Effect of Dapagliflozin Combined with Cognitive Behavior Training on Quality of Life and Cognitive Function in Elderly Patients with Type 2 Diabetes Mellitus Complicated with Mild Cognitive Impairment

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Abstract

Background: To investigate the effect of dapagliflozin combined with cognitive behavior training on quality of life and cognitive function in elderly patients with type 2 diabetes mellitus (T2DM) complicated with mild cognitive impairment.

Methods: Ninety-six elderly patients with T2DM and mild cognitive impairment treated in Shenzhen People's Hospital, Guangdong Province China from June 2019 to December 2020 were selected and equally randomized into control group (CG) and experimental group (EG). The CG received conventional intervention, while the EG received dapagliflozin combined with cognitive behavior training based on the CG. The clinical observation indexes of both groups were compared to assess the clinical intervention effect of dapagliflozin combined with cognitive behavior training on elderly patients with T2DM complicated with mild cognitive impairment.

Results: After intervention, the blood glucose levels of both groups decreased, and compared with the CG, the blood glucose level of the EG was markedly lower (*P*<0.05). The scores of C-DMSES, ADL and MMSE of both groups were higher than those before intervention, and compared with the CG, the scores of the EG were obviously higher (*P*<0.05). The QOL-AD scores of both groups gradually increased, and compared with the CG, the QOL-AD scores of the EG were higher at 3 and 6 months after intervention (*P*<0.05).

Conclusion: For elderly patients with T2DM complicated with mild cognitive impairment, dapagliflozin combined with cognitive behavior training intervention can obviously improve their cognitive function, self-efficacy of diabetes management and quality of life, which should be promoted in clinic.

Keywords: Dapagliflozin; Cognitive behavior training; Elders; Type 2 diabetes mellitus

Introduction

According to the clinical statistics, about 60% of diabetic patients have mild or moderate cognitive impairment. Type 2 diabetes mellitus (T2DM) may do damage to the central nervous system, and then accelerate the degeneration of brain tissue in patients, which is a high-risk factor of triggering cognitive impairment (1-4). In fact, cognitive impairment is a common cognitive disease in

clinic, with the impairment degree usually between normal aging and dementia. However, about 13% of patients with cognitive impairment will develop into dementia in clinic. Therefore, applying effective treatment is the crux to improve patients' cognition and ensure their self-care ability (5-8).

Dapagliflozin is a new hypoglycemic drug and with a unique mechanism, it plays a hypoglycemic effect not depending on insulin. Therefore, a new method for the treatment of T2DM is initiated, especially in patients without obvious effect by using metformin (9-12). At present, there are very few clinical studies on non-drug treatment of T2DM complicated with cognitive impairment, but in recent years, cognitive behavior training could efficaciously improve patients' cognition, with an absolute advantage in mental diseases, orthopedics and students' moral education (13).

We explored dapagliflozin combined with cognitive behavior training for elderly patients with T2DM complicated with mild cognitive impairment.

Methods

Research subjects

Inclusion criteria. 1) Patients met the WHO clinical diagnostic criteria for elderly T2DM combined with mild cognitive impairment (14). 2) Patients had hypomnesis for more than 6 months. 3) Patients had no mental illness, language disorders and limb movement disorders. 4) Patients and their families participated voluntarily after knowing the purpose, process and significance of this study in detail. Exclusion criteria. 1) Patients had severe liver and kidney function diseases. 2) Patients were complicated with other malignant tumors. 3) Patients quit halfway and were with low treatment compliance. 4) Patients were allergic to dapagliflozin. 5) Patients were in severe and extremely unstable condition.

According to the selection criteria above, 96 elderly patients with T2DM complicated with mild cognitive impairment treated in Shenzhen People's Hospital, Guangdong Province China from June 2019 to December 2020 were enrolled in this study.

Grouping

According to the patients' hospitalization number, 48 patients were randomly selected into the control group (CG), and the other 48 patients were included into the experimental group (EG). The study was approved by the ethics committee of Shenzhen People's Hospital (approval no. 20190455) and signed written informed consents were obtained from the patients.

Intervention methods

The CG received conventional intervention. ① The nursing team gave scientific evaluation about patients' blood glucose and cognitive level, and organized routine health education for patients in the form of groups, which mainly involved the pathogenesis of diabetes, dietary guidance, disease changes and exercise suggestions (15-18). ② Patients received conventional symptomatic and supportive treatment according to their conditions. ③ Memory training for patients were carried out collectively. The nurses drew 5-7 pictures according to patients' familiar objects. The patients were allowed to see the pictures for 5 seconds first, and then were asked to write down the names of the objects. The training could be repeated for many times with gradually increasing number of cards and picture complexity to train the patients' memory. The training time was 60 min. The patients would be followed up by telephone after discharge.

The EG received dapagliflozin combined with cognitive behavior training intervention on the basis of the CG. ① Before taking dapagliflozin, the renal function should be evaluated. When the glomerular filtration rate (GFR) was less than $60ml/min/1.73m^2$, dapagliflozin could not be taken. The initial dose was 5mg/time, once a day in the morning. If the patient was tolerant to dapagliflozin and needed to control blood glucose, the dose could be increased to 10mg/time, once a day (19,20). ② Cognitive behavior training. Based on the patients' condition, the primary nurses implemented the one-to-one comprehen-

sive management intervention for patients, assessed their cognition of diabetes, and formulated education programs focusing on their cognitive misunderstanding and ignorance, which mainly involved one-to-one learning and discussion about the content of the pictures so as to further deepen patients' cognition of diabetes. The intervention tool was the diabetes figure dialogue. Nurses taught beside the bed about insulin injection skills, medication methods, pathological characteristics and daily precautions for association and memory training. When measuring blood glucose every day, nurses should also publicize the knowledge of diabetic cognitive impairment and answer patients' questions. Nurses conducted behavior training from the aspects of patients' attention, memory, calculation and self-care ability, and often asked patients questions to deepen their memories. The cognitive behavior training should be conducted step by step, once every two days and each for one hour. Nurses ought to communicate with patients, encourage them to be the leading speakers, help to recall something impressive from the past, and guide them to tell by themselves with the purpose of arousing their long-term memory. After patients' discharge, nurses should formulate follow-up plans, organize remote cognitive behavior training once a week and telephone them every two weeks to know about their recovery of cognitive function.

Observation indexes

General data. Age, gender, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), 2h postprandial blood glucose (2h PBG), fasting blood glucose (FBG), haemoglobin A1c (HbA1c), triacylglycerol (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), mean blood glucose (MBG), largest amplitude of glycemic excursion (LAGE), standard deviation of blood glucose level (SDBG), postprandial glucose excursion (PPGE) and other data were recorded.

Blood glucose levels. The levels of FBG, PBG and HbA1c were detected.

The Chinese version of the diabetes management self-efficacy (C-DMSES) scale. It included 20 items, with 10 points for each one, and a total score of 200 points. The score was in direct proportion to the patients' self-efficacy.

Activity of daily living (ADL) scale. It included 10 items with a total score of 100 points. 0-20 points indicated that patients had extremely serious functional deficit and had no self-care ability. 20-40 points indicated that patients needed a lot of help in their lives. 40-60 points indicated that patients needed help in their lives. 60-100 points indicated patients had basic self-care ability.

Mini-mental state examination (MMSE) scale. It included 19 items, with a total score of 30 points. It was mainly used to evaluate patients' memory, orientation, language, calculation, and attention. The score was in direct proportion to the patients' cognitive function level.

Quality of life in Alzheimer's disease (QOL-AD) scale. It included 13 items, with a total score of 65 points. According to Linker 5-point scoring method, it comprehensively evaluated patients' quality of life from the aspects of spirit, family, life, self and psychology. The score was in direct proportion to the patients' quality of life.

Statistical processing

All statistical data of the study were processed by SPSS 22.0 (IBM Corp., Armonk, NY, USA) to calculate differences between groups, and the pictures were graphed by GraphPad Prism 7 (GraphPad Software, San Diego, USA). Including enumeration data and measurement data in the form of [n (%)] and ($\bar{x}\pm s$) respectively, the study used x^2 test and *t* test. The differences were statistically significant at *P*<0.05.

Results

General data

According to the general data of the two groups, *P*>0.05 was obtained, with no obvious difference (Table 1). The subjects met the grouping criteria of the control experiment.

Table 1: Comparison of general data (n=48)

Indexes	CG	EG	X²/t	P
Age (yr)	59.41±7.96	61.05±8.43	0.9800	0.3296
Gender ratio	26/22	28/20	0.1693	0.681
BMI (kg /m2)	24.65±2.83	23.77±2.58	1.5921	0.1147
DBP (mmHg)	82.39±10.22	84.26±11.07	0.8599	0.3920
SBP (mmHg)	145.38±17.13	143.81±16.75	0.4540	0.6509
2h PBG (mmol/L)	16.89±4.90	17.12±5.34	0.2199	0.8265
FPG (mmol/L)	10.35±3.37	10.06±3.28	0.4272	0.6702
HbAlc (%)	9.31±1.51	9.47±1.60	0.5039	0.6155
TG (mmol/L)	2.68±0.55	2.74±0.61	0.5061	0.6140
TC (mmol/L)	5.38±0.76	5.32±0.74	0.3919	0.6960
HDL-C (mmol/L)	1.18±0.33	1.20±0.37	0.2795	0.7805
LDL-C (mmol/L)	3.19±0.75	3.27±0.68	0.5475	0.5853
MBG (mmol/L)	14.71±5.12	14.68±5.06	0.0289	0.9770
LAGE (mmol/L)	6.75±1.24	6.83±1.30	0.3085	0.7584
SDBG (mmol/L)	3.88±1.42	3.94±1.41	0.2077	0.8359
PPGE (mmol/L)	5.20±1.91	5.36±2.09	0.3915	0.6963

Blood glucose levels

After intervention, the blood glucose levels of both groups showed a downward trend, and compared with the CG, the blood glucose levels of the EG were conspicuously lower ($P<0.05$) (Table 2).

Table 2: Comparison of blood glucose changes ($\bar{x}\pm s$)

Indexes		CG	EG	t	P
Fasting blood glucose (mmol/L)	Before intervention	9.75±1.72	1.83±1.66		
	After intervention	7.52±0.48	6.30±0.51	12.0687	<0.001
Postprandial blood glucose (mmol/L)	Before intervention	14.64±2.51	14.70±2.23		
	After intervention	8.75±1.57	7.36±1.64	4.2417	0.0001
HbAlc (%)	Before intervention	9.72±1.55	9.80±1.63		
	After intervention	8.39±0.85	6.77±0.82	9.5031	<0.001

C-DMSES scores

After intervention, the C-DMSES scores of both groups increased, and compared with the CG, the C-DMSES score of the EG was conspicuously higher (*P*<0.05), with a statistical difference (Table 3).

Table 3: Comparison of C-DMSES scores ($\bar{x}\pm s$)

Group	Before intervention	After intervention	t	P
CG	129.83±6.78	159.90±14.28	13.179	<0.001
EG	131.02±6.82	170.11±13.56	17.843	<0.001
t		3.5921		
P		<0.001		

ADL scores

Compared with the CG, the ADL score of the EG after intervention was conspicuously higher (*P*<0.05), with an obvious difference between groups (Fig. 1).
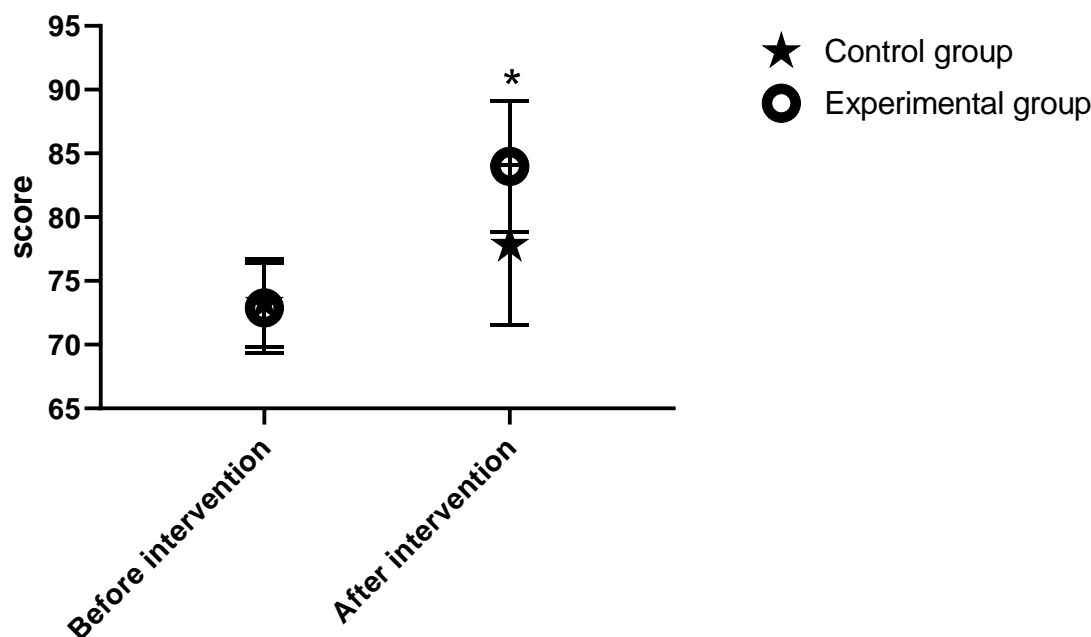

Fig. 1: Comparison of ADL scores ($\bar{x}\pm s$)
Note: The abscissa indicated before and after intervention, and the ordinate indicated the score.
The ADL scores of the CG before and after intervention were (73.26±3.47) and (77.81±6.28) respectively.
The ADL scores of the EG before and after intervention were (72.89±3.51) and (83.99±5.16) respectively.
* indicated a significant difference in the ADL scores between the two groups after intervention (*t*=5.2678, *P*<0.001)

MMSE scores

After intervention, the MMSE scores of the two groups were higher than those before intervention, and compared with the CG, the MMSE score of the EG after intervention was conspicuously higher (*P*<0.05) (Table 4).

Table 4: Comparison of MMSE scores ($\bar{x}\pm s$)

Group	Before intervention	After intervention	t	P
CG	20.41±1.50	23.02±2.54	6.130	P<0.001
EG	20.28±1.46	25.61±2.53	12.642	*P*<0.001
t		5.005		
P		*P*<0.001		

QOL-AD scores

After intervention, the QOL-AD scores of both groups gradually increased, and compared with the CG, the QOL-AD scores of the EG were higher at 3 months and 6 months after intervention (*P*<0.05) (Table 5).

Table 5: Comparison of QOL-AD scores ($\bar{x}\pm s$)

Group	Before intervention	3 months after intervention	6 months after intervention
CG	24.53±4.12	34.75±4.63	47.62±5.01
EG	25.48±4.18	43.16±5.84	58.31±5.16
t	1.1214	9.1492	10.2978
P	0.2650	<0.001	<0.001

Discussion

At present, the pathogenesis of cognitive impairment caused by diabetes is not very clear in clinic, which results in a lack of effective intervention methods. Furthermore, in fact, the symptoms of cognitive impairment are too inconspicuous to be noticed, which also aggravates the disease itself, therefore, clinical treatment is in the stage of active exploration (21-24). In terms of the cognitive impairment caused by T2DM, comprehensive intervention is usually implemented in clinic on the basis of common treatment approaches such as controlling blood glucose, blood pressure and blood lipid. Some scholars have previously proposed that although the cognitive ability of the patients is damaged to some extent, the patients still have the learning ability. In this way, scholars have realized the value of cognitive behavior training in improving the cognitive function of patients. However, comprehensive intervention is also closely related to effective blood glucose control. Therefore, this study explored the effect of dapagliflozin combined with cognitive behavior training on quality of life and cognitive function in elderly patients with T2DM complicated with mild cognitive impairment.

The results showed that, after intervention, the blood glucose levels of both groups demonstrated a downward trend, and compared with the CG, the blood glucose levels of the EG were obviously lower (*P*<0.05), which was in line with the study of Richard-Devantoy et al (25). The results implied that dapagliflozin combined with cognitive behavior training had a good effect on controlling the blood glucose level of patients, which was attributed to the hypoglycemic effect of dapagliflozin by inhibiting SGLT2 and reducing the reabsorption of glucose. With high selectivity of SGLT2, dapagliflozin had a specific hypoglycemic effect, and the external intervention of cognitive behavior training could deepen the cognition of diabetes for patients. Coordinating with each other, these two treatment methods delivered a good result. In addition, after intervention, the scores of C-DMSES, ADL and MMSE in both groups were higher than those before intervention, and compared with the CG, the scores in the EG were remarkably higher

(*P*<0.05). The results demonstrated that dapagliflozin combined with cognitive behavior training could effectively improve the patients' self-efficacy of diabetes management, cognitive level and ability of activities of daily living. The reasons are as follows. Cognitive behavior training mainly focuses on words like diabetic diet and exercise, which will enhance the patients' cognition of diabetes. Furthermore, in reaction and calculation training, patients will also learn how to calculate dietary calories according to their weight, and how to shape reasonable diet for better self-management. In addition, proper exercise together with finger and palm training can improve patients' body coordination, enhance muscle exercise, prevent or improve the symptoms of limb numbness and decrease in grip strength caused by degenerative diseases, facilitate the recovery of damaged brain cells and promote the generation of brain metabolic substances. Therefore, patients' cognitive ability and quality of life are gradually improved.

The deficiencies of this study are as follows. ① At present, there are few clinical data on the safety of dapagliflozin in the long run, and its common adverse reactions are mainly urinary tract infection and electrolyte disorder. None were addressed in the study regarding long-term safety of dapagliflozin, so whether this combined intervention program can be applied for a long time remains uncertainties. ② Cognitive behavior training methods in this study are relatively single, therefore, it is expected to innovate training methods for elderly patients with T2DM complicated with cognitive impairment.

Conclusion

For elderly patients with T2DM complicated with mild cognitive impairment, dapagliflozin combined with cognitive behavior training intervention can obviously improve their cognitive function, self-efficacy of diabetes management and quality of life, which should be promoted in clinic.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

Conflict of interest

The authors declare that there is no conflict of interest.

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