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Research Article
Comparing Efficacy and Safety of Glucagon-Like Peptide 1 (GLP-1) Agonist Versus Sodium-Glucose Cotransporter 2 (SGLT-2) Inhibitors in Chinese Patients with Type 2 Diabetes Mellitus: A Preliminary Study

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Abstract

Background and Objective: Several selective glucagon-like peptide 1 receptor inhibitors have been developed for the treatment of Type 2 Diabetes (T2DM) but their dosing is limited by gastrointestinal adverse effects. Sodium-glucose cotransporter 2 inhibitors are approved by the USFDA for clinical use along with diet and exercise in elderly T2DM patients. The present study compared the efficacy and safety of Dulaglutide (Dula) versus Dapagliflozin in T2DM patients. **Materials and Methods:** Chinese T2DM patients with an age of at least 18 years with a history of poorly controlled blood glucose levels were enrolled. Subjects who met the suitability conditions were randomized to receive (1:1:1) either Dula (0.75 mg, weekly once, given subcutaneously, n = 100) or Dula (1.5 mg, weekly once, given subcutaneously, n = 100) or Dapagliflozin (10 mg daily, n = 100). Each enrolled patient was carefully monitored and followed up for 26 weeks. **Results:** Dula 1.5 mg had the greatest reduction in HbA1c (%) as compared to Dula 0.75 mg and Dapagliflozin. A similar trend of reduction was observed while comparing the reduction that occurred in Dapagliflozin-treated patients. Dula 0.75 mg reported a greater decrease in HbA1c levels from baseline. Dula 1.5 mg reported a greater decrease in HbA1c levels than Dapagliflozin. The incidence of gastrointestinal-related events more in Dula compared to Dapagliflozin, however, there were no serious gastrointestinal-related adverse events that led to discontinuation of Dula. **Conclusion:** Dula and Dapagliflozin were found effective in the management of diabetes. Glycemic control was higher in patients who received Dula, especially 1.5 mg compared to Dapagliflozin.

Key words: Dapagliflozin, diabetes mellitus, Dulaglutide, glucagon-like peptide-1, HbA1c, sodium-glucose cotransporter-2 inhibitor

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Regular blood glucose measurement is important in evaluating the therapeutic response of new anti-diabetic drugs. The Glucagon-Like Peptide 1 (GLP-1) that is secreted from the gut following a meal[1-5] sensitizes the release of insulin for a series of physiological actions that help to utilize the blood glucose. In addition, Glucose-Dependent Insulinotropic Polypeptide Receptor (GIPR)s are generally available in adipose cells and their stimulation is the main key to balance the utilization of sugar and triglycerides load in these tissues and the postprandial nutrient disposal. Type 2 Diabetes (T2DM) patients have impaired incretin responses. Several selective Glucagon-Like Peptide 1 Receptor Inhibitors (GLP-1Ras) are formulated for the management of T2DM. The dosing of GLP-1RAs is limited mainly by gastrointestinal (GI) unwanted adverse effects. The frequency of these unwanted adverse events (AEs) could be managed by dose oscillation program. Among GLP-1RAs available for clinical use[2-9]. Dulaglutide (Dula) acts via GLP-1 produces increased secretion of insulin and inhibits the glucagon release from endocrine cells. Along with these actions, Dula also causes loss of body weight and delayed gastric emptying effect[10]. Another recently approved anti-diabetic drug in China is Sitagliptin, which is an oral medicine commonly indicated in patients with T2DM and acts by slowing down the effect of incretin hormone. Also, another class of anti-diabetes drugs recently approved are Sodium-Glucose Cotransporter 2 (SGLT-2) inhibitors by the USFDA for clinical use along with diet and exercise in elderly patients with diabetes. These drugs block the SGLT-2 protein present in the kidney (within renal tubes) which is responsible for absorbing glucose from the blood further decreasing the blood sugar and offering effective management of diabetes. These drugs are effective in reducing HbA1c thereby controlling glucose levels so offer long-term management. The SGLT-2 inhibitors are also called Gliflozins (Dapagliflozin, ertugliflozin and canagliflozin etc.). Another novel treatment option for diabetes management was Tirzepatide which enables albumin binding to prolong the duration of action[11-16]. The GIPR-mediated and GLP-1R-mediated mechanisms are managed insulin and glucagon secretions using body energy turnover. Therefore, tripeptide could have important in achieving greater glucose-lowering effects in comparison to selective GLP-1RAs. Tripeptide is at present investigated in trials for its effect on hyperglycemia and other diseases related with T2DM. It is mainly used once weekly (QW) by subcutaneous (SC) route of administration[10-18].

There is no head-to-head study comparing the efficacy and safety of GLP 1 agonists versus SGLT-2 inhibitors in Chinese T2DM patients. Thus, the present study compared the efficacy and safety of Dula versus Dapagliflozin in Chinese T2DM patients.

MATERIALS AND METHODS

Study area: From 15 January, 2021 to 15 March, 2023 study was conducted at the Henan Provincial People's Hospital, Zhengzhou, Henan, China and the Yuzhou Municipal Hospital of TCM, Yuzhou, Henan, China.

Patients and ethics: Chinese 200 T2DM patients at least 18 years old with a history of poorly controlled blood glucose levels were enrolled. The patients were excluded if patient were clinically unstable and had severe hepatic and kidney diseases which may jeopardize. Each patient was informed about the use of allowed/disallowed medications at the time of the informed consent process. Written informed consent was obtained from each enrolled patient.

Ethical consideration: The study received approval from the institutional ethics committee of Xuchang University vide ICE approval no. 17d2tmXU. The procedures used in the study were as per the local and international guidance on human research. Also, the patients with a history of severe liver disease, lung disease, severe heart and thyroid disease were excluded.

Treatments and procedures: Subjects were randomized to receive (1:1:1) either Dula (0.75 mg, weekly once, given subcutaneously) or Dula (1.5 mg, weekly once, given subcutaneously) or Dapagliflozin (10 mg daily). Each enrolled patient was carefully monitored and followed up for 26 weeks. The dose of Dula was adjusted accordingly if needed.

Assessment of efficacy and safety profiles: The baseline characteristics of each patient were assessed. The primary endpoint was changes in HbA1c from baseline W26. The secondary endpoints of interest change in body weight (kg) from baseline to endpoint (at W26); % of patients who achieved HbA1c targets at endpoint visit (W26); fasting blood glucose (FBG) levels from baseline to W26; blood glucose (BG) profiles at the specific time point of the day; HbA1c (%) from baseline to W26. Safety was monitored and reported.

Statistical analysis: Considering this was a preliminary study, the, sample size was not calculated, however, approximately 300 patients (100 patients per arm) were planned to be

included to conclude this study. Appropriate statistical tests were used to analyze data (quantitative data) based on type and distribution (normal and non-normal). In the case of non-normal data, the Mann-Whitney test was used whereas for normal data, an unpaired t-test was used. In the case of categorical data, data were analyzed using Fisher's exact or Chi-square test based on the size of the data. Analysis was done using GraphPad (version 3.01) software, San Diego, California, USA. All results were considered significant at p-values less than 0.05.

RESULTS

Three hundred patients (100 patients per arm) were randomized and all patients completed the study. Demography data were similar across groups. In all the groups, the majority of patients enrolled were female with a duration of diabetes was approximately 2-3 years. The majority of patients in treatment groups were aged more than 50 years. Overall, the patient characteristic was found comparable across treatment groups. Median age was also found similar in all the groups (Table 1).

Outcome measures: A summary of the primary outcome was presented in Fig. 1. Dula 1.5 mg had a greater reduction in HbA1c (%) than Dula 0.75 mg and Dapagliflozin. All study drugs were effective in reducing HbA1c as evidenced after looking reduction trend from baseline. All study drugs were found effective in improving glycemic control when compared to baseline. Compared to Dula 0.75 mg, the decrease in HbA1c was more pronounced among Dula 1.5 mg treated patients. A similar trend of reduction was observed while comparing the reduction that occurred in the Dapagliflozin group. Compared to Dapagliflozin, the patients treated with Dula 0.75 mg reported a greater reduction in HbA1c levels from baseline. In comparison with Dapagliflozin, Dula 1.5 mg reported a greater decrease in HbA1c levels. Overall, both doses of Dula had significantly greater reduction HbA1c from baselines when compared to the patients treated with Dapagliflozin.

Dula 1.5 mg demonstrated the greatest reduction in body weight (kg) as compared to Dula 0.75 mg and Dapagliflozin (Fig. 2). All study drugs were effective in decreasing body weight as evidenced after looking at the reduction trend from baseline. Compared to Dula 0.75 mg, the reduction in body weight was more pronounced among Dula 1.5 mg. A similar trend of reduction was observed while comparing the reduction that occurred in Dapagliflozin. In comparison to Dapagliflozin, Dula 0.75 mg reported a greater reduction in body weight levels from baseline. Compared to Dapagliflozin, Dula 1.5 mg reported a greater decrease in body weight levels from baseline. Overall, both doses of Dula had a significantly greater decrease in body weight from baselines when compared to Dapagliflozin.

A summary of % of patients reaching HbA1c targets at W26 was presented in Fig. 3. Dula 1.5 mg had the greatest % of patients reaching HbA1c targets at W26 as compared to Dula 0.75 mg and Dapagliflozin. All study drugs were effective in reducing HbA1c as evidenced after looking reduction trend from baseline. All study drugs were found effective in improving glycemic control when compared to baseline. In comparison to Dula 0.75 mg, % of patients reaching HbA1c targets at W26 is more evident in Dula 1.5 mg. A similar trend of reduction was observed while comparing glycemic control with Dapagliflozin. In comparison to Dapagliflozin, Dula 0.75 mg reported a greater proportion of achieving HbA1c

Table 1: Patient characteristics before the study

Parameter	Total	Dulaglutide (1.5 mg)	Dulaglutide (0.75 mg)	Dapagliflozin	Comparisons among cohorts			
Numbers of patients	300	100	100	100	p-value	Test value	Df	95% CI
Median (Q3-Q1) age (years)	53 (55-51)	54 (55-51)	53 (55-52)	52 (55-51)	0.282 (Kruskal-Wallis' test)	2.532	N/A	N/A
Gender								
Female sex (%)	165 (55)	58 (58)	52 (52)	55 (55)	0.6951 (Chi-squared test for Independence)	0.7273	2	N/A
Male sex (%)	135 (45)	42 (42)	48 (48)	45 (45)				
Weight (kg)	63 (65-62)	63 (64-63)	63.5 (65-62)	63 (64-62)	0.2434 (Kruskal-Wallis' test)	2.826	N/A	N/A
BMI (kg/m^2)	25 (25.5-24.5)	25 (25.8-24.3)	25 (25.5-24.9)	25 (25.2-24.5)	0.0734 (Kruskal-Wallis' test)	5.224	N/A	N/A
Diabetes duration (years)	2.3 (2.5-2.1)	2.2 (2.5-2.1)	2.4 (2.6-2.2)	2.3 (2.5-2.2)	0.081 (Kruskal-Wallis' test)	6.123	N/A	N/A
SBP (mmHg)	122.65±1.82	123.3±17.5	120.3±15.5	121.6±11.2	0.062 (One-way ANOVA)	5.423	298	1.324-2.431
Heart rate (beats/min)	74.48±8.02	75.32±8.41	73.33±7.41	73.52±7.82	0.982 (One-way ANOVA)	5.5621	298	2.4321-2.5212
HbA1c (%)	7.6±1.5	7.8±1.2	7.2±1.7	7.9±2.9	0.6241 (One-way ANOVA)	6.2311	298	2.451-3.4521
FBG (mmol/L)	200±20	198±12.4	197±17.4	202±24.4	0.0851 (One-way ANOVA)	5.4212	298	3.4123-3.8541

Categorical variables are presented as frequencies with percentages in parenthesis, continuous normal variables are presented as Mean±Standard Deviation (SD) and continuous non-normal variables are presented as medians with Q3-Q1 in parenthesis, Df: Degree of freedom, CI: Confidence interval, BMI: Body Mass Index, FBG: Fasting blood glucose, SBP: Systolic blood pressure, HbA1c: Glycated Hemoglobin, test value (Chi-squared value for Chi-squared test; Kruskal-Wallis' statistics for Kruskal-Wallis' test, F-value for ANOVA) and all results were considered significant if the p-value was less than 0.05

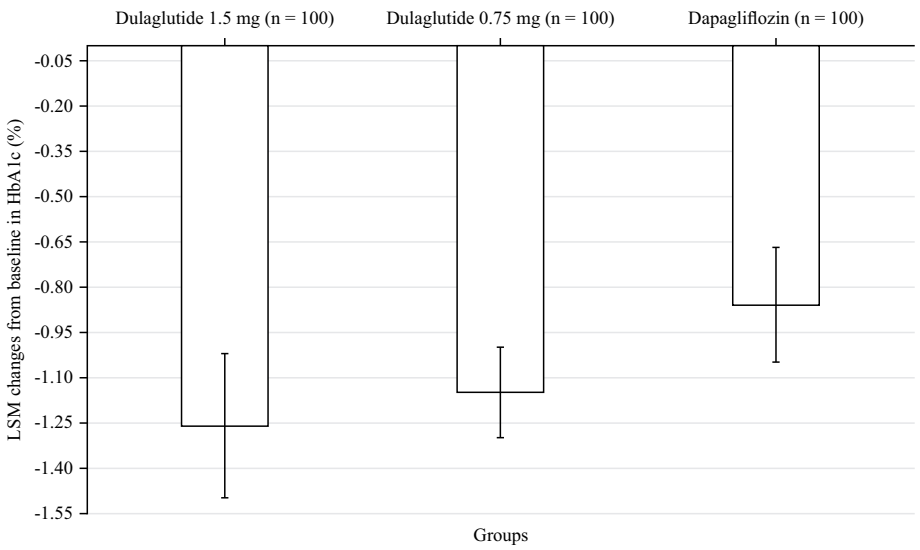

Fig. 1: Results of the primary endpoint

LSM: Least square mean, HbA1c: Glycated Hemoglobin and variables are presented as Mean±Standard Deviation

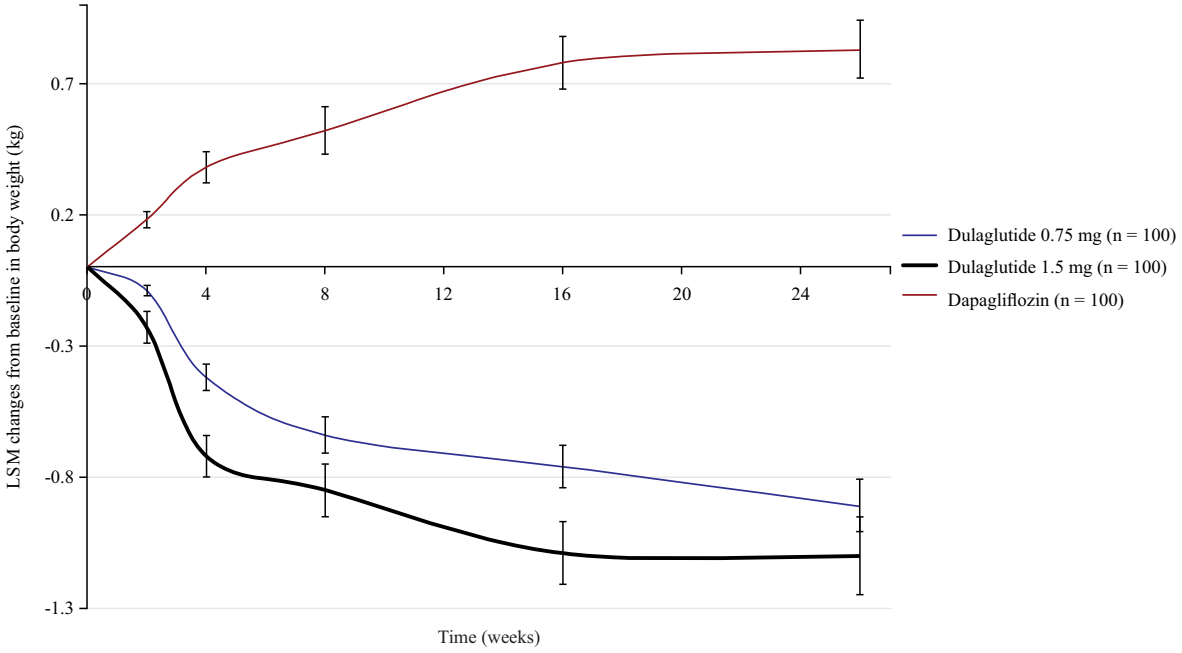

Fig. 2: Body weight change from baseline to 26 weeks

LSM: Least square mean and variables are presented as Mean±Standard Deviation

targets at W26. In comparison to Dapagliflozin, Dula 1.5 mg reported a greater proportion of achieving HbA1c targets at W26. Overall, both doses of Dula had a significantly greater proportion in achieving HbA1c targets at W26 in comparison to Dapagliflozin.

A summary of FBG (mmol/L) data from baseline to W26 was presented in Fig. 4. Dula 1.5 mg had the greatest reduction in FBG as compared to Dula 0.75 mg and Dapagliflozin. All study drugs were effective in reducing FBG as evidenced after looking reduction trend from baseline. All study drugs were found effective in improving glycemic control when compared to baseline. Compared to Dula 0.75 mg, the reduction in FBG was more pronounced with Dula 1.5 mg. A similar trend of reduction was observed while comparing the reduction that occurred in patients treated with Dapagliflozin. Compared to Dapagliflozin, the patients

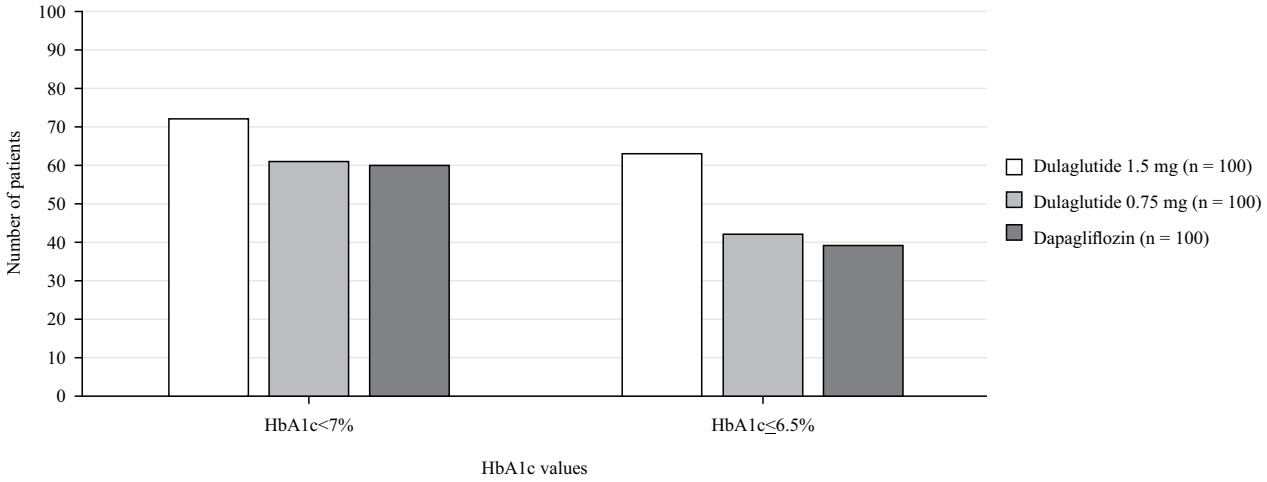

Fig. 3: Percentage of patients reaching HbA1c targets at 26 weeks

HbA1c: Glycated Hemoglobin, p<0.05 vs. Dapagliflozin (Fisher's exact test), Dulaglutide and variables are presented as percentages

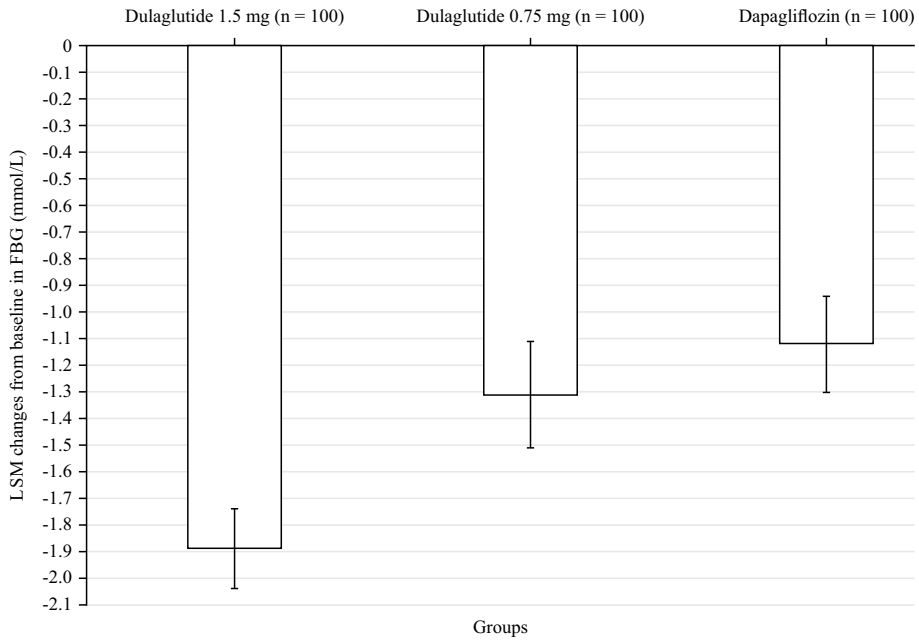

Fig. 4: LSM change in FBG (mmol/L) from baseline to 26 weeks

LSM: Least square mean, SE: Standard error and variables are presented as Mean±Standard error

treated with Dula 0.75 mg reported a greater decrease in FBG levels from baseline. Compared to Dapagliflozin, the patients treated with Dula 1.5 mg reported a greater reduction in FBG levels from baseline.

A summary of 7-point BG profiles (mmol/L) by time of day was presented in Fig. 5. Patients treated with Dula 1.5 mg had the greatest reduction in BG as compared to Dula 0.75 mg and Dapagliflozin. All study drugs were effective in reducing BG as evidenced after looking reduction trend from baseline. All study drugs were found effective in improving glycemic control when compared to baseline. Compared to Dula 0.75 mg, the reduction in FBG was more pronounced with Dula 1.5 mg. A similar trend of reduction was observed while comparing the reduction that occurred with Dapagliflozin. Compared to Dapagliflozin, the patients treated with Dula 0.75 mg reported a greater reduction in BG levels from baseline. Compared to Dapagliflozin, the patients treated with Dula 1.5 mg reported a greater reduction in BG levels from baseline. Overall, both doses of Dula had a significantly greater reduction in BG from baselines when compared with Dapagliflozin.

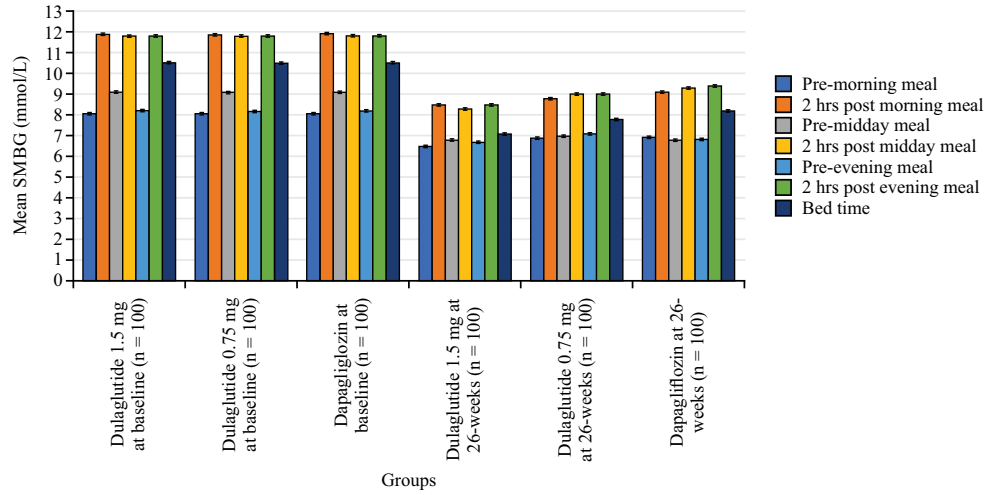

Fig. 5: 7-point BG profiles (mmol/L)

BG: Blood glucose and SMBG: Self-monitoring of blood glucose

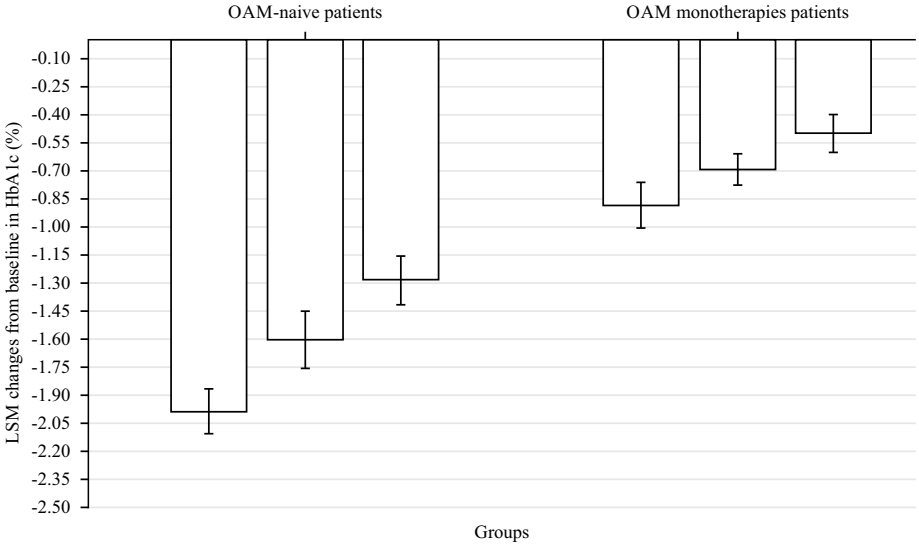

Fig. 6: HbA1c (%) by OAM patients

OAM: Oral antihyperglycemic medication, LSM: Least square mean, SE: Standard error and variables are presented as Mean±Standard Error

A summary of HbA1c (%) by oral antihyperglycemic medication patients was presented in Fig. 6. Dula 1.5 mg had the greatest reduction in HbA1c (%) as compared to Dula 0.75 mg and Dapagliflozin. All study drugs were effective in reducing HbA1c as evidenced after looking reduction trend from baseline. All study drugs were found effective in improving glycemic control when compared to baseline. Compared to Dula 0.75 mg, the decrease in HbA1c was more pronounced with Dula 1.5 mg. A similar trend of decrease was observed while comparing the reduction that occurred in patients treated with Dapagliflozin. In comparison to Dapagliflozin, Dula 0.75 mg reported a greater reduction in HbA1c levels from baseline. In comparison to Dapagliflozin, the Dula 1.5 mg reported a greater reduction in HbA1c levels from baseline. Overall, both doses of Dula had significantly greater reduction HbA1c from baselines when compared to the patients treated with Dapagliflozin.

Side effects: The frequent side effects noted across the treatment group were GI-related, although the incidence of GI-related events more in Dula compared to Dapagliflozin, however, there were no GI events that led to discontinuation of Dula and none of them were serious. All GI events that occurred in this study were of milder severity and did not

Table 2: Results of assumption tests

Variables	Test	
Categorical	Contingency table	
	A large contingency table: Chi-square for Independence	
	2×2 contingency tables: Chi-square with Yate's correction for >40 sample size otherwise Fisher exact test	
Continuous		
	Normality test	Sub-test
Age (years), BMI (kg/m^2)	Two columns failed the normality test with p<0.05, i.e., Kruskal-Wallis' test (nonparametric ANOVA)	Not applicable
Weight (kg), Years of diabetes	All columns failed the normality test with p<0.05, i.e., Kruskal-Wallis' test (nonparametric ANOVA)	Not applicable
SBP, Heart rate, HBA1c (%), FBG	All columns passed the normality test with p>0.05, i.e., one-way ANOVA	SD (standard deviation) is normally distributed
Normal continuous parameters between and within the cohort	All columns passed the normality test with p>0.05, i.e., one-way ANOVA	SD normally distributed

rescue treatment to manage the GI events. Overall, both the study drugs had acceptance safety profiles and the risk-benefit ratio was favorable.

The results of the assumption tests were presented in Table 2.

DISCUSSION

There is no head-to-head study comparing the efficacy and safety of GLP-1 agonists versus SGLT-2 inhibitors in Chinese T2DM patients (either in English or Chinese). To our knowledge, this is the first clinical study carried out to evaluate the efficacy and safety of Dula versus Dapagliflozin in Chinese T2DM patients. Current results were consistent with previous studies[9-17] in which Dula was found effective in improving glycemic control when compared to baseline. In comparison to Dula 0.75 mg, the decrease in HbA1c was more pronounced with Dula 1.5 mg. A similar trend of reduction was observed while comparing the reduction that occurred with Dapagliflozin. In comparison to Dapagliflozin, Dula 0.75 mg reported a greater reduction in HbA1c levels from baseline. In comparison to Dapagliflozin, Dula 1.5 mg reported a greater reduction in HbA1c levels from baseline. Overall, both doses of Dula had a significantly greater reduction of HbA1c from baselines when compared to Dapagliflozin. In both Dula groups, it was noted that the reduction in HbA1c was more among the patients with greater HbA1c at baseline. A similar trend of results was noted in previous studies with Dula 1.5 mg/0.75 mg in global studies and Dula 0.75 mg in the previous studies[4,8-10,18-20]. The finding of current study was consistent with the previous reports demonstrating a significant reduction of HbA1c. Patients treated with Dula 1.5 mg had the greatest % of patients reaching HbA1c targets at W26 as compared to Dula 0.75 mg and Dapagliflozin. All study drugs were effective in reducing HbA1c as evidenced after looking reduction trend from baseline. All study drugs were found effective in improving glycemic control when compared to baseline. In comparison to Dula 0.75 mg, % of patients reaching HbA1c targets at W26 is more evident among those with Dula 1.5 mg. A similar trend of reduction was observed while comparing glycemic control with Dapagliflozin. In comparison to Dapagliflozin, Dula 0.75 mg reported a greater % of patients reaching HbA1c targets at W26. In comparison to Dapagliflozin, Dula 1.5 mg reported a greater % of patients reaching HbA1c targets at W26. Overall, both doses of Dula had a significantly greater % of patients reaching HbA1c targets at W26 when compared with Dapagliflozin.

Weight management is essential in diabetes treatment. Current findings related to the weight reduction effect of Dula and are consistent with previous reports of Dula[9,10,19-23]. In the present study, patients treated with Dula 1.5 mg had the greatest reduction in body weight (kg) as compared to Dula 0.75 mg and Dapagliflozin. All study drugs were effective in reducing body weight as evidenced after looking reduction trend from baseline. In comparison to Dula 0.75 mg, the reduction in body weight was more pronounced with Dula 1.5 mg. A similar trend of reduction was observed while comparing the reduction that occurred in patients treated with Dapagliflozin. In comparison to Dapagliflozin, Dula 0.75 mg reported a greater reduction in body weight levels from baseline. In comparison to Dapagliflozin, Dula 1.5 mg reported a greater reduction in body weight levels from baseline. Overall, both doses of Dula had a significantly greater reduction in body weight from baselines when compared with Dapagliflozin. Earlier reports of Dula demonstrated that Dula produces weight reduction by altering eating habits and increases utilization of energy, this was consistent with the previous reports.

Reduction in blood glucose levels (fasting and post-prandial) was very evident after treatment with Dula. Our study results in reducing FBG were consistent with the previous reports of Dula[9,10,19-25], which demonstrated that patients treated with Dula 1.5 mg had the greatest reduction in FBG as compared to Dula 0.75 mg and Dapagliflozin. Compared to Dula 0.75 mg, the reduction in FBG was more pronounced among the patients treated with Dula 1.5 mg. A similar trend of reduction was observed while comparing the reduction that occurred in patients treated with Dapagliflozin. Compared to Dapagliflozin, Dula 0.75 mg reported a greater reduction in FBG levels from baseline. Compared to Dapagliflozin, Dula 1.5 mg reported a greater reduction in FBG levels from baseline. Overall, both doses of Dula had a significantly greater reduction in FBG from baselines when compared to the patients treated with Dapagliflozin. Dula 1.5 mg had the greatest reduction in BG as compared to Dula 0.75 mg and Dapagliflozin. All study drugs were effective in reducing BG as evidenced after looking reduction trend from baseline. All study drugs were found effective in improving glycemic control when compared to baseline. Compared to Dula 0.75 mg, the reduction in FBG was more pronounced with Dula 1.5 mg. A similar trend of reduction was observed while comparing the reduction that occurred in patients treated with Dapagliflozin. Compared to Dapagliflozin, Dula 0.75 mg reported a greater reduction in BG levels from baseline. Compared to Dapagliflozin, Dula 1.5 mg reported a greater reduction in BG levels from baseline. Overall, both doses of Dula had a significantly greater reduction in BG from baselines when compared to the patients treated with Dapagliflozin.

Patients treated with Dula 1.5 mg had the greatest reduction in HbA1c (%) as compared to Dula 0.75 mg and Dapagliflozin. All study drugs were effective in reducing HbA1c as evidenced after looking reduction trend from baseline. All study drugs were found effective in improving glycemic control when compared to baseline. Compared to Dula 0.75 mg, the reduction in HbA1c was more pronounced with Dula 1.5 mg. A similar trend of reduction was observed while comparing the reduction that occurred in patients treated with Dapagliflozin. Compared to Dapagliflozin, Dula 0.75 mg reported a greater reduction in HbA1c levels from baseline. Compared to Dapagliflozin, Dula 1.5 mg reported a greater reduction in HbA1c levels from baseline. Overall, both doses of Dula had significantly greater reduction HbA1c from baselines when compared to the patients treated with Dapagliflozin. The frequent side effects noted across all treatment groups were GI-related, although the incidence of GI-related events more in Dula compared to Dapagliflozin, however, there were no GI events that led to discontinuation of Dula and none of them were serious. All GI events that occurred in this study were of milder severity and did not rescue treatment to manage the GI events. Overall, both the study drugs had acceptance safety profiles and the risk-benefit ratio was favorable.

Overall, current study results demonstrated that Dula and Dapagliflozin were found effective in the management of diabetes. However, on compassion, noted the improvement in glycemic control was meaningfully larger in patients who were treated with Dula compared to Dapagliflozin. Overall, Dula was a better alternative in the treatment of diabetes. Overall, both the study drugs had acceptance safety profiles and the risk-benefit ratio was favorable. In the limitations of the study, for example, the results of this study may not be generalized to the Chinese population due to relatively low samples (for diabetes) used. Thus, a study with a large sample size is required to validate the results reported here. In addition, diverse patients population and small choice of medication types.

CONCLUSION

This study has demonstrated that Dulaglutide could be a better alternative as compared to Dapagliflozin in the management of diabetes among Chinese patients. Overall, both the study drugs had acceptance safety profiles and the risk-benefit ratio was favorable. The present study encourages to conduct of a larger randomized multicentric study to confirm the findings of the present study.

SIGNIFICANCE STATEMENT

A preliminary study has demonstrated that 0.75 mg once weekly Dulaglutide could be a better alternative as compared to 10 mg daily Dapagliflozin with manageable adverse effects in the management of type 2 diabetes among Chinese patients with a history of poorly controlled blood glucose levels. Dulaglutide has dose related response. In addition, Dulaglutide and Dapagliflozin both have acceptance safety profiles and the risk-benefit ratio is favorable. The findings will help physicians uncover critical areas of the management of type 2 diabetes that many clinicians have not evaluated.

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REFERENCES

1. Iqra, H., S.R. Masoodi, S.A. Mir, M. Nabi, K. Ghazanfar and B.A. Ganai, 2015. Type 2 diabetes mellitus: From a metabolic disorder to an inflammatory condition. World J. Diabetes, 6: 598-612.
2. Wang, L., P. Gao, M. Zhang, Z. Huang and D. Zhang *et al*., 2017. Prevalence and ethnic pattern of diabetes and prediabetes in China in 2013. JAMA, 317: 2515-2523.
3. Wang, C., J. Li, H. Xue, Y. Li and J. Huang *et al*., 2015. Type 2 diabetes mellitus incidence in Chinese: Contributions of overweight and obesity. Diabetes Res. Clin. Pract., 107: 424-432.
4. Unger, J.R. and C.G. Parkin, 2011. Glucagon-like peptide-1 (GLP-1) receptor agonists: Differentiating the new medications. Diabetes Ther., 2: 29-39.
5. Zhang, F., L. Tang, Y. Zhang, Q. Lü and N. Tong, 2017. Glucagon-like peptide-1 mimetics, optimal for Asian type 2 diabetes patients with and without overweight/obesity: Meta-analysis of randomized controlled trials. Sci. Rep., Vol. 7. 10.1038/s41598-017-16018-9.
6. Boyle, J.G., R. Livingstone and J.R. Petrie, 2018. Cardiovascular benefits of GLP-1 agonists in type 2 diabetes: A comparative review. Clin. Sci., 132: 1699-1709.
7. Davies, M.J., D.A. D'Alessio, J. Fradkin, W.N. Kernan and C. Mathieu *et al*., 2018. Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care, 41: 2669-2701.
8. Chen, Y.H., C.N. Huang, Y.M. Cho, P. Li and L. Gu *et al*., 2018. Efficacy and safety of dulaglutide monotherapy compared with glimepiride in East-Asian patients with type 2 diabetes in a multicentre, double-blind, randomized, parallel-arm, active comparator, phase III trial. Diabetes Obesity Metab., 20: 2121-2130.
9. Wang, W., L. Nevárez, E. Filippova, K.H. Song and B. Tao *et al*., 2019. Efficacy and safety of once-weekly dulaglutide versus insulin glargine in mainly Asian patients with type 2 diabetes mellitus on metformin and/or a sulphonylurea: A 52-week open-label, randomized phase III trial. Diabetes Obesity Metab., 21: 234-243.
10. Gallwitz, B., S. Dagogo-Jack, V. Thieu, L.E. Garcia-Perez and I. Pavo *et al*., 2018. Effect of once-weekly dulaglutide on glycated haemoglobin (HbA1c) and fasting blood glucose in patient subpopulations by gender, duration of diabetes and baseline HbA1c. Diabetes Obesity Metab., 20: 409-418.
11. Gentilella, R., G. Sesti, L. Vazquez, H. Sapin, V. Reed, I. Romera and P. Pozzilli, 2019. Dulaglutide is an effective treatment for lowering HbA1c in patients with type 2 diabetes regardless of body mass index. Diabetes Obesity Metab., 21: 2660-2666.
12. Kim, Y.G., S. Hahn, T.J. Oh, K.S. Park and Y.M. Cho, 2014. Differences in the HbA1c-lowering efficacy of glucagon-like peptide-1 analogues between Asians and non-Asians: A systematic review and meta-analysis. Diabetes Obesity Metab., 16: 900-909.
13. Carls, G.S., R. Tan, J.Y. Zhu, E. Tuttle, J. Yee, S.V. Edelman and W.H. Polonsky, 2017. Real-world weight change among patients treated with glucagon-like peptide-1 receptor agonist, dipeptidyl peptidase-4 inhibitor and sulfonylureas for type 2 diabetes and the influence of medication adherence. Obesity Sci. Pract., 3: 342-351.
14. Conget, I., D. Mauricio, R. Ortega and B. Detournay, 2016. Characteristics of patients with type 2 diabetes mellitus newly treated with GLP-1 receptor agonists (CHADIG Study): A cross-sectional multicentre study in Spain. BMJ Open, Vol. 6. 10.1136/bmjopen-2015-010197.
15. Lapolla, A., C. Berra, M. Boemi, A.C. Bossi and R. Candido *et al*., 2018. Long-term effectiveness of liraglutide for treatment of type 2 diabetes in a real-life setting: A 24-month, multicenter, non-interventional, retrospective study. Adv. Ther., 35: 243-253.
16. Hamano, K., H. Nishiyama, A. Matsui, M. Sato and M. Takeuchi, 2017. Efficacy and safety analyses across 4 subgroups combining low and high age and body mass index groups in Japanese phase 3 studies of dulaglutide 0.75 mg after 26 weeks of treatment. Endocr. J., 64: 449-456.
17. Wolffenbuttel, B.H.R., L. van Gaal, S. Durán-Garcia and J. Han, 2016. Relationship of body mass index with efficacy of exenatide twice daily added to insulin glargine in patients with type 2 diabetes. Diabetes Obesity Metab., 18: 829-833.
18. Geiser, J.S., M.A. Heathman, X. Cui, J. Martin, C. Loghin, J.Y. Chien and A. de la Peña, 2016. Clinical pharmacokinetics of dulaglutide in patients with type 2 diabetes: Analyses of data from clinical trials. Clin. Pharmacokinet., 55: 625-634.
19. Henry, R.R., J.B. Buse, G. Sesti, M.J. Davies, K.H. Jensen, J. Brett and R.E. Pratley, 2011. Efficacy of anti hyperglycemic therapies and the influence of baseline hemoglobin A_{1C}: A meta-analysis of the liraglutide development program. Endocr. Pract., 17: 906-913.
20. Blonde, L., P. Chava, T. Dex, J. Lin, E.V. Nikonova and R.M. Goldenberg, 2017. Predictors of outcomes in patients with type 2 diabetes in the lixisenatide GetGoal clinical trials. Diabetes Obesity Metab., 19: 275-283.
21. Onishi, Y., T. Oura, H. Nishiyama, S. Ohyama, M. Takeuchi and N. Iwamoto, 2016. Subgroup analysis of phase 3 studies of dulaglutide in Japanese patients with type 2 diabetes. Endocr. J., 63: 263-273.

22. Pencek, R., A. Blickensderfer, Y. Li, S.C. Brunell and P.W. Anderson, 2012. Exenatide twice daily: Analysis of effectiveness and safety data stratified by age, sex, race, duration of diabetes, and body mass index. Postgrad. Med., 124: 21-32.
23. Pencek, R., A. Blickensderfer, Y. Li, S.C. Brunell and S. Chen, 2012. Exenatide once weekly for the treatment of type 2 diabetes: Effectiveness and tolerability in patient subpopulations. Int. J. Clin. Pract., 66: 1021-1032.
24. Seufert, J., T. Bailey, S.B. Christensen and M.A. Nauck, 2016. Impact of diabetes duration on achieved reductions in glycated haemoglobin, fasting plasma glucose and body weight with liraglutide treatment for up to 28 weeks: A meta-analysis of seven phase III trials. Diabetes Obesity Metab., 18: 721-724.
25. Pratley, R.E., M.A. Nauck, A.H. Barnett, M.N. Feinglos and F. Ovalle *et al.*, 2014. Once-weekly albiglutide versus once-daily liraglutide in patients with type 2 diabetes inadequately controlled on oral drugs (HARMONY 7): A randomised, open-label, multicentre, non-inferiority phase 3 study. Lancet Diabetes Endocrinol., 2: 289-297.