MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2018; 24: 8707-8715
DOI: 10.12659/MSM.913603

Received: 2018.10.13
Accepted: 2018.11.12
Published: 2018.12.02

Long-Term Patterns of Antidiabetic Medication Use in Patients with Type 2 Diabetes

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ACDEF 1 Yang Xu
DE 2 Zhirong Yang
B 3 Hongbo Lin
B 3 Peng Shen
D 4 Haining Wang
DG 1 Siyan Zhan

1 Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing, P.R. China
2 Department of Public Health and Primary Care, School of Clinical Medicine, University of Cambridge, Cambridge, U.K.
3 Yinzhou District Center for Disease Control and Prevention, Ningbo, Zhejiang, P.R. China
4 Department of Endocrinology, Peking University Third Hospital, Beijing, P.R. China

Corresponding Author: Siyan Zhan, e-mail: siyan-zhan@bjmu.edu.cn
Source of support: This work was supported by the National Natural Science Foundation of China, Grant Number 91646107

Background: This study aimed to investigate the patterns of use of antidiabetic medication among patients with newly diagnosed type 2 diabetes mellitus (T2DM), focusing on the comparison in glycemic control between sulfonylureas and metformin.

Material/Methods: Data from patients newly diagnosed and treated for T2DM between 2011 and 2014, who were ≥18 years of age were obtained from the Yinzhou Regional Health Care Database, and patterns of medication and glycemic control were analyzed. The Poisson probability distribution was used to determine the rate ratio (incidence density ratio) of uncontrolled hyperglycemia between sulfonylureas and metformin. Cox regression analysis was used to determine the association between initial treatment with sulfonylureas and metformin and the requirement for additional medications.

Results: Of the 4,017 patients included in the study, 33.58% began treatment with sulfonylureas and 20.41% began treatment with metformin, and during follow-up, 21.13% and 22.68%, respectively were treated with a second drug. After adjustment for body mass index (BMI) and fasting blood glucose (FBG), the rate ratio of uncontrolled blood glucose for sulfonylurea monotherapy compared with metformin monotherapy was 1.30 (95% CI, 1.17–1.45). Patients who began treatment with sulfonylureas were 18% less likely to progress to dual medication compared with metformin (HR=0.82; 95% CI, 0.68–0.99).

Conclusions: Sulfonylurea monotherapy was the most common initial treatment for patients with newly diagnosed T2DM and was associated with an increased risk of uncontrolled hyperglycemia, but patients were less likely to receive additional drugs when compared with patients initially treated with metformin monotherapy.

MeSH Keywords: Diabetes Mellitus, Type 2 • Drug Utilization Review • Metformin • Sulfonylurea Compounds

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/913603

2985 3 4 28

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Background

During the past 30 years, the prevalence of type 2 diabetes mellitus (T2DM) has significantly increased in China as a result of lifestyle changes, urbanization, and increased life expectancy [1–3]. According to current data from the International Diabetes Federation, China had 114.4 million adults with diabetes in 2017 [4].

T2DM is characterized by progressive loss of pancreatic beta cell function, and serious complications can arise due to poor control of blood glucose levels (hyperglycemia) [5–7]. Guidelines developed by the Chinese Diabetes Society (CDS) recommend that the target levels for fasting blood glucose (FBG) that indicate disease control should be between 4.4–7.0 mmol/L [8,9]. To achieve and maintain the target blood glucose levels, progressive treatment strategies commonly used in newly diagnosed T2DM include lifestyle changes, and pharmacotherapy when lifestyle interventions fail to control blood glucose levels. First-line pharmacotherapy is commonly used with the oral antidiabetic drug (OAD), metformin, with sulfonylureas used for patients who have contraindications for metformin treatment.

However, some cross-sectional studies have indicated that the use of first-line antidiabetic pharmacotherapy in China does not comply with current evidence-based management guidelines [10,11]. The prevalence of patients with T2DM on sulfonylurea monotherapy in China is up to 40%, which is much higher than that in Europe [12,13], and in the USA [14]. In China, the low body mass index (BMI) and high FBG level may contribute to the high prevalence of sulfonylureas use [15]. However, baseline data for newly diagnosed patients with T2DM from previous cross-sectional studies have not provided sufficient information on antidiabetic drug use patterns over time, including drug initiation and modification patterns, and glycemic control after starting antidiabetic therapy. Also, the situation of clinical inertia in diabetic management commonly exists, which is defined as the failure to escalate treatment to achieve blood glucose targets [16], but little is known about this phenomenon in China. However, clinical information that reflects the management of T2DM in real-world settings is of help in making clinical decisions and for making public health policy to improve the quality of future diabetes management.

Therefore, the aim of this cohort study was to investigate the patterns of use of antidiabetic medication in patients with newly diagnosed T2DM, focusing on the comparison in glycemic control between sulfonylurea and metformin treatment. Data from the Yinzhou Regional Health Care Database were analyzed from patients newly diagnosed and treated for T2DM between 2011 and 2014.

Material and Methods

The data source for patients with type 2 diabetes mellitus (T2DM)

Data were extracted from the diabetes management database that was part of the Yinzhou Regional Health Care Database [17]. Yinzhou is the largest district in Ningbo City, an eastern coastal city in China, with a relatively stable population of nearly 1.2 million inhabitants. In 2008, the Center for Disease Control and Prevention (CDC) of Yinzhou District began to routinely collect the information of diabetic patients, including name, age, sex, diabetes type, date of first diagnosis, family history, body mass index (BMI), blood pressure, fasting blood glucose (FBG), and glycated hemoglobin (HbA1c).

Once the patient information had been recorded, community physicians followed up the patients at least four times a year. At each follow-up, the community physicians measured the patient's blood pressure, FBG, and HbA1c, and recorded their smoking history, alcohol intake, and antidiabetic drug use patterns since the last follow-up. When the FBG was >7.0 mmol/L, community physicians considered increasing the drug dose or adding another drug. Until the end of December 2015, 31,932 patients with diabetes mellitus were included in the diabetes management system. The Peking University Health Science Center Ethics Committee approved this study with a waiver of informed consent.

Study population

The study included patients aged ≥18 years who were newly diagnosed with T2DM and initiation of antidiabetic pharmacotherapy between 01/01/2011 and 12/31/2014. Patients who had been on any antidiabetic pharmacotherapy before entering the diabetes management system were excluded. Follow-up began from the date of the patient starting drug treatment for diabetes until the occurrence of an outcome of interest, the end date of enrollment in the diabetes management system, the date of death or the date of 12/31/2015, whichever occurred first.

Data recording

The FBG measurements at baseline and at each follow-up were recorded in the diabetes management database. Any blood glucose values <1.1 mmol/L or >33.3 mmol/L were excluded because the measurement range of the glucose meters used by community physicians of Yinzhou District was between 1.1–33.3 mmol/L.

The BMI was calculated from the patient's weight and height measured at time of the initial diagnosis of T2DM. The BMI

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

values were considered valid if they were between 14–80 kg/m^2 and within one year before pharmacotherapy began, and was classified as underweight (<18.5 kg/m^2), normal weight (18.5–23.9 kg/m^2), overweight (24.0–27.9 kg/m^2), and obese (≥28.0 kg/m^2) [18]. All drugs recorded during the follow-up were coded using the Anatomical Therapeutic Chemical (ATC) classification system.

Drug use modifications and uncontrolled blood glucose

Periods of longer than 180 days without any antidiabetic drug use was considered as drug discontinuation. Receiving a new antidiabetic drug after a discontinuation was defined as a restart. Addition was defined as any other classes of antidiabetic drugs, including both oral antidiabetic drugs (OADs) and insulin, being added to previous pharmacotherapy. Switching occurred when patients discontinued previous antidiabetic drugs with the concomitant initiation of other antidiabetic drugs. Reduction was defined as discontinuation of at least one but not all of the antidiabetic drug classes used previously. Discontinuation, addition, switching, or reduction of drugs was defined as drug use modifications. Uncontrolled blood glucose was defined as any FBG value >7.0 mmol/L.

Statistical analysis

Baseline characteristics of included patients were descriptive and included the mean and standard deviation (SD), or the median and interquartile range (IQR) for continuous variables, and proportions were included for categorical variables. For patients who were initially treated with metformin and initially treated with sulfonylureas, the baseline characteristics were compared and changes in medication patterns were described. The standardized mean difference (SMD) was used to evaluate the baseline characteristics between the two groups. An SMD <0.1 indicated a negligible difference between the baseline characteristics between the treatment groups [19]. Kaplan-Meier survival curves were plotted to describe the time to the first drug addition. Cox regression analysis was used to determine the association between initial treatment with sulfonylureas and metformin and the requirement for additional medications. Hazard ratios (HR) were calculated in an unadjusted model and in a full model that simultaneously adjusted for gender, age, BMI, duration of diabetes, and FBG. In the time-to-event analysis, drug discontinuation and drug switching were considered as censoring. The proportional hazards assumption was assessed by the Schoenfeld residuals plot. Since non-proportional hazards were observed, a time-partitioned analysis was conducted, and the follow-up period was partitioned at 800 days after drug initiation when the pattern of first drug addition changed (identified through the cumulative incidences).

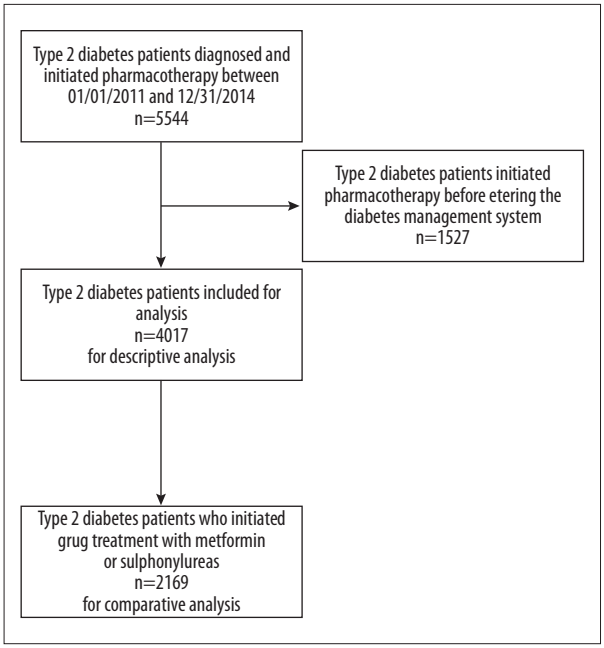

Figure 1. Flowchart of the study design and patient inclusion.

The Poisson probability distribution was used to determine the rate ratio (incidence density ratio) of uncontrolled hyperglycemia between sulfonylureas and metformin. Potential confounders in the adjustment model were the same as those accounted for in the above Cox model. In this analysis, patients with baseline uncontrolled blood glucose were excluded. All statistical analysis was conducted in R version 3.3.2. A P-value of <0.05 was considered to represent statistical significance.

Results

Characteristics of patients with type 2 diabetes mellitus (T2DM) and initial antidiabetic treatment

This study included 4,017 patients with newly diagnosed T2DM. The study design and patient inclusion process are shown in Figure 1. The baseline characteristics of the patients at diagnosis are shown in Table 1. The study population was equally divided between men and women and the mean age was 61.44 years. The median follow-up time was 838 days. The mean fasting blood glucose (FBG) value of the patients before initiating pharmacotherapy was 8.51 mmol/L.

Patients who began treatment for T2DM with monotherapy, dual therapy, triple or multiple therapies were 69.98%, 27.46% and 2.56%, respectively (Table 1). These three groups differed in gender, age, FBG, body mass index (BMI), and duration of diabetes (Table 2). Among monotherapy, sulfonylurea treatment ranked first (33.58%), followed by metformin (20.41%). These two oral antidiabetic drugs (OADs) were most commonly used

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 1. Baseline characteristics of patients at first treatment for type 2 diabetes mellitus (T2DM).

	n (Total=4,017)
Male	1974 (49.14%)
Age (mean ±SD) years	61.44±11.58
Follow-up (median ±IQR) days	838 (568±1179)
FBG (mean ±SD) mmol/L	8.51±3.20
First antidiabetic treatment	
Mono therapy	2811 (69.98%)
Sulfonylureas	1349 (33.58%)
Metformin	820 (20.41%)
Alpha-glucosidase inhibitors	290 (7.22%)
Thiazolidinediones	80 (1.99%)
Glinides	164 (4.08%)
Insulin	108 (2.69%)
Dual therapy	1103 (27.46%)
Metformin + Sulfonylureas	556 (13.84%)
Insulin + one OAD	53 (1.32%)
Other combinations	494 (12.30%)
Triple or combination therapy	103 (2.56%)

FBG – fasting blood glucose; IQR – interquartile range; SD – standard deviation; OAD – oral antidiabetic drug.

between 2011 and 2014 and the prevalence of use for each drug was stable over time (Figure 2). There were 108 patients who began treatment with insulin, who had significantly increased FBG levels at diagnosis (mean, 9.73 mmol/L) (95% CI, 8.79–10.66) compared with the FBG for patients treated with OAD monotherapies (mean, 8.12 mmol/L) (95% CI, 8.01–8.23).

For patients who were treated with dual therapy, the combination of metformin and sulfonylureas were most widely used (13.84%). The combinations of insulin and one OAD were used by 53 patients (1.32%) and their FBG level was significantly higher compared with patients receiving two OADs, 10.92 mmol/L (95% CI, 9.42–12.43) versus 9.11 mmol/L (95% CI, 8.91–9.31).

Changes in treatment patterns for patients who began monotherapy with metformin or sulfonylurea

As the initial monotherapy, metformin and sulfonylureas were prescribed for 820 and 1,349 patients, respectively. The baseline characteristics comparisons are shown in Table 3. Baseline characteristics, BMI and FBG were unbalanced between the two groups. Figure 3 shows the first and second drug modifications for patients who initially received metformin or sulfonylureas. The median follow-up duration was 458 days, and 44.51% of the 820 patients initially treated with metformin remained on metformin without any drug modification throughout follow-up, 14.88% switched to other drugs, and 22.68% received a second drug added to metformin. With switching or

Table 2. Comparison of baseline characteristics among three treatment groups for type 2 diabetes mellitus (T2DM), monotherapy, dual therapy, and triple or combined therapy.

	Monotherapy N=2811	Dual therapy N=1103	Triple or combined therapy N=103
Gender			
Male	1303 (46.35%)	606 (54.94%)	65 (63.11%)
Female	1508 (53.65%)	497 (45.06%)	38 (36.89%)
Age (mean ±SD) years	62.07±11.56	60.07±11.48	58.83±11.67
BMI (mean ±SD) kg/m^2	24.01±3.14	24.40±3.45	24.12±2.75
Underweight	61 (2.18%)	17 (1.54%)	0 (0.00%)
Normal	1460 (52.12%)	512 (46.50%)	56 (54.90%)
Overweight	980 (34.99%)	453 (41.14%)	38 (37.25%)
Obese	300 (10.71%)	119 (10.81%)	8 (7.84%)
Duration* (median ±IQR) days	85 (23,299)	50 (18,217)	55 (23,295)
FBG (mean ±SD) mmol/L	8.18±2.94	9.20±3.46	10.18±4.93

* Duration between diagnosis and initiation of pharmacotherapy. BMI – body mass index; FBG – fasting blood glucose; IQR – interquartile range; SD – standard deviation.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

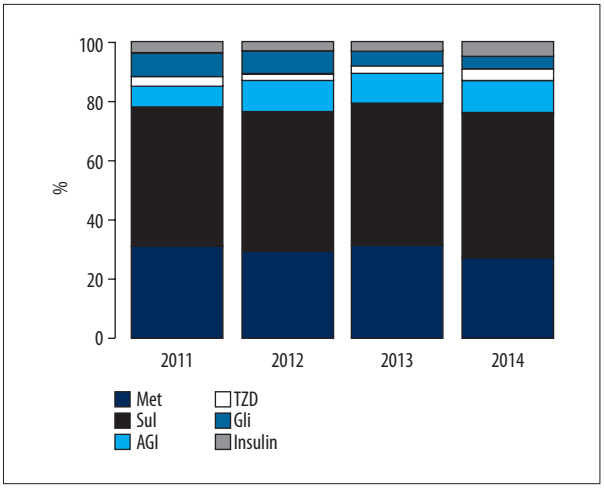

Figure 2. Initial antidiabetic monotherapy from patients newly diagnosed with type 2 diabetes mellitus (T2DM) between 2011 to 2014. Met – metformin; Sul – sulfonylurea; AGI – alpha-glucosidase inhibitors; TZD – thiazolidinediones; Gli – glinides.

addition, sulfonylureas were the most frequently prescribed OAD, accounting for 59.84% and 67.20% of switched or added drugs, respectively.

The patients who had therapy initiated with sulfonylureas were followed up for a median of 509 days. During this period, 52.63% of patients did not change the initial treatment. 9.04% switched to other antidiabetic drugs, most of whom received metformin as a substitute for sulfonylureas (30.32%). An additional drug was prescribed for 285 patients (21.13%), 69.12% of whom received metformin.

Uncontrolled blood glucose occurred in 133 patients initially receiving metformin, and 55 patients (41.35%) additionally received another drug after the first occurrence of uncontrolled blood glucose, and 30 patients (22.56%) started second-line therapy after the second episode. For the 226 patients initially treated with sulfonylureas, 28.31% received another drug after the first occurrence of uncontrolled blood glucose, and 23.45% started second-line therapy after the second episode.

Uncontrolled blood glucose in patients who began monotherapy with metformin or sulfonylurea

The 725 patients without uncontrolled blood glucose at baseline were included in the Poisson regression model, including 298 patients in the metformin group and 427 patients in the sulfonylureas group. The crude rate ratio (incidence density ratio) of uncontrolled hyperglycemia between sulfonylureas and metformin was 1.33 (95% CI, 1.20–1.48). After adjustment for BMI and FBG, the rate ratio was 1.30 (95% CI, 1.17–1.45).

The first drug additional drug required in patients who began monotherapy with metformin or sulfonylurea

The probability of receiving the first drug addition over time for both sulfonylureas and metformin initiation groups are

Table 3. Comparison of baseline characteristics between patients who began metformin monotherapy and patients who began sulfonylurea monotherapy.

	Metformin initiation N=820 (%)	Sulfonylurea initiation N=1349 (%)	SMD
Gender			
Male	351 (42.80%)	622 (46.11%)	0.067
Female	469 (57.20%)	727 (53.89%)	
Age (mean ±SD) years	61.53±11.16	62.33±11.49	0.071
BMI (mean ±SD) kg/m^2	24.42±3.06	23.88±3.19	0.173
Underweight	10 (1.22%)	32 (2.38%)	0.187
Normal	387 (47.31%)	737 (54.80%)	
Overweight	314 (38.39%)	437 (32.49%)	
Obese	107 (13.08%)	139 (10.33%)	
Duration* (median ±IQR) days	106 (28±324)	68 (20±287)	0.092
FBG (mean ±SD) mmol/L	7.87±2.37	8.29±2.76	0.166

* Duration between diagnosis and initiation of pharmacotherapy. BMI – body mass index; FBG – fasting blood glucose; IQR – interquartile range; SMD – standardized mean difference; SD – standard deviation.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

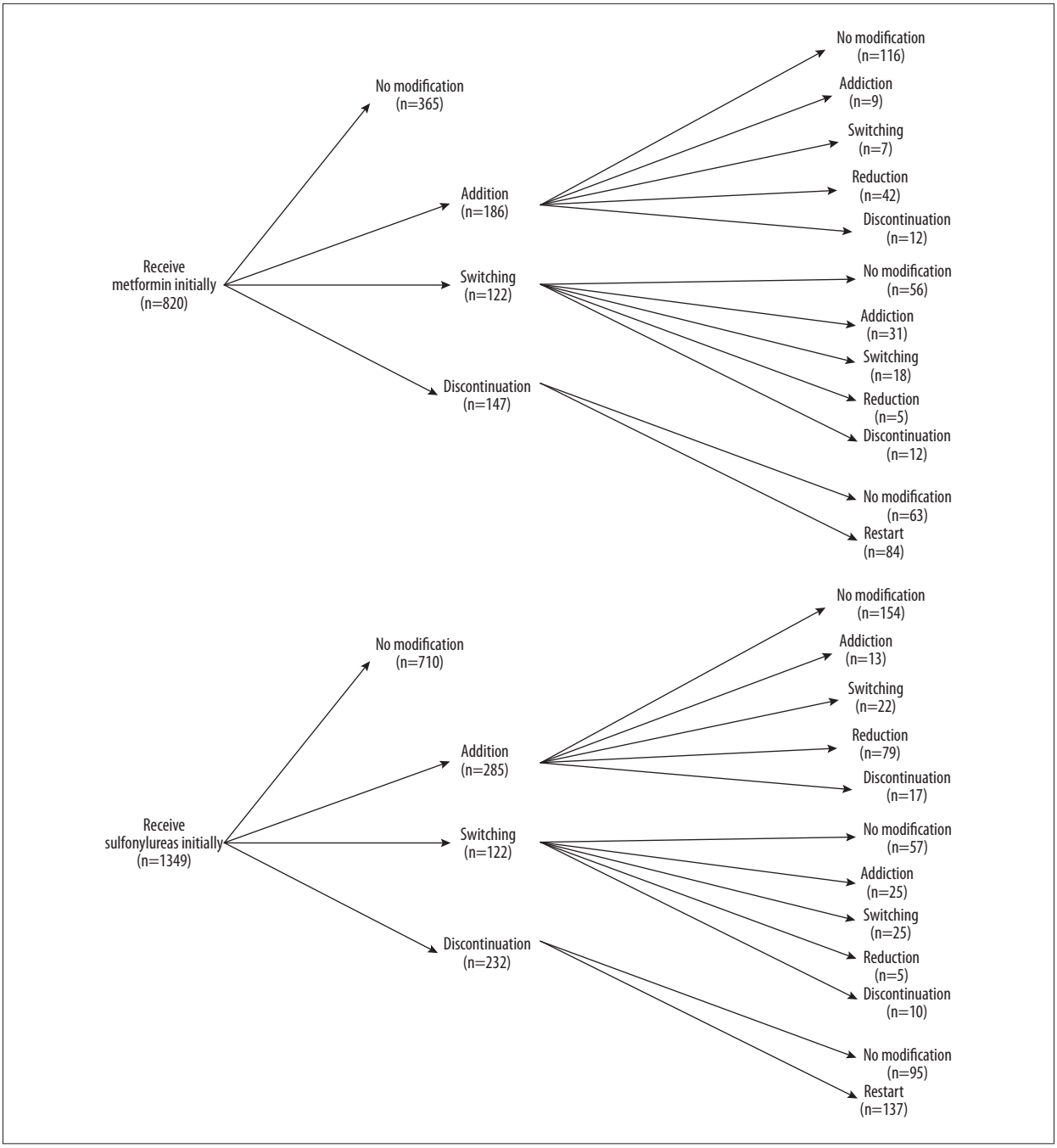

Figure 3. The first two drug modification patterns for the two groups of patients with newly diagnosed with type 2 diabetes mellitus (T2DM) who began metformin monotherapy or sulfonylurea monotherapy.

shown in the Kaplan-Meier survival curves in Figure 4. The crude hazard ratio (HR) of sulfonylureas compared with metformin was 0.87 (95% CI, 0.73–1.05). After adjusting for the BMI and FBG, the hazard ratio over the whole period of follow-up was 0.82 (95% CI 0.68–0.99). In the time-partitioned analysis, the adjusted HR during the first 800 days after drug initiation was 0.84 (95% CI, 0.69–1.03) and the adjusted HR after the first 800 days was 0.66 (95% CI, 0.37–1.17).

Discussion

In this study, the initial treatment patterns for new-onset type 2 diabetes mellitus (T2DM) were analyzed. Almost 70% of patients who began antidiabetic treatment with monotherapy were treated mainly by sulfonylureas, followed by metformin. Patients who began drug treatment with dual therapy had higher fasting blood glucose (FBG) levels compared with

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

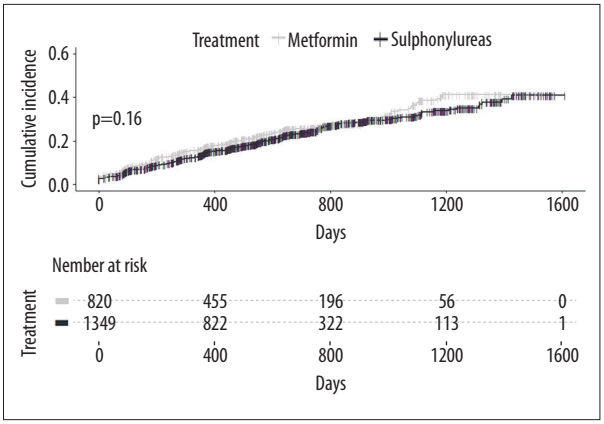

Figure 4. Kaplan-Meier survival curves following the addition of a second drug for patients with newly diagnosed with type 2 diabetes mellitus (T2DM) who began metformin monotherapy or sulfonylurea monotherapy.

patients with initial monotherapy. During follow-up, almost 40% of patients changed their initial treatment patterns in both the sulfonylurea and metformin monotherapy groups. The findings of the study showed that patients who began sulfonylurea monotherapy were 30% more likely than patients who began metformin monotherapy to develop uncontrolled diabetes but were 18% less likely to receive an additional drug.

Sulfonylureas were by far the most commonly used initial antidiabetic drug therapy used in the Yinzhou District in Ningbo City, and the prevalence of initial usage of sulfonylureas remained unchanged from 2011 to 2014. These findings are supported by those of other studies conducted at communities in other cities in China after 2011 [20,21]. These findings do not conform to the clinical guidelines developed by the Chinese Diabetes Society (CDS) released in 2010, in which metformin was recommended as the first-line drug treatment, with sulfonylureas as an optional first-line drug for patients with renal or hepatic insufficiency, serious infections, hypoxia, or for patients undergoing major surgery [9]. This inconsistency may indicate problems with non-adherence of community physicians to the guidelines, but it may also be explained in part by the baseline FBG levels and patient body mass index (BMI). Patients who initiated treatment with sulfonylureas had higher mean FBG values before initiation of pharmacotherapy and they started treatment earlier than patients who initiated treatment with metformin after being newly diagnosed with diabetes. The findings might imply that patients initially treated with sulfonylureas represented more severe cases and required a more effective glucose lowering agent, sulfonylureas rather than metformin, to achieve a rapid therapeutic response. However, patients who began metformin monotherapy had a higher prevalence of being overweight and of obesity than patients who began sulfonylurea monotherapy, which indicated that the risk of weight gain was a major concern of physicians in not choosing sulfonylureas as first-line therapy for patients with an increased BMI. However, sulfonylureas used at Yinzhou District were mostly gliclazide (88.42%), glipizide (5.59), and glimepiride (5.59%), which were not likely to put patients at an increased risk of weight gain [22–24]. As shown by the use of sulfonylureas in clinical practice, the risk of weight gain should not be a concern when initiating sulfonylureas treatment for overweight and obese patients [25].

The findings of the present study showed that patients starting pharmacotherapy with sulfonylureas had a higher rate of developing uncontrolled blood glucose levels compared with patients who commenced pharmacotherapy with metformin before adding a second antidiabetic drug, as is shown in the Poisson regression model. However, the use of a second antidiabetic drug, for patients with uncontrolled blood glucose levels, were less likely used among patients who began sulfonylurea monotherapy, even if initiation of treatment tended to be delayed. The associations of initial treatments (sulfonylureas versus metformin) with uncontrolled blood glucose and the first drug addition were both independent of BMI, FBG, age, gender and duration between diagnosis and initiation of pharmacotherapy. The findings that patients who began sulfonylurea monotherapy had worse glycemic control but decreased the probability of the use of second drugs compared with patients who began metformin monotherapy, supported the phenomenon of clinical inertia [26], which was more significant in the sulfonylurea group than in the metformin group. The clinical inertia that occurred in sulfonylurea initiation group was probably because sulfonylureas dose adjustment may precede a drug addition when treatment modification was needed. Sulfonylureas had a wider dosage range for dose adjustment than metformin so that dosage adjustment could be done before another antidiabetic drug was added. In the present study, most patients started using low-dose sulfonylureas. When uncontrolled blood glucose occurred in these patients, dosage adjustment was first considered. While around one-third of patients received dosage adjustment, their blood glucose remained uncontrolled. This finding indicated that the dose adjustment was inappropriate and an additional drug was not timely, possibly due to the lack of sufficient clinical experience of community physicians, or because of concerns regarding hypoglycemia [27].

To our knowledge, this was the first study using longitudinal data to explore the patterns of use of antidiabetic drugs in China. The present study has two main strengths. First, it provided longitudinal data on the use of antidiabetic drugs, which overcame the limitations of the cross-sectional data provided by most previous studies in China [10,11,28]. Second, the study included data on FBG for patients at each follow-up, which allowed evaluation of the association between drug utilization patterns with glycemic control conditions over time, which was

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

rarely analyzed in most previous longitudinal studies of antidiabetic drug use patterns [14].

This study also had several limitations. First, the study analyzed FBG data, instead of glycated hemoglobin (HbA1c), to determine glycemic control. HbA1c would be more suitable as an indicator of blood glucose control. However, HbA1c data was incomplete in the diabetes management database, with more than 85% missing values, as HbA1c was not widely measured at Yinzhou District. Second, although several important variables were used for adjustment analysis, the changes in the efficacy of antidiabetic drugs may be influenced by other factors, such as blood cholesterol and blood pressure, but this clinical information was poorly recorded in the database, which limited the analysis. Finally, because the study used data from the Yinzhou Regional Health Care Database, the results of this study might not be representative of the whole diabetic population in China.

Conclusions

The findings of this study showed that sulfonylureas were still widely used as first-line therapy for patients with newly diagnosed type 2 diabetes mellitus (T2DM). These findings were not consistent with the clinical guidelines developed by the Chinese Diabetes Society (CDS). Patients who began sulfonylurea monotherapy when first diagnosed with T2DM had a higher risk of uncontrolled hyperglycemia than patients who began metformin monotherapy but were less likely to receive an additional drug. More attention should be paid to these patients in clinical practice and in public health policymaking. Further studies are needed to provide more real-world evidence to support the use of antidiabetic medications.

Acknowledgments

The authors gratefully acknowledge Jinzhu Jia for advice on the statistical analysis.

Conflict of interest

None.

References:

1. Yang W, Lu J, Weng J et al: Prevalence of diabetes among men and women in China. N Engl J Med, 2010; 362(12): 1090–101
2. Li LM, Rao KQ, Kong LZ et al: [A description on the Chinese national nutrition and health survey in 2002]. Zhonghua Liu Xing Bing Xue Za Zhi, 2005; 26(7): 478–84 [in Chinese]
3. Pan XR, Yang WY, Li GW, Liu J: Prevalence of diabetes and its risk factors in China, 1994. National Diabetes Prevention and Control Cooperative Group. Diabetes Care, 1997; 20(11): 1664–69
4. International Diabetes Federation. Diabetes Atlas (8th edition). Available from: *http://diabetesatlas.org/resources/2017-atlas.html*
5. Vijan S, Hofer TP, Hayward RA: EStimated benefits of glycemic control in microvascular complications in type 2 diabetes. Ann Intern Med, 1997; 127(9): 788–95
6. Klein R, Klein BK, Moss SE: RElation of glycemic control to diabetic microvascular complications in diabetes mellitus. Ann Intern Med, 1996; 124(1Pt2): 90–96
7. Coutinho M, Gerstein HC, Wang Y, Yusuf S: The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. Diabetes Care, 1999; 22(2): 233–40
8. Weng J, Ji L, Jia W et al: Standards of care for type 2 diabetes in China. Diabetes Metab Res Rev, 2016; 32(5): 442–58
9. Chinese Diabetes Society: Standards of care for type 2 diabetes in China (version 2010). Chinese Journal of Diabetes, 2012; 20(1): 1–36
10. Ji L, Lu J, Weng J et al: China type 2 diabetes treatment status survey of treatment pattern of oral drugs users. J Diabetes, 2015; 7(2): 166–73
11. Pan C, Yang W, Jia W et al: Management of Chinese patients with type 2 diabetes, 1998–2006: The Diabcare-China surveys. Curr Med Res Opin, 2009; 25(1): 39–45
12. Datta-Nemdharry P, Thomson A, Beynon J, Donegan K: Patterns of antidiabetic medication use in patients with type 2 diabetes mellitus in England and Wales. Pharmacoepidemiol Drug Saf, 2017; 26(2): 127–35
13. Liatis S, Dafoulas GE, Kani C et al: The prevalence and treatment patterns of diabetes in the Greek population based on real-world data from the nation-wide prescription database. Diabetes Res Clin Pract, 2016; 118: 162–67
14. Lamberts EJ, Nijpels G, Welschen LM et al: Long term patterns of use after initiation of oral antidiabetic drug therapy. Pharmacoepidemiol Drug Saf, 2011; 20(4): 351–58
15. Fujihara K, Hanyu O, Heianza Y et al: Comparison of clinical characteristics in patients with type 2 diabetes among whom different antihyperglycemic agents were prescribed as monotherapy or combination therapy by diabetes specialists. J Diabetes Investig, 2016; 7(2): 260–69
16. Pantalone KM, Misra-Hebert AD, Hobbs TM et al: Clinical inertia in type 2 diabetes management: Evidence from a large, real-world data set. Diabetes Care, 2018; 41(7): e113–14
17. Yang Y, Zhou X, Gao S et al: Evaluation of electronic healthcare databases for post-marketing drug safety surveillance and pharmacoepidemiology in China. Drug Saf, 2018; 41(1): 125–37
18. Chen CM, Kong LZ: Guidelines for the prevention and control of overweight and obesity in chinese adults. Beijing: People Health Publishing House, 2006: 44–45
19. Normand ST, Landrum MB, Guadagnoli E et al: Validating recommendations for coronary angiography following acute myocardial infarction in the elderly: A matched analysis using propensity scores. J Clin Epidemiol, 2001; 54(4): 387–98
20. Li R, Shi L, Yang QD et al: Glycemic control conditions and medication use patterns of patients with type 2 diabetes at communities in Shanghai. J Occup Environ Med, 2016; 4: 329–33
21. Liao L, Zong ZY: Analysis of rationality of anti-diabetic medication use at a community medical service center in Dongguan. Journal of North Pharmacy, 2016; 4: 160
22. Campbell IW, Menzies DG, Chalmers J et al: One year comparative trial of metformin and glipizide in type 2 diabetes mellitus. Diabete Metab, 1994; 20(4): 394–400
23. Schernthaner G, Grimaldi A, Di Mario U et al: GUIDE study: Double-blind comparison of once-daily gliclazide MR and glimepiride in type 2 diabetic patients. Eur J Clin Invest, 2004; 34(8): 535–42
24. Holstein A, Plaschke A, Egberts EH: Lower incidence of severe hypoglycaemia in patients with type 2 diabetes treated with glimepiride versus glibenclamide. Diabetes Metab Res Rev, 2001; 17(6): 467–73

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

25. Mu YM, Yang WY, Zhu DL et al: Expertise of sulfonylureas use in clinical practice. Drug Eval, 2017; 1: 5–12
26. Phillips LS, Branch WT, Cook CB et al: Clinical inertia. Ann Intern Med, 2001; 135(9): 825–34
27. Khunti S, Davies MJ, Khunti K: Clinical inertia in the management of type 2 diabetes mellitus: A focused literature review. Br J Diabetes, 2015; 15(2): 65
28. Ji LN, Lu JM, Guo XH et al: Glycemic control among patients in China with type 2 diabetes mellitus receiving oral drugs or injectables. BMC Public Health, 2013; 13: 602

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]