ORIGINAL ARTICLE

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Y. L. Zhang[1], C. Zho [2], X. F. Li[1], M. N. Yang[1], L. Tao[2], X. Y. Zheng[2] and Y. S. Jia[3]

[1]Depar men of Endocrinolog , Qianan Yan han Ho pi al, Hebei, China; [2]Depar men of Endocrinolog , Qinh angdao Ho pi al of Tradi ional Chine e Medicine, Qinh angdao, Hebei, China; [3]Nor h China Uni er i of Science and Technolog , Tang han, Hebei, China;

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Addre for corre pondence: Y. L. Zhang, Depar men of Endocrinolog , Qianan Yan han Ho pi al, Qianan 064000, Hebei, China.
E-mail: anli hang_ @163.com
Y. S. Jia, Nor h China Uni er i of Science and Technolog , Tang han 063210, Hebei, China.
E-mail: jia ong en@126.com

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Aims

The p rpo e of hi d a o e amine he effec i ene of beinagl ide on bod eigh , gl ca ed haemoglobin (HbA_{1c}), blood pre re and lipid profile in pa ien i h pe 2 diabe e melli (T2DM) in a real orld e ing in China.

Materials and methods

Thi a a m l icen re, ob er a ional, re ro pec i e, open-label d cond c ed in China. Da a ere collec ed from T2DM pa ien ho ar ed rea men i h beinagl ide be een 2017 and 2018.

Results

A o al of 314 pa ien ere incl ded in he d . Af er 3 mon h of rea men i h beinagl ide, here ere ignifican red c ion in bod eigh (−10.05 kg [95% confidence in er al −9.29 o −10.80]), HbA_{1c} (−2.87% [−2.62 o −3.11]), 2-h po prandial pla ma gl co e (−5.46 mmol L^{-1} [−4.96 o −

increa ing a en ion o ing o heir comprehen i e effec on bo h gl caemic con rol and eigh lo i h lo h pogl caemia incidence.

Beinagl ide (formerl kno n a benagl ide), a GLP-1RA, i recombinan h man gl cagon-like pep ide-1 and hare 100% homolog i h h man GLP-1(7-36) (5). The dr g a appro ed b he China Food and Dr g Admini ra ion for he rea men of T2DM in December 2016. Beinagl ide i one of he GLP-1RA recommended for he rea men of T2DM b he Chine e g ideline for he pre en ion and rea men of pe 2 diabe e (2017 edi ion) (6). The efficac and afe of beinagl ide ha e been a e ed in randomi ed con rolled rial (RCT) in China (7–9). Similar o o her GLP-1RA , beinagl ide a effec- i e in lo ering gl ca ed haemoglobin (HbA_{1c}), fa ing pla ma gl co e (FPG) and po prandial pla ma gl co e (PPG) in pa ien i h T2DM (7,8). In addi ion, beinagl ide red ced bod eigh and bod ma inde (BMI) in T2DM pa ien i h o e eigh and obe i (7,9). The e RCT pro ided e idence of he effec i ene of beinagl ide in a ell-defined pa ien pop la ion nder a ric l con rolled en ironmen , e i i ncer ain o ha e en he re l can be ran la ed o real orld clinical prac ice here a more general pa ien pop la ion i rea ed i h he ne in er en ion in o pa ien clinic .

Real orld die are er impor an o f r her e al- a e he performance of ne dr g once he reach he marke . S ch die can complemen RCT and a e heir re l in a more general pa ien pop la ion. The real orld effec of beinagl ide ha e no been repor ed o da e. Th , he p rpo e of hi d a o e amine he effec i ene of beinagl ide on HbA_{1c}, bod eigh , blood pre re, and lipid profile in a real orld e ing in China. The a hor h po he i ed ha he efficac of beinagl ide in RCT ill al o be ob er ed in he real- orld d .

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Thi a a m l icen re, ob er a ional, re ro pec i e, open-label d cond c ed in o ho pi al in Hebei Pro ince (nor hern China). The GLP-1RA beinagl ide a la nched in Febr ar 2017 in China. Since hen, da a from T2DM pa ien rea ed i h beinagl ide nder ro ine clinical prac ice condi ion ere con ec i el collec ed n il March 2018, i.e. o er a ime frame of 14 mon h . Da a ere e rac ed from he elec ronic medical record em and ga hered in an E cel da a hee b he re earcher . Ad l T2DM pa ien (≥18 ear) ere eligible for he d . The e cl ion cri eria ere pa ien i h pe 1 diabe e melli and ho e ho ref ed o pro ide informed con en . The follo ing da a ere collec ed a ba eline and/or hree b eq en i i (af er 1, 2 and 3 mon h of rea men): age, e , diabe e d ra ion, HbA_{1c}, 2-h PPG, FPG, bod eigh , BMI, ai circ mference (WC), C-pep ide, hear ra e, olic blood pre re (SBP), dia olic blood pre re (DBP), rigl ceride , lo -den i lipopro ein chole erol (LDL-C), high-den i lipopro ein chole erol (HDL-C), an i- h per en i e and lipid-lo ering herapie and hi or of pre io an i-diabe ic medica ion . Moreo er, he do age of beinagl ide and concomi an an i-diabe ic herapie a recorded. The al e of HbA_{1c}, FPG, 2-h PPG, C-pep ide, rigl ceride , LDL-C and HDL-C ere e rac ed from andardi ed labora or e re l . Bod eigh , WC, hear ra e, SBP and DBP ere mea red b profi- cien n r e ing andard eq ipmen .

The primar d objec i e a o a e he effec- i ene of beinagl ide in con rolling gl caemia af er 3 mon h of rea men . Secondar objec i e incl ded a e ing change in bod eigh , he propor ion of pa ien i h eigh lo ≥ 5% and ≥10% and o her clinical parame er rela ed o diabe e af er 3 mon h of rea men . Ad er e e en , h pogl caemic e en and di con in a ion of beinagl ide ere al o racked.

Thi d a appro ed b he local e hical commi- ee and performed in accordance i h he Declara ion of Hel inki (re i ed in 2013).

S a i ical anal i

The Kolmogoro –Smirno e a ed o de ermine if al e ere normall di rib ed. Da a for con in o ariable ere e pre ed a he mean (andard de ia- ion [SD]). Da a for ca egorical ariable ere e pre ed a percen age (%). Ba eline charac eri ic are repor ed on he ba i of he f ll anal i e (FAS), hich incl ded all pa ien ho me he eligibili cri eria and had ba eline mea re for HbA_{1c} or eigh . Efficac anal i incl ded all pa ien ho recei ed a lea one do e of beinagl ide and had a lea one po ba eline mea re- men for HbA_{1c} or bod eigh . Mi ing al e ere imp ed ing he la ob er a ion carried fo ard (LOCF) me hod. For paired ample , he paired *t*- e or Wilco on ma ched-pair igned-rank e a ed for o ime poin , and repea ed-mea re anal i of ariance or he Friedman e follo ed b D nn' m l iple- compari on e a ed for m l iple ime poin . The mean (SD), mean difference, andard error (SE) and 95% confidence in er al (CI) ere calc la ed for each ime poin . S bgro p anal e for paired ample ere performed i h he ame a i ical me hod . The change in HbA_{1c} and eigh ere a e ed b anal i of co ariance, adj ing for ba eline mea re and he do e of beinagl ide a co aria e . A m l i aria e lin- ear regre ion model a applied o iden if de erminan

of HbA_{1c} reduction and weight loss. Independent variables included age, sex, diabetes duration, baseline HbA_{1c}, BMI, SBP, triglycerides, LDL-C, HDL-C and hepatic dose of beinaglutide. $p < 0.05$ was considered statistically significant (two-tailed). Data were analysed using SPSS 23 software (IBM SPSS, USA).

Based on the data with imputation for missing values (i.e. observed data only), a sensitivity analysis was conducted using the LOCF method for handling missing data might have influenced any critical conclusions.

Results

Baseline characteristics of patients

From January 2017 to March 2018, data from 323 patients treated with beinaglutide were extracted from the electronic medical record system. Of those, nine patients lacked baseline data for HbA_{1c} and body weight (unknown reason) and were excluded from the analysis. The remaining 314 patients were included in the FAS (see flow chart in Figure 1). There were 163 (51.9%) men and 151 (48.1%) women, with an overall mean age of 47.6 (10.5) years. Most patients (60.3%) had a diabetes duration < 5 years. On average, baseline body weight was 77.94 (10.91) kg, BMI was 27.95 (4.07) kg m^{-2}, HbA_{1c} was 9.05 (1.48)%, 2-h PPG was 14.23 (3.23) mmol L^{-1} and FPG was 9.25 (1.77) mmol L^{-1}. Baseline characteristics of the FAS population are summarized in Table 1. Approximately 27.7% of the FAS population were drug-naive patients who were newly diagnosed with T2DM. Regarding the history of previous anti-diabetic medications before initiating beinaglutide, 30.3% of patients had been treated previously with metformin, 14.0% with repaglinide, 12.7% with acarbose, 10.8% with sulfonylurea, 8.6% with short-acting insulin, 7.0% with basal insulin, 1.9% with DPP4 inhibitor and 1.0% with liraglutide. In addition, 48.1% of patients had received one anti-diabetic agent, 21.0% received two anti-diabetic agents and a small proportion (3.2%) received three anti-diabetic agents prior to beinaglutide treatment. Regarding diabetic complications, 12.7% and 1.3% of patients presented with a personal history of coronary heart disease and brain infarction, respectively. Diabetic peripheral neuropathy, nephropathy and retinopathy were present in 40.4%, 13.7% and 2.2% of patients, respectively. A total of 10.5% of patients presented with both diabetic peripheral neuropathy and nephropathy, and a small proportion (0.1%) presented with diabetic peripheral neuropathy, nephropathy and retinopathy. Hypertension was present in 51.9% of patients, 84.0% of whom

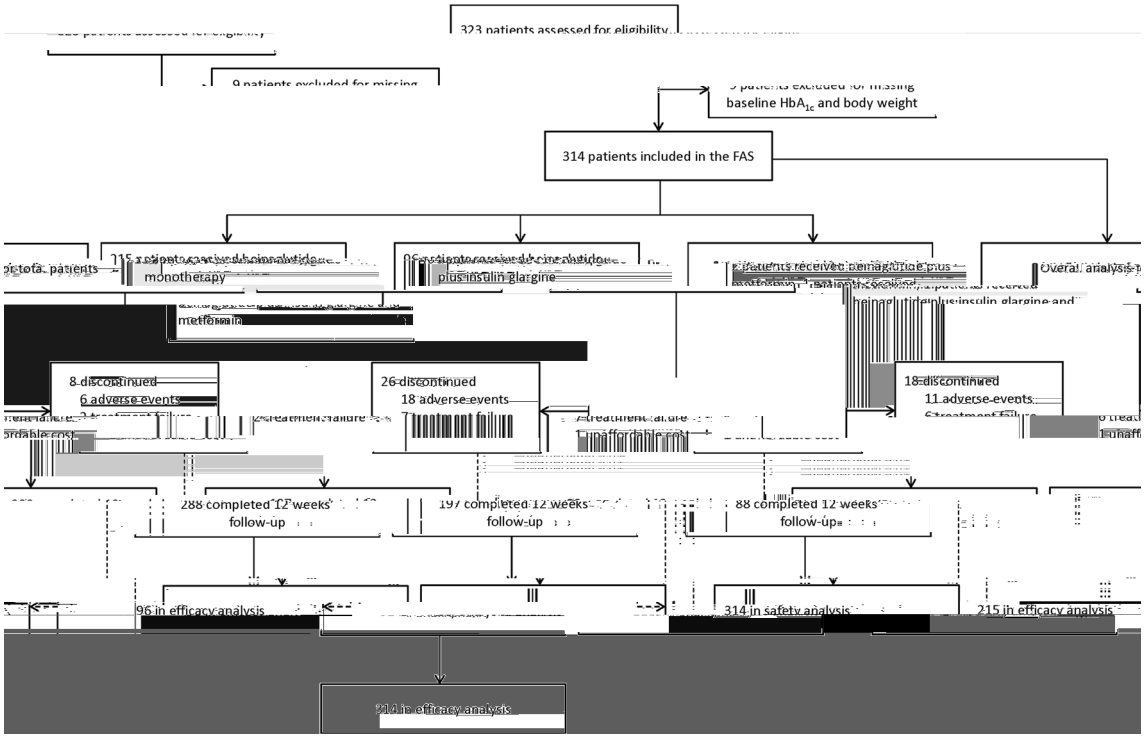

Figure 1 Study flow chart. FAS, full analysis set; HbA_{1c}, glycated haemoglobin.

recei ed an i-h per en i e rea men . D lipidaemia a pre en in 33.4% of pa ien , 79.0% of hom recei ed lipid-l ering rea men .

Beinagl ide admini ra ion

A ba eline, 215 pa ien (68.5%) ed beinagl ide mono herap , 96 (30.6%) ed beinagl ide in combina- ion i h in lin glargine, o (0.6%) in combina ion i h me formin and one (0.3%) in combina ion i h in lin glargine and me formin. A ba eline, 37.6% of he pa ien ere pre cribed a dail do e of 0.2 mg, 52.3% recei ed 0.3 mg, 5.5% recei ed 0.4 mg, 0.5% recei ed 0.45 mg and 4.1% recei ed 0.6 mg of beinagl ide. Follo ing a period of do e e cala ion of 1–2 eek , pre crip ion of 0.2, 0.3, 0.4, 0.42, 0.48 and 0.6 mg of beinagl ide ere gi en o 31.2%, 5.7%, 2.1%, 11.3%, 22.7% and 27.1% of he pa ien , re pec i el . In addi- ion, 96.0% of pa ien carried o pplemen al life le in er en ion .

Clinical o come af er 3 mon h of beinagl ide rea men

Clinical parame er a ba eline and he 3-mon h follo - p are pre en ed in Table 2. Compared i h ba eline, af er 3 mon h of rea men , he pa ien ho ed ignifi- can red c ion in bod eigh , HbA_{1c}, 2-h PPG, FPG, BMI, WC, hear ra e, SBP, DBP, rigl ceride and LDL-C and a ignifican ele a ion in HDL-C (all $p < 0.0001$). In bgro p , pa ien recei ing beinagl ide mono herap or beinagl ide in combina ion i h in lin glargine ho ed imilar re l ($p < 0.001$). C-pep ide ho ed a ignifican red c ion from ba eline o 3 mon h in he o al pop la ion of pa ien ($p = 0.0016$) and he pa ien ho recei ed mono herap ($p < 0.0001$), b no in ho e re- cei ing beinagl ide in combina ion i h in lin glargine ($p = 0.4464$).

Temporal rend in bod eigh change are ho n in Fig re 2. Significan eigh lo a ob er ed a all ime poin . For he o al pop la ion of pa ien , bod eigh a decrea ed b −10.05 kg (−9.29 o −10.80) and −12.90% (−12.02 o −13.78) af er 3 mon h (all $p <$ 0.0001). Af er 3 mon h , 84.96% and 72.18% of pa ien a ained eigh lo of ≥5% and ≥10%, re pec i el . S bgro p anal e ho ed imilar re l . Af er 3 mon h , bod eigh a decrea ed b −9.98 kg (−8.97 o −10.99) and −12.81% (−11.64 o −13.97) in beinagl ide mono herap pa ien and b −10.30 kg (−9.43 o −11.16) and 13.33% (−12.28 o −14.38) hen admini ered in combina ion i h in lin glargine (all $p <$ 0.0001). F r hermore, a 3 mon h , he propor ion of pa- ien i h eigh lo of ≥5% and ≥10% ere 80.75% and 68.45% for mono herap and 97.37% and 85.53% for he combina ion herap i h in lin glargine, re pec i el .

Temporal rend in HbA_{1c}, 2-h PPG and FPG are ho n in Fig re 3. For he o al pop la ion of pa ien , he a erage change in HbA_{1c} 97admini ered(Te6.2(pple(9-389.(glarClof)-42.90%)-

T 2 Clinical parame er compared‑ i h ba eline af er 3-mon h beinagl ide rea men

					S bgro p							
					Beinagl ide (*N* = 215)				Beinagl ide + in lin glargine (*N* = 96)			
	To al (*N* = 314)											
Variable	*N*	Ba eline	Af er rea men	*p*	*N*	Ba eline	Af er rea men	*p*	*N*	Ba eline	Af er rea men	*p*
Bod ‑ eigh , kg	266	77.84 (10.70)	67.80 (10.42)	<0.0001	187	77.63 (11.19)	67.65 (10.75)	<0.0001	76	77.49 (8.28)	67.19 (8.10)	<0.0001
HbA_{1c}, %	208	9.02 (1.53)	6.16 (0.87)	<0.0001	134	8.78 (1.36)	5.96 (0.93)	<0.0001	73	9.46 (1.72)	6.52 (0.63)	<0.0001
2-h PPG, mmol L^{-1}	255	14.21 (3.29)	8.75 (1.99)	<0.0001	186	14.41 (3.11)	8.98 (2.21)	<0.0001	67	13.36 (3.31)	8.12 (0.95)	<0.0001
FPG, mmol L^{-1}	256	9.24 (1.79)	6.20 (1.00)	<0.0001	187	9.11 (1.65)	6.13 (1.09)	<0.0001	67	9.42 (1.76)	6.33 (0.59)	<0.0001
C-pep ide, nmol L^{-1}	97	0.98 (0.45)	0.86 (0.20)	0.0016	35	1.13 (0.30)	0.94 (0.10)	<0.0001	62	0.89 (0.50)	0.82 (0.23)	0.4464
BMI, kg m^{-2}	262	27.93 (4.11)	24.05 (2.95)	<0.0001	187	27.96 (4.47)	24.03 (2.90)	<0.0001	76	27.64 (2.48)	23.85 (2.33)	<0.0001
WC, cm	244	95.84 (14.63)	86.01 (12.50)	<0.0001	177	100.20 (13.96)	89.04 (12.78)	<0.0001	67	84.37 (9.17)	78.01 (7.09)	<0.0001
Hear ra e, bpm	105	76.55 (6.78)	73.86 (4.27)	<0.0001	39	76.56 (7.24)	73.87 (4.12)	0.0029	66	76.55 (6.54)	73.85 (4.39)	<0.0001
SBP, mmHg	178	143.60 (19.04)	128.50 (8.78)	<0.0001	108	147.70 (16.61)	129.60 (8.37)	<0.0001	69	136.60 (20.45)	126.80 (9.27)	<0.0001
DBP, mmHg	178	87.97 (8.29)	81.95 (5.02)	<0.0001	108	88.92 (7.84)	81.91 (5.05)	<0.0001	69	86.55 (8.86)	82.32 (4.34)	<0.0001
Trigl ceride, mmol L^{-1}	188	3.09 (1.78)	1.52 (0.65)	<0.0001	115	3.18 (1.87)	1.55 (0.66)	<0.0001	73	2.95 (1.63)	1.46 (0.65)	<0.0001
LDL-C, mmol L^{-1}	148	3.38 (0.94)	1.84 (0.83)	<0.0001	79	3.44 (0.80)	2.03 (0.84)	<0.0001	69	3.31 (1.07)	1.62 (0.77)	<0.0001
HDL-C, mmol L^{-1}	147	1.31 (0.54)	2.30 (1.02)	<0.0001	78	1.18 (0.47)	1.91(0.97)	<0.0001	69	1.46 (0.59)	2.74 (0.88)	<0.0001

Da a are e pre ed a mean (SD).

BMI, bod ma inde ; bpm, bea min^{-1}; DBP, dia olic blood pre re; FPG, fa ing pla ma gl co e; HbA_{1c}, gl ca ed haemoglobin; HDL-C, high-den i lipopro ein chole erol; LDL-C, lo‑ - den i lipopro ein chole erol; PPG, po prandial gl co e; SBP, olic blood pre re; SD; andard de ia ion; WC, ‑ ai circ mference.

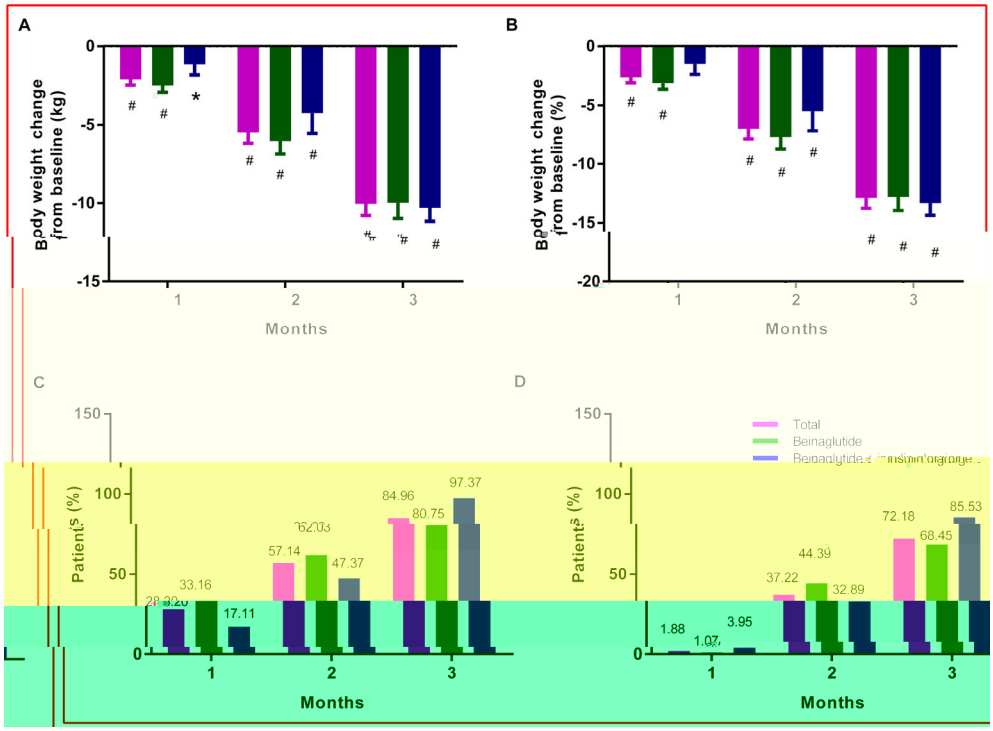

Figure 2 Temporal trends in body weight between baseline and 3 months. (A) Absolute change in body weight (kg). (B) Relative change in body weight (%). (C) The proportion of patients with body weight loss of ≥5%. (D) The proportion of patients with body weight loss of ≥10%. The bars show 95% CI. Significant changes from baseline are indicated (*$p < 0.01$, #$p < 0.0001$). [Correction added on 10 July 2019, after first online publication: Figure 2 has been replaced in this version.]

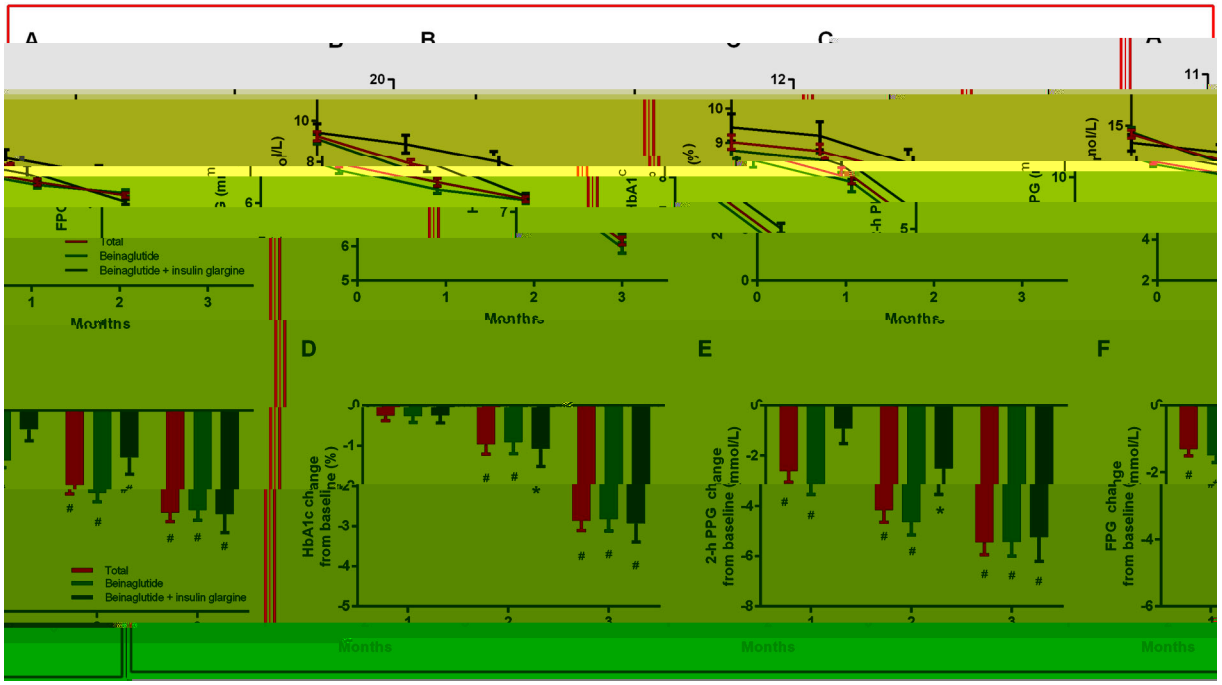

Figure 3 Temporal trends of glycaemic parameters between baseline and 3 months. (A) Mean values of HbA_{1c}. (B) Mean values of PPG. (C) Mean values of FPG. (D) Mean change in HbA_{1c}. (E) Mean change in PPG. (F) Mean change in FPG. The bars show 95% CI. Significant changes from baseline are indicated (*$p < 0.01$, #$p < 0.0001$). FPG, fasting plasma glucose; HbA_{1c}, glycated haemoglobin; PPG, postprandial glucose.

change in 2-h PPG and FPG after 3 months reached −5.46 mmol L^{-1} (−4.96 to −5.95) and −3.04 mmol L^{-1} (−2.78 to −3.31) (all $p < 0.0001$), respectively. The statistical results of the subgroup showed a similar trend. For patients receiving beinaglutide monotherapy, the average change in HbA_{1c}, 2-h PPG and FPG gradually decreased over 3 months and reached −2.83% (−2.53 to −3.12), −5.44 mmol L^{-1} (−4.88 to −5.99) and −2.97 mmol L^{-1} (−2.67 to −3.27) (all $p < 0.0001$) after 3 months of treatment, respectively. For patients receiving combination therapy with beinaglutide and insulin glargine, the average change in HbA_{1c}, 2-h PPG and FPG after 3 months reached −2.94% (−2.49 to −3.39), −5.24 mmol L^{-1} (−4.27 to −6.21) and −3.10 mmol L^{-1} (−2.55 to −3.64) (all $p < 0.0001$), respectively.

Detailed results (mean difference, standard error and 95% CI) of the temporal trend in HbA_{1c}, 2-h PPG, FPG and body weight are reported in Table S1–S3.

Change in body weight and HbA_{1c} according to baseline characteristics and the dose of beinaglutide

The change in body weight did not significantly vary by age ($p = 0.097$), age ($p = 0.157$), diabetes duration ($p = 0.157$) or baseline HbA_{1c} categories ($p = 0.949$). The change in HbA_{1c} also did not significantly vary by age ($p = 0.471$), age ($p = 0.249$), diabetes duration ($p = 0.169$) or baseline BMI categories ($p = 0.964$). However, the changes in body weight were significantly greater in patients with ≥28 kg m^{-2} of baseline BMI and in patients receiving beinaglutide 0.60 mg ($p = 0.007$ and $p < 0.0001$, respectively); and the changes in HbA_{1c} were significantly greater in patients with ≥9.0% baseline HbA_{1c} and in patients receiving beinaglutide of 0.40–0.48 mg (all $p < 0.0001$) (Figure S1).

Determinants of weight loss and HbA_{1c} reduction

The results of multiple linear regression models showed that weight loss from baseline to 3 months positively correlated with baseline BMI levels and the dose of beinaglutide, and the HbA_{1c} reduction from baseline to 3 months positively correlated with baseline HbA_{1c} levels and the dose of beinaglutide (Table S4 and S5).

Adverse events, hypoglycaemic events and discontinuation

Among patients in the FAS, the most common adverse events were gastrointestinal symptoms (51.0%) and vomiting (18.2%). Other reported adverse events were dizziness (17.2%) and headache (8.3%). The adverse events mainly occurred in the first month after initiation of treatments, and most were mild to moderate. A total of 14 symptomatic hypoglycaemic events were recorded within the 3 months prior to beinaglutide treatments, but no such events were reported after beinaglutide treatments. A total of 26 patients (8.3%) discontinued beinaglutide therapy within 3 months citing gastrointestinal side effects (5.7%), treatment failure (2.2%) or unaffordable cost (0.3%).

Sensitivity analysis performed on the completer's data with LOCF imputations generally consistent with the conclusion of the aforementioned dataset (data not shown).

Discussion

The present study is the first multicentre, observational, retrospective, open-label analysis of beinaglutide effectiveness in T2DM patients, most of whom were with overweight and obesity, in China. The data demonstrated a mean weight loss of 10.05 kg and a mean reduction of 2.87% in HbA_{1c} after 3 months of treatments. The observations confirmed the effectiveness of beinaglutide in a real-world setting.

The patients included in the present study represented a general T2DM population in a real-world setting in China. Baseline data indicated that beinaglutide therapy was commonly prescribed for patients with overweight and obesity who had a relatively short disease duration. Notably, 27.7% of the patients were newly diagnosed with T2DM, indicating that beinaglutide was generally accepted as a second-line treatment.

For the Chinese people, a BMI between 24.0 and 27.9 kg m^{-2} is defined as overweight, and a BMI ≥ 28.0 kg m^{-2} is categorized as obese (10). In the present study, 56.5% of patients were overweight, 41.2% were obese and only 2.3% were normal weight. When analysing the weight-loss effects of beinaglutide on the basis of baseline BMI, patients with overweight and obesity experienced greater weight-loss effects. This BMI-dependent effect was similar to that in a previous study of liraglutide (11,12). Data for normal weight Chinese patients were only available for individual, making estimates for this subgroup unreliable. Similar to other studies of GLP-1RA (13,14), the weight-loss effects of beinaglutide was dose dependent, with the highest dose (0.6 mg) providing the greatest weight loss. In addition, based on other results, sex, age and disease duration had no impact on drug efficacy with regard to either glycaemic control or weight loss, which was a consistent with previous studies of GLP-1RA (11,15).

The mean reduction in HbA_{1c} in this study was higher than mean reduction reported in previous RCT of

beinaglutide, in which mean reduction from baseline between 0.7% and 1.2% have been reported (7,9). This relatively interesting because HbA_{1c} reduction in real‐world groups have all been smaller than those in RCT according to Edelman and Polonsky's data (16). Previous studies have reported that baseline HbA_{1c} level might predict an early response to GLP-1RA in terms of HbA_{1c} reduction (15,17). In the present study, HbA_{1c} reduction was a potential correlated with baseline HbA_{1c} level; that is, i.e. patients with higher baseline HbA_{1c} level had a greater HbA_{1c} reduction after 3 months of treatment. Compared with previous RCT of beinaglutide (mean baseline HbA_{1c} between 7.97% and 8.05%) (7,9), the higher baseline HbA_{1c} level (9.02%) in this study may be an important reason for the increased efficacy observed with beinaglutide treatment.

This discrepancy might also be explained by a change in the formulation of beinaglutide. In previous RCT, beinaglutide lyophilized powder was used for injection; that is, i.e. the powder had to be dissolved and then subcutaneously injected with a disposable sterile syringe (7–9). This formulation increased the difficulty for patients to the drug, and the accuracy of the drug dose and patient compliance were affected. However, a new formulation (beinaglutide injection) was developed before entering the market. In clinical practice, patients can easily use an injection pen for subcutaneous administration, providing great convenience for patients prescribed beinaglutide. Thus, the change in the formulation may be another reason for the increased efficacy of beinaglutide treatment in the real‐world setting. In addition, the HbA_{1c} reduction were more significant in the relative high-dose group (0.40–0.48 and 0.60 mg), and this finding was consistent with that of previous studies of GLP-1RA (18,19).

Decreased fasting C-peptide level after beinaglutide monotherapy suggested potential efficacy for improving both perinatal hyperglycaemia and β-cell rest. As a short-acting meal-time GLP-1RA, beinaglutide has a short half-life (15 min) and duration of action (2 h) (6). Beinaglutide simulate post prandial insulin secretion in a glucose-dependent manner (20), but the insulinotropic effect is not maintained in the fasting state owing to rapid degradation of the drug. This outcome is beneficial because β-cell rest offers potential β-cell again other improvement and improve islet function (21,22). This phenomenon of β-cell rest was also observed in previous studies of GLP-1 (7-36) and exendin-4 in post prandial state (23–25). For patients receiving beinaglutide plus insulin glargine, there was a decrease in C-peptide level, but there was no significant difference, which might be due to lower baseline C-peptide level (i.e. poor β-cell function) in this group.

The present study also provide new information about the benefit of beinaglutide on other health indicators in a real‐world setting. After 3 months of treatment, significant reductions in heart rate, SBP, DBP, total cholesterol and LDL-C were observed, whereas HDL-C increased significantly. These improvements in cardiovascular and lipid profiles were related to beinaglutide treatment and only partially contributed by concomitant anti-hypertensive or lipid-lowering treatments. These benefits together with high implied a potential impact of beinaglutide on overall cardiovascular outcomes. However, this comprehensive beneficial efficacy was not new expected, as indicated by previous studies of GLP-1RA (13,26).

The safety characteristics of beinaglutide were also consistent with previous findings of GLP-1RA (27–29). Gastrointestinal adverse events were common but mostly transient. No symptomatic hypoglycaemic events were reported during the 3-month treatment, which may be explained by the glucose-dependent insulinotropic effect and short half-life of beinaglutide. The main cause of beinaglutide discontinuation was adverse events (5.7%), which was similar to previous studies of GLP-1RA (30,31).

The present study has significant strengths, such as extensive clinical information and minimal exclusion criteria, resulting in more truly real data gained from a wide range of T2DM patients. Additionally, however, the lack of randomization and a control group are the main limitations of this study. In addition, the follow-up period was limited to the first 3 months from the start of beinaglutide. Additional RCT and real‐world studies are needed to evaluate the effectiveness and safety of long-term beinaglutide treatment.

In summary, this study confirmed the effectiveness of beinaglutide on Chinese T2DM patients in a real‐world setting. Significant improvements were observed in body weight, HbA_{1c}, blood pressure and lipid profile after 3 months of treatment with beinaglutide. A trend of improvement in both perinatal hyperglycaemia and β-cell rest also emerged. Such benefits were observed despite a wide range of patient baseline characteristics. These observational results suggest beinaglutide may be an effective treatment for T2DM, especially for patients with overweight and obesity, in clinical practice.

Author contributions

Study design was performed by Y. Z. and Y. J. Data collection and analysis were conducted by C. Z., X. L., M. Y., L. T. and X. Z. Manuscript writing was carried out by Y. Z. and Y. J. All authors reviewed and approved the final version of the manuscript.

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The a hor ackno- ledge Yale D an, Ning D and G i Zhao (Shanghai Benemae Pharmace ical Corpora ion) for a i ical and edi orial a i ance.

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