (HOMA-IR) index [21]: FPG level (mmol/L) × fasting plasma insulin level (mIU/L)/22.5. (4) PPGE: calculated from peripheral blood glucose level before and after breakfast in the present study. (5) The standards of high quality rate (HQR) [22] included (a) no hypoglycaemia, (b) weight gain < 2%, and (c) HbA1c level < 7% at week 24.

A sleep quality questionnaire was used in this study. Sleep quality was considered poor if it affected normal work during the day. Patients were also asked whether they took medication to promote sleep.

The following safety indicators were evaluated: (1) hypoglycaemia: hypoglycaemia was diagnosed at a blood glucose level lower than 3.9 mmol/L [20]. In this study, hypoglycaemia diagnosis was based on patient self-reports and blood glucose monitoring [23]. Severe hypoglycaemic events were considered when disturbance of consciousness or symptoms that could not be self-managed occurred. (2) Identification of serious adverse events (SAEs): SAEs included myocardial infarction, cardiac surgery or revascularisation, unstable angina pectoris, congestive heart failure, transient ischemic attack, severe cerebrovascular disease, severe hypoglycaemic events, hypertonic coma, and ketoacidosis. All events were reported to the investigators. To ensure compliance with the protocol definitions, rigorous measures were implemented to ensure data quality, including source data verification for reported outcomes and safety events and a thorough review of events.

2.5. Efficacy and Safety Endpoints. Glycaemic efficacy endpoints were changes from baseline in HbA1c, 2 h incremental PPGE, 2hPG, and FPG levels and the proportion of patients who achieved an HbA1c goal of < 7% at week 24. Safety endpoints included AEs, hypoglycaemia, or urinary tract infection.

Other indicators included changes in body weight, blood lipid levels, and blood pressure from baseline to week 24.

2.6. Statistical Analyses. In this study, the GPower software was used to estimate the required sample size and assist in evaluating the effect size and statistical efficacy. The Statistical Program for Social Sciences 26.0 software (SPSS, Inc., Chicago, IL, USA) was used for data collection and analysis. The Kolmogorov–Smirnov normal test was performed on the
measurement data, the mean ± standard deviation was used to describe variables conforming to a normal distribution, and percentage (%) was used for counting data. An independent sample t-test was used to compare measurement data between the two groups, and a paired sample t-test was used to compare the groups before and after treatment. The chi-square test was used to compare the observed data. All statistical tests were performed using bilateral tests with an alpha of 0.05.

3. Results

3.1. Patient Disposition and Characteristics and Dapagliflozin/Liraglutide Doses. A total of 360 patients were eligible for enrolment and volunteered to participate in the study from October 2019 to January 2020. There were 180 participants in each group, but only a total of 309 patients completed the study (Figure 1). There were 166 and 143 participants in each group, but only a total of 309 patients completed the study (Figure 1). There were 166 and 143 patients in the dapagliflozin and liraglutide groups, respectively, at week 24. The mean age of the participants was 51.8 ± 11.2 years, and 190 patients (61.5%) were male. Patients had a mean BMI of 29.5 ± 4.0 kg/m², a mean waist circumference of 90 ± 4.0 cm, and average T2DM duration of 6.3 ± 5.7 years. The baseline demographics and clinical parameters of the two groups are shown in Table 1. More-
### Table 2: Efficacy endpoints (HbA1c, FPG, and 2hPG) at week 24.

| Parameter | Liraglutide (n = 143) | Dapagliflozin (n = 166) |
|-----------|----------------------|------------------------|
| HbA1c (%) |                      |                        |
| Baseline  | 8.92 ± 1.49          | 8.80 ± 1.41            |
| Week 24   | 6.78 ± 1.00          | 7.02 ± 1.05            |
| Change from baseline<sup>a</sup> | -2.14<sup>c</sup> (-2.45--1.85) | -1.78<sup>c</sup> (-2.01--1.55) |
| Change vs. dapagliflozin<sup>b</sup> | \( t = 1.910 \) | \( p = 0.057 \) |
| FPG (mmol/l) |                  |                        |
| Baseline  | 10.04 ± 2.99        | 10.41 ± 3.13           |
| Week 24   | 7.20 ± 1.63         | 7.59 ± 2.16            |
| Change from baseline<sup>a</sup> | -2.95<sup>c</sup> (-3.52--2.39) | -2.83<sup>c</sup> (-3.40--2.26) |
| Change vs. dapagliflozin<sup>b</sup> | \( t = 0.304 \) | \( p = 0.761 \) |
| 2hPG (mmol/l) |                  |                        |
| Baseline  | 17.30 ± 4.39        | 17.90 ± 4.39           |
| Week 24   | 10.13 ± 4.15        | 10.12 ± 2.47           |
| Change from baseline<sup>a</sup> | -7.47<sup>c</sup> (-9.14--5.79) | -6.36<sup>c</sup> (-7.87--4.85) |
| Change vs. dapagliflozin<sup>b</sup> | \( t = 0.988 \) | \( p = 0.326 \) |

Abbreviations: FPG: fasting peripheral blood glucose; 2hPG: 2-hour postprandial peripheral blood glucose. <sup>a</sup>Test of paired samples before and after treatment, \( p = 0.000 \). <sup>b</sup>Independent sample \( t \) test of change value between two groups. <sup>c</sup>Mean change (95% confidence interval).

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![Figure 2: Comparison of PPGE between the two groups at week 12 and week 24. Abbreviations: PPGE: 2-hour incremental postprandial glucose excursion.](image-url)
in both groups (Table 2). There were no significant differences in the HQR between the liraglutide and dapagliflozin groups (21 (14.7%) and 29 (17.5%) patients in the liraglutide and dapagliflozin groups, respectively). No significant differences between the two groups were noted ($\chi^2 = 0.439, p = 0.508$). A total of 20 patients had urinary tract infection, including 5 and 15 in the liraglutide and dapagliflozin groups, respectively, and 2 of them stopped treatment with dapagliflozin due to a severe urinary tract infection. There was no significant difference between the two groups ($\chi^2 = 3.788, p = 0.052$).

During the observation period, nine patients experienced chest tightness, feelings of suffocation, and other discomfort. Five patients were relieved of their symptoms after psychological counselling. Four patients were diagnosed with angina pectoris and were further hospitalised (two in each group). No serious AEs, such as severe hypoglycaemia, heart failure, or myocardial infarction, were noted in either group.

3.5. Sleep Quality. Following the start of the COVID-19 outbreak, the proportion of patients with poor sleep quality significantly increased from 27.5% to 41.7% ($\chi^2 = 13.839, p = 0.001$). The number of patients taking sleep-promoting drugs significantly increased from 15 (4.9%) to 29 (9.4%) ($\chi^2 = 4.796, p = 0.029$).
4. Discussion

The results showed that both liraglutide and dapagliflozin significantly reduced HbA1c and fasting and postprandial blood glucose levels in patients with overweight or obesity and T2DM. This study showed that even in the initial stage of the COVID-19 outbreak, when the lifestyle of patients was seriously affected, HbA1c levels were consistently reduced. Few current studies have compared these drugs, but a meta-analysis found that compared to other antidiabetic drugs (including SGLT2I), GLP-1RAs, including liraglutide and dulaglutide, provided better hypoglycaemic effects [24]. A retrospective multicentre study conducted at 46 diabetes specialist outpatient clinics in Italy compared the hypoglycaemic efficacy of dapagliflozin (10 mg/d) and liraglutide (1.2 mg/d) in real-world patients between 2015 and 2016, and the results showed similar endpoints [25]. A study in China from 2017 to 2018 found that after a 24-week treatment period, higher reductions in HbA1c level were observed with dapagliflozin (10 mg/d) than with liraglutide (1.8 mg/d) [26]. However, the results of our study showed no differences in the changes in FPG, 2hPG, PPGE, or HbA1c levels between the two groups before and after 24 weeks of treatment.

Liraglutide, a GLP-1RA, mediates several positive effects, including lowering glucose dependence and reducing appetite and body weight; furthermore, it provides antiatherosclerosis, neural protection, natriuresis, and bone osteogenesis benefits [27]. Dapagliflozin is a new oral hypoglycaemic drug that increases urinary glucose excretion by inhibiting glucose reabsorption in proximal renal tubules. SGLT2is can reduce HbA1c levels without increasing the risk of hypoglycaemia, induce weight loss, and improve various metabolic parameters, including blood pressure, lipid profile, and hyperuricemia [28].

Obesity is one of the main risk factors for T2DM, and both constitute a major global health crisis [29]. Weight

### Table 3: Changes in other metabolic indicators (body weight, Tg, LDL-C, DBP, and SBP) at week 24.

| Parameter          | Liraglutide n = 143                     | Dapagliflozin n = 166                  |
|--------------------|----------------------------------------|----------------------------------------|
| Body weight (kg)   |                                        |                                        |
| Baseline           | 85.5 ± 14.5                            | 84.3 ± 15.0                            |
| Week 24            | 85.5 ± 16.4                            | 82.7 ± 12.9                            |
| Change from baseline | -0.08 (-1.78--1.94)                   | -0.61 (-1.23--0.01)                    |
| t value            | -0.086                                 | 1.939                                  |
| p value            | 0.931                                  | 0.055                                  |
| SBP (mmHg)         |                                        |                                        |
| Baseline           | 143.9 ± 22.5                           | 144.1 ± 19.1                           |
| Week 24            | 140.6 ± 23.7                           | 139.7 ± 16.2                           |
| Change from baseline | -3.98 (-8.87--0.92)                   | -5.28 (-8.43--2.12)                    |
| t value            | 1.608                                  | 3.306                                  |
| p value            | 0.111                                  | 0.001                                  |
| DBP (mmHg)         |                                        |                                        |
| Baseline           | 83.5 ± 13.0                            | 85.5 ± 11.9                            |
| Week 24            | 84.0 ± 12.7                            | 84.6 ± 10.6                            |
| Change from baseline | 0.38 (2.92--1.28)                   | -1.12 (-2.91--0.67)                    |
| t value            | -0.296                                 | 1.233                                  |
| p value            | 0.767                                  | 0.220                                  |
| Tg (mmol/l)        |                                        |                                        |
| Baseline           | 2.34 ± 1.50                            | 2.62 ± 1.88                            |
| Week 24            | 2.27 ± 1.91                            | 2.46 ± 1.85                            |
| Change from baseline | -0.24 (-0.49--0.01)                   | -0.15 (-0.49--0.18)                    |
| t value            | 1.974                                  | 0.907                                  |
| p value            | 0.053                                  | 0.367                                  |
| LDL-C (mmol/l)     |                                        |                                        |
| Baseline           | 3.48 ± 1.06                            | 3.21 ± 0.94                            |
| Week 24            | 3.29 ± 1.13                            | 2.98 ± 0.89                            |
| Change from baseline | -0.24 (-0.49--0.02)                   | -0.24 (-0.42--0.05)                    |
| t value            | 1.837                                  | 2.512                                  |
| p value            | 0.071                                  | 0.014                                  |

Abbreviations: SBP: systolic blood pressure; DBP: diastolic blood pressure; Tg: triglycerides; LDL-C: low-density lipoprotein cholesterol. *Mean change (95% confidence interval).
management is becoming increasingly important for the diagnosis and treatment of T2DM [30]. Liraglutide and dapagliflozin are potent hypoglycaemic drugs that have been widely recommended in China for managing the weight of patients with T2DM [20]. Treatment with liraglutide was found to attenuate cardiometabolic dysregulation and improve cardiac function, while dapagliflozin treatment improved glucose handling but had only a mild effect on an animal model of heart failure with preserved ejection fraction [31].

However, in the present study, there were no significant changes in body weight between the two groups before and after the 24-week treatment period. Body weight is regulated by the interaction of a number of processes, including homoeostatic, environmental, and behavioural factors. Interventions based on lifestyle modifications are integral to the management of body weight [32]. It is possible that the sudden outbreak of the epidemic and local policies had a certain impact on the activities and emotions of patients and may even have affected thyroid function [33]. In our study, we also found that the quality of sleep had deteriorated in patients during the outbreak. Studies have suggested a potential causal relationship between poor sleep and rapid weight gain, which may be related to the effects of sleep on dietary intake or physical activity [34].

The SBP of patients in the dapagliflozin group decreased significantly before and after the 24-week treatment period compared to the liraglutide group. Dapagliflozin at a dose of 10 mg has been found to induce a modest reduction in blood pressure compared to placebo in patients with diabetes with a low risk of orthostatic reactions, regardless of baseline blood pressure, and without increasing the heart rate [35]. The associated mechanisms include osmotic diuresis, bulbar balance, and weight loss [28]. In addition, recent studies have suggested that dapagliflozin has an important effect on lipid metabolism. It is also known that dapagliflozin can reduce blood TG [36] and blood uric acid [37] levels and increase the level of high-density lipoprotein cholesterol [38]. One study showed that LDL-C level increases significantly in patients after SGLT-2i treatment [39], whereas the levels of small and dense LDL decrease significantly, which is beneficial for atherosclerotic diseases [36]. In contrast with previous studies, our study showed a significant reduction in LDL-C levels in patients treated with dapagliflozin. This result could be related to interfering factors, such as the use of lipid-lowering drugs, as well as the impact of COVID-19. In patients receiving metformin-based background therapy who have an increased cardiovascular risk, specific GLP-1RAs and SGLT-2is have demonstrated favourable effects on certain cardiovascular outcomes [40]. However, studies have also shown that the effects of dapagliflozin and liraglutide on bone material properties are not identical and are not only mediated by low blood glucose levels [41]. Therefore, other effects of these two new hypoglycaemic drugs need to be confirmed in further studies.

Both treatments were well-tolerated. In the dapagliflozin group, two patients left the study after contracting urinary tract infections. SGLT2is increased the overall risk of genital system infection but did not increase the risk of other safety events, such as amputation, fracture, acute renal injury, and hyperkalaemia. The safety outcomes of the study were consistent with those of previous studies [42].

5. Conclusions and Limitations

Even under the impact of COVID-19, liraglutide and dapagliflozin have strong hypoglycaemic effects in patients with overweight or obesity and T2DM. Compared to liraglutide, dapagliflozin may greatly improve blood pressure and blood lipid levels. Further research is needed to confirm this assumption. This study, however, has many limitations. The study is a single-centre study, and the enrolled patients were limited to the northern area of Tianjin. Since liraglutide is an injectable drug and dapagliflozin is an oral hypoglycaemic drug, the study was not double-blinded, and the conclusions need further verification.

Data Availability

Data are available upon reasonable request by email.

Disclosure

The funding sources had no role in the study design, data collection, analysis, and interpretation, or in the writing of the manuscript or in the decision to submit the manuscript for publication.

Conflicts of Interest

The authors declare that they have no competing interests.

Authors’ Contributions

Hao Zhaohu was a major contributor in writing the manuscript. Huang Xiao analysed and interpreted the patient data. All authors read and approved the final manuscript. Shao Hailin and He Feng proposed the necessity and design of the study. All authors have read and approved the final manuscript.

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References

[1] Y. Li, D. Teng, X. Shi et al., “Prevalence of diabetes recorded in mainland China using 2018 diagnostic criteria from the American Diabetes Association: national cross sectional study,” BMJ, vol. 369, article m997, 2020.
[2] G. Roglic, N. Unwin, P. H. Bennett et al., “The burden of mortality attributable to diabetes,” Diabetes Care, vol. 28, no. 9, pp. 2130–2135, 2005.
[3] Y. Zhang, J. Niu, and H. K. Choi, “Excess mortality among persons with type 2 diabetes,” The New England Journal of Medicine, vol. 374, no. 8, p. 788, 2016.
[4] N. Cheng, Y. Zhang, J. Yang et al., “Association between fasting blood glucose and all-cause mortality in a rural Chinese population: 15-year follow-up cohort study,” *Diabetes Therapy*, vol. 11, no. 11, pp. 2691–2701, 2020.

[5] L. La Sala and A. E. Pontiroli, “Prevention of diabetes and cardiovascular disease in obesity,” *International Journal of Molecular Sciences*, vol. 21, no. 21, p. 8178, 2020.

[6] G. Liu, J. Dou, D. Zheng et al., “Association between abnormal glycemic phenotypes and microvascular complications of type 2 diabetes mellitus outpatients in China,” *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, vol. Volume 13, pp. 4651–4659, 2020.

[7] Z. Lv and Y. Guo, “Metformin and its benefits for various diseases,” *Frontiers in endocrinology*, vol. 11, p. 191, 2020.

[8] S. Kinoshita, K. Hosomi, S. Yokoyama, and M. Takada, “Inverse association between metformin and amiodarone-associated extracardiac adverse events,” *International Journal of Medical Sciences*, vol. 17, no. 3, pp. 302–309, 2020.

[9] A. Nicolucci, B. Charbonnel, M. B. Gomes et al., “Treatment patterns and associated factors in 14 668 people with type 2 diabetes initiating a second-line therapy: results from the global DISCOVER study programme,” *Diabetes, Obesity & Metabolism*, vol. 21, no. 11, pp. 2474–2485, 2019.

[10] Y. An, P. Zhang, J. Wang et al., “Cardiovascular and all-cause mortality over a 23-year period among Chinese with newly diagnosed diabetes in the Da Qing IGT and diabetes study,” *Diabetes Care*, vol. 38, no. 7, pp. 1365–1371, 2015.

[11] B. Akinci, “Dapagliflozin and cardiovascular outcomes in type 2 diabetes,” *The New England Journal of Medicine*, vol. 380, no. 19, p. 1881, 2019.

[12] A. B. van der Aart-van der Beek and H. J. L. Heerspink, “Renal outcomes of SGLT2 inhibitors and GLP1 agonists in clinical practice,” *Nature Reviews Nephrology*, vol. 16, no. 8, pp. 433–434, 2020.

[13] D. C. Wheeler, B. V. Stefánsson, N. Jongs et al., “Effects of dapagliflozin on major adverse kidney and cardiovascular events in patients with diabetic and non-diabetic chronic kidney disease: a prespecified analysis from the DAPA-CrKD trial,” *The Lancet Diabetes and Endocrinology*, vol. 9, no. 1, pp. 22–31, 2021.

[14] J. J. V. McMurray, S. D. Solomon, S. E. Inzucchi et al., “Dapagliflozin in patients with heart failure and reduced ejection fraction,” *The New England Journal of Medicine*, vol. 381, no. 21, pp. 1995–2008, 2019.

[15] T. Singhal, “A review of coronavirus disease-2019 (COVID-19),” *Indian Journal of Pediatrics*, vol. 87, no. 4, pp. 281–286, 2020.

[16] Chinese Medical Association, “Guideline for primary care of obesity (2019),” *Chinese Journal of General Practice*, vol. 19, no. 2, pp. 95–101, 2020.

[17] K. Shah, S. Mann, R. Singh, R. Bangar, and R. Kulkarni, “Impact of COVID-19 on the mental health of children and adolescents,” *Careus*, vol. 12, no. 8, article e10051, 2020.

[18] X. Lan, Y. Long, F. Shao, and Y. Song, “Expert consensus on the safety prevention and control of nuclear medicine diagnosis and treatment during the outbreak of COVID-19 (1st edition): (translated from Chinese version),” *European Journal of Nuclear Medicine and Molecular Imaging*, vol. 48, no. 4, pp. 1134–1143, 2021.

[19] M. M. Hossain, S. Tasnim, A. Sultana et al., “Epidemiology of mental health problems in COVID-19: a review,” *F1000Research*, vol. 9, p. 636, 2020.

[20] Chinese Diabetes Society, “Guideline for the prevention and treatment of type 2 diabetes mellitus in China (2017 edition),” *Chinese Journal of Diabetes Mellitus*, vol. 10, no. 1, pp. 4–67, 2018.

[21] S. Placzkowska, L. Pawlik-Sobecka, I. Kokot, and A. Piwowar, “Indirect insulin resistance detection: current clinical trends and laboratory limitations,” *Biomedical Papers of the Medical Faculty of the University Palacky, Olomouc*, Czech Republic, vol. 163, no. 3, pp. 187–199, 2019.

[22] J. Rosenstock, S. E. Kahn, O. E. Johansen et al., “Effect of linagliptin vs glimepiride on major adverse cardiovascular outcomes in patients with type 2 diabetes: the CAROLINA randomized clinical trial,” *Journal of the American Medical Association*, vol. 322, no. 12, pp. 1155–1166, 2019.

[23] R. Silbert, A. Salcido-Montenegro, R. Rodriguez-Gutierrez, A. Katabi, and R. G. McCoy, “Hypoglycemia among patients with type 2 diabetes: epidemiology, risk factors, and prevention strategies,” *Current Diabetes Reports*, vol. 18, no. 8, p. 53, 2018.

[24] H. Inoue, Y. Tamaki, Y. Kashiha et al., “Efficacy of DPP-4 inhibitors, GLP-1 analogues, and SGLT2 inhibitors as add-ons to metformin monotherapy in T2DM patients: a model-based meta-analysis,” *British Journal of Clinical Pharmacology*, vol. 85, no. 2, pp. 393–402, 2019.

[25] G. P. Fadini, V. Sciannameo, I. Franzetti et al., “Similar effectiveness of dapagliflozin and GLP-1 receptor agonists concerning combined endpoints in routine clinical practice: a multicentre retrospective study,” *Diabetes, Obesity & Metabolism*, vol. 21, no. 8, pp. 1886–1894, 2019.

[26] J. Jiang, L. Lin, and P. Chen, “Comparison of dapagliflozin and liraglutide in patients with poorly controlled type 2 diabetes mellitus: a 24-week, open, double-centered, head to head trial,” *Endocrine, Metabolic & Immune Disorders Drug Targets*, vol. 21, no. 7, pp. 1366–1374, 2021.

[27] X. Zhao, M. Wang, Z. Wen et al., “GLP-1 receptor agonists beyond their pancreatic effects,” *Frontiers in endocrinology*, vol. 12, article 721135, 2021.

[28] Y. Saisho, “SGLT2 inhibitors: the star in the treatment of type 2 diabetes?,” *Diseases*, vol. 8, no. 2, p. 14, 2020.

[29] C. M. Apovian, J. Okemah, and P. M. O’Neil, “Body weight considerations in the management of type 2 diabetes,” *Advances in Therapy*, vol. 36, no. 1, pp. 44–58, 2019.

[30] S. M. Fruh, “Obesity: risk factors, complications, and strategies for sustainable long-term weight management,” *Journal of the American Association of Nurse Practitioners*, vol. 29, no. 51, pp. S3–S14, 2017.

[31] C. Witthaar, L. M. G. Meems, G. Markoussis-Mavrogenis et al., “The effects of liraglutide and dapagliflozin on cardiac function and structure in a multi-hit mouse model of heart failure with preserved ejection fraction,” *Cardiovascular Research*, vol. 117, no. 9, pp. 2108–2124, 2021.

[32] F. L. Greenway, “Physiological adaptations to weight loss and factors favouring weight regain,” *International Journal of Obesity*, vol. 39, no. 6, pp. 1188–1196, 2015.

[33] D. Weiwei, W. Bei, W. Hong et al., “Thyroid hormone changes in the northern area of Tianjin during the COVID-19 pandemic,” *International Journal of Endocrinology*, vol. 2022, Article ID 5720875, 7 pages, 2022.

[34] R. P. Ogilvie and S. R. Patel, “The epidemiology of sleep and obesity,” *Sleep Health*, vol. 3, no. 5, pp. 383–388, 2017.

[35] C. D. Sjöström, P. Johansson, A. Ptaszynska, J. List, and E. Johnsson, “Dapagliflozin lowers blood pressure in
hypertensive and non-hypertensive patients with type 2 diabetes," *Diabetes & Vascular Disease Research*, vol. 12, no. 5, pp. 352–358, 2015.

[36] T. Hayashi, T. Fukui, N. Nakanishi et al., "Dapagliflozin decreases small dense low-density lipoprotein-cholesterol and increases high-density lipoprotein 2-cholesterol in patients with type 2 diabetes: comparison with sitagliptin," *Cardiovascular Diabetology*, vol. 16, no. 1, p. 8, 2017.

[37] Z. Hao, X. Huang, H. Shao, and F. Tian, "Effects of dapagliflozin on serum uric acid levels in hospitalized type 2 diabetic patients with inadequate glycemic control: a randomized controlled trial," *Therapeutics and Clinical Risk Management*, vol. 14, pp. 2407–2413, 2018.

[38] A. Jiang, Z. Feng, L. Yuan, Y. Zhang, Q. Li, and Y. She, "Effect of sodium-glucose co-transporter-2 inhibitors on the levels of serum asprosin in patients with newly diagnosed type 2 diabetes mellitus," *Diabetology and Metabolic Syndrome*, vol. 13, no. 1, p. 34, 2021.

[39] S. A. Cha, Y. M. Park, J. S. Yun et al., "A comparison of effects of DPP-4 inhibitor and SGLT2 inhibitor on lipid profile in patients with type 2 diabetes," *Lipids in Health and Disease*, vol. 16, no. 1, p. 58, 2017.

[40] A. Tsapas, I. Avgerinos, T. Karagiannis et al., "Comparative effectiveness of glucose-lowering drugs for type 2 diabetes: a systematic review and network meta-analysis," *Annals of Internal Medicine*, vol. 173, no. 4, pp. 278–286, 2020.

[41] A. Mieczkowska, P. Millar, D. Chappard, V. A. Gault, and G. Mabilleau, "Dapagliflozin and liraglutide therapies rapidly enhanced bone material properties and matrix biomechanics at bone formation site in a type 2 diabetic mouse model," *Calciﬁed Tissue International*, vol. 107, no. 3, pp. 281–293, 2020.

[42] M. I. Maiorino, M. Longo, L. Scappaticcio et al., "Improvement of glycemic control and reduction of major cardiovascular events in 18 cardiovascular outcome trials: an updated meta-regression," *Cardiovascular Diabetology*, vol. 20, no. 1, p. 210, 2021.