

Biological interaction between sleep quality and depression in type 2 diabetes

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Abstract. – OBJECTIVE: To explore the interaction of sleep quality and depression among patients with type 2 diabetes mellitus (T2DM).

PATIENTS AND METHODS: With multistage cluster sampling, the living quality of all participants was investigated. The indicator of interaction was calculated according to the delta method and non-conditional logistic regression model.

RESULTS: There were 944 residents involved in the final analysis including 365 males and 579 females. The average age was (64 ± 10.2) years. The rate of poor sleep quality and poor sleep quality combined depression were 33.6% and 40.1%, respectively. Due to poor sleep quality and depression in patients with T2DM, the combined interaction index was 2.48 (95% CI 1.44-4.29), the relative excess risk was 3.42 (95% CI 2.16-4.67), and the attributable proportion was 0.51 (95% CI 0.32-0.70).

CONCLUSIONS: An additive interaction rather than a multiplicative interaction of poor sleep quality and depression in affecting the quality of life was found in T2DM patients. When both factors existed at the same time, the interaction effect of these 2 factors was greater than the sum of the two factors.

Key Words

Type 2 diabetes mellitus, Quality of life, Depression, Sleep quality, Interaction.

Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disorder caused by many factors. Due to the long course of the disease, patients' psychological, physical and social functions would be significantly decreased, leading to a serious decline in the quality of life¹. Existing studies have confirmed that gender, age, smoking, activity level, insulin use, depression are closely correlated with the living quality of T2DM patients with²⁻⁴. After these potential confounding factors are adjusted,

depression is still an independent risk factor for reducing the living quality of T2DM patients^{5,6}. Meanwhile, an increasing number of literature reports that poor sleep quality of can also lead to a decline in the living quality of patients with T2DM^{7,8}. However, when depression and poor sleep quality co-exist in T2DM patients, their interactive influence on T2DM patients has not been studied. So we made a survey on the living quality of T2DM patients from November 2012 to January 2013 to investigate their interactive influence on T2DM patients when depression and poor sleep quality co-exist.

Patients and Methods

Patients

A total of 1040 cases were enrolled in our study using a multi-stage cluster and simple randomization method. Firstly, 9 counties/districts in Xuzhou city were numbered randomly. According to random number table, we randomly selected 4 towns/districts Fengxian, Pizhou, Jiawang District and Gulou. Then used the same method to randomly select 3-5 towns/streets from each county/district and 1 village per community from each county per street. A total of 37 villages per communities were selected. T2DM patients from these villages per communities that conformed to the inclusion criteria were selected as our study objects. A validated self-designed general situation questionnaire and the existing DSQL, SDSL, PSQI scales were used for face-to-face investigation on the quality of life of these T2DM patients. HbA1C was detected.

Methods

Inclusion criteria for studies cases were (1) confirmed case and confirmed diagnosis time ≥6 months (2) age ≥18 years old (3) clear conscious-

ness and able to communicate normally and sign informed consent (4) patients with malignant tumors and complicated by severe physical damages were excluded. Several factors were considered for selected cases, e.g. gender, age, educational level, course of the disease, complications, smoking and drinking, etc. Smokers were selected for having at least 100 cigarettes in the past and present. Drinkers were considered as average weekly alcohol consumption ≥ 30 l for ≥ 1 year. Complications include diabetic cardiovascular diseases, retinopathy, nephropathy, neuropathy and diabetic foot. The dichotomy was performed according to the occurrence or nonoccurrence of complication.

Blood glucose control standard generally, HbA1C reflects the average blood glucose level of patients in recent 8-12 weeks, irrelevant to factors, including fasting, insulin use and so on. It is a favorable index for judging the long-term control of diabetes. According to Guidelines for Prevention and Treatment of Diabetes, HbA1C $< 7\%$ is set up as the standard for blood glucose control of diabetics.

Diabetes-Specific Quality of Life (DSQL)

It was composed by 4 dimensions and 27 entries. Linear scoring from 1-5 is made in sequence according to the options. The sum of the point of each entry is defined as total points. The higher the points are, the more serious the patient is affected, and the poorer is his living quality. Four dimensions (1) physiological function: a total of 12 entries, to understand the physical discomfort caused by diabetes, the effects of diabetes complications, as well as the impact of this disease on intelligence and sensory functions (2) psychological/mental functions: a total of 8 entries, to understand the impact of diabetes on patients, including adverse psychological problems and the degree of confidence in treatment (3) social relations: a total of 4 entries, to understand the effects of diabetes on the patient's interpersonal relationship, and the social as well as family status (4) treatment: a total of 3 entries, to understand the patient's satisfaction degree on treatment, adverse drug reactions, the occurrence of hypoglycemia and dietary control. After testing, it has been confirmed that the scale had a good structure validity and it has been commonly used for domestic research in the field. Meanwhile, DSQL < 40 is defined as a good quality of life.

Self-rating Depression Scale (SDS)

It was mainly used to assess the time frequency of patient's depressive symptoms in recent times. It is one of the scales for psychopharmacology research recommended by Health Education and Welfare Department USA and is widely used because of its simplicity in operation. It includes 20 entries, and each entry is scored from 1-4. Cumulative scores of each entry are defined as total depression scores. Multiplying the total depression scores by 1.25 and took the integer part, ranging from 25-100. According to Zung standard, ≤ 50 is defined as depression-free.

Pittsburgh Sleep Quality Index (PSQI) Scale

It was used to assess the sleep quality of patients in recent one month¹⁰. This scale is composed of 18 entries, including 7 dimensions, such as subjective sleep quality, fall-sleep time, sleep time, sleep efficiency, sleep disturbance, hypnotic drug application, and daytime dysfunction. Each dimension is scored from 0-3. The cumulative scores were the PSQI total score, ranging from 0-21. The higher the score is, the poorer is the sleep quality. Generally, PSQI > 7 is defined as poor sleep quality.

Statistical Analysis

Epidata 3.1 was applied to build a database. Conformance test was performed after data were input individually by two people. SPSS 18 software was applied for statistical analysis, $\alpha = 0.05$ was taken as an inspection level. The Excel table compiled by Andersson et al¹¹ was introduced into the database using Delta and relevant indicators of interaction were computed. The value obtained from logistic regression model was taken as the estimated value of relative risk (RR). Interaction indexes include: (1) relative excess risk of interaction (RERI), used to evaluate the difference between the combined effect when A and B coexist and the independent effect when either A or B exists. (2) Attributable proportion (AP), used to evaluate the ratio that could be attributable to the interaction of both factors when A and B coexist. (3) Interaction index (S). When interaction doesn't exist, the credibility interval of RERI and AP shall include 0, and the credibility interval of S shall include 1. $p < 0.05$ was considered statistically significant.

Table I. Rating scale of sleep quality and living quality of T2DM patients ($\bar{x}\pm S$).

Sleep quality	Physiology	Psychology	Social relation	Treatment	Total DSQL scores
Good (n=627)	21.3±6.3	15.7±3.9	5.8±2.0	4.7±1.4	47.6±10.7
Poor (n=317)	27.3±8.2	18.0±4.9	6.3±2.8	5.3±1.7	56.9±14.5
t	11.41	7.42	2.75	5.32	10.21
p	<0.01	<0.01	<0.01	<0.01	<0.01

Computational Method

$RERI = RR_{11} - RR_{10} - RR_{01} + 1$
 $AP = RERI / RR_{11}$
 $S = (RR_{11} - 1) / (RR_{01} - 1)$
 RR_{11} represents the RR value when A and B coexist; RR_{10} and RR_{01} represent the RR value when either of A or B exists.

Results

General Materials of T2DM Patients

944 T2DM patients were involved in the final analysis, among which were 365 males and 579 females and being aged from 27-87 years old, on average (64.0 ± 10.2) years old. The course of disease was from 0.5-35 years, on average (5.6 ± 5.1) years; smoking rate was 17.3%; drinking rate was 12.0%. HbA1c was (7.96 ± 1.82)%, standard rate (HbA1c < 7%) was 31.7%. 317 patients had poor sleep quality, accounting for 33.6%; 379 T2DM patients were complicated by depression, accounting for 40.1%.

Independent Influence of Sleep Quality and Depression on the Living Quality of T2DM Patients

Total DSQL scores and scores of each dimension of poor sleep quality group (PSQI>7) were higher than the good sleep quality group ($p<0.01$); total DSQL scores and scores of each dimension of poor sleep quality & depression group (PSQI>7) were higher than the normal group ($p<0.01$) (Tables I and II).

Multiplicative Interaction of Depression and Sleep Quality on Patients' Living Quality

Patients were grouped according to the occurrence of depression and the quality of sleep. Table III shows the number of patients in each group. The quality of life was taken as the dependent variable, and sleep quality, depression and sleep quality and depression were taken as independent variable to make Logistic regression analysis (Table IV).

Additive interaction of depression and sleep quality on patients' living quality

$\beta_1, \beta_2, (\beta_1 + \beta_2 + \beta_3)$ in logistic regression analysis and variance and covariance between factors were input into the Excel tables that Andersson and others compiled (Tables V, VI).

Discussion

T2DM is a kind of physical and mental disease in need of long-term comprehensive treatment. As the course of disease gradually extend, the number of complication increase and the economic burden become aggravated; diabetic patients would be lack of confidence in the future life, overwhelmed by negative emotions, and even troubled by depression. Studies^{5,6} have shown that the living quality of T2DM patients complicated by depression was relatively poor. The result of our study also showed that the quality of life in patients with depression was lower than that in patients without depression. It might be because

Table II. Rating scale of depression and living quality in each dimension ($\bar{x}\pm S$).

Group	Physiology	Psychology	Social relation	Treatment	Total DSQL scores
Normal (n=572)	21.8±6.7	15.8±3.8	5.5±1.8	4.7±1.4	47.7±10.7
Depression (n=372)	25.7±8.0	17.5±4.9	6.8±2.7	5.3±1.8	55.2±14.6
t	7.78	5.64	8.28	5.76	8.61
p	<0.01	<0.01	<0.01	<0.01	<0.01

Table III. Sleep quality and depression grouping.

Sleep quality	Depression	Quality of life	
		High	Low
Good	No	121	308
Good	Yes	40	158
Poor	No	17	119
Poor	Yes	10	171

the self-management initiative and treatment compliance of patients with depression were relatively poor, thus affecting the control of disease, and finally reducing the quality of life. Results of our work and the previous studies^{7,8} showed that poor sleep quality of T2DM patients would also reduce their quality of life.

The occurrence and development of diabetes was the result of mutual interactions of multiple factors. Only a few of these factors could work independently. Most factors would not take effect directly but through a few independent risk factors or in other words they would interact with each other and take effect. Since biological interaction was different from the analysis of product term in statistical model, Rothman¹² deemed that the assessment of biological interaction shall be based on additive scale rather than multiplication scale, so he recommended to evaluate the additive interaction of logistic regression model by REROI, AP and S. In our study, there was no multiplicative interaction but additive interaction between sleep quality and depression. When both factors existed at the same time, the interaction effect

Table IV. Outcome of multiple logistic regression analysis.

Project	β	p-value	OR (95%)
Sleep quality	1.012	<0.01	2.75 (1.59-4.77)
Depression	0.439	0.034	1.55 (1.03-2.33)
Sleep quality* depression	0.454	0.329	1.57 (0.63-3.91)

Table V. OR of additive interaction.

Variable	OR	Lower limit	Upper limit
Sleep quality	1.55	1.08	2.24
Depression	2.75	1.77	4.28
Sleep and depression	6.72	5.42	8.51

Table VI. Calculating table for relevant index of additive interaction.

Index	Point estimation	Lower limit	Upper limit
Relative excess risk of interaction	3.42	2.16	4.67
Attribution ratio(AP)	0.51	0.32	0.70
Interaction index(S)	2.48	1.44	4.29

of these two factors was greater than the sum of the two factors. 51% of poor quality of life shall be attributable to the interaction of poor sleep and depression. Therefore, improving the T2MD patients' sleep quality and mental health was extremely significant for improving their quality of life.

The biological mechanism of interaction between depression and poor sleep quality has not been reported in literature¹³. But some scholars have found that depression would affect endocrine system through hypothalamic-pituitary-adrenal, make the blood glucose uncontrollable, reduce patients' physical functions, and finally affect the patients' quality of life^{14,15}. Poor sleep quality would stimulate central system to secrete a large number of catecholamine substances, which once being released into blood, would lead blood glucose to increase⁸ and reduce the quality of life^{16,17}. So we could come to that the decreased quality of life of patients resulted from the interaction between poor sleep quality and depression might be closely related with blood glucose.

Conclusions

Although the biological mechanism between depression and poor sleep quality is still unclear, the result of our study has confirmed that improving T2DM patients' sleep quality and mental health were extremely important for improving their quality of life. While controlling the patients' glucose, the medical staff shall also strengthen their interference in the patients' psychology and sleep so as to keep them in a good physical and mental state, thus improving their quality of life.

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Conflict of Interests:

The Authors declare that they have no conflict of interests.

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