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Anti-depressant treatment-related changes in risk factors and their impact on the prognosis of sleep disturbances in patients with depression.

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Abstract

This study aimed to elucidate the risk factors of Sleep Disturbances in Depression (SDD) and to determine improvements related to anti-depressant treatment. One-hundred-and-forty-six patients with depression were included. The Simplified Coping Style Questionnaire (SCSQ) was used to determine patients' coping styles, while the Hamilton Depression Scale (HAMD) and Hamilton Anxiety Scale (HAMA) were used to assess depression and anxiety. The Pittsburgh Sleep Quality Index Scale (PSQI) was used to assess sleep quality, and the Beck Scale for Suicide Ideation (BSS) and Suicide Attitude Questionnaire (QSA) were used to observe patients' suicidal tendencies. Except for the SCSQ, all other scales were assessed before and 3 months after anxiolytic therapy, for comparison. Sleep-associated factors were also analysed. In addition to relief from depression and anxiety, the patients' sleep conditions improved and their suicidal tendency declined after antidepressant treatment. Correlation analysis revealed that the risk factors of sleep disturbances included sex, anxiety and depression status, negative coping style, and suicidal tendency. After antidepressant treatment, some of the above-mentioned risk factors were corrected and only anxiety and depression status, coping style, and suicidal tendency remained as risk factors. In conclusion, antidepressant treatment can bring about many benefits to patients with depression.

Keywords: Depression, Sleep disturbances, Impact factors, Prognosis, Prediction.

Abbreviations

SCSQ: Simplified Coping Style Questionnaire; HAMD: Hamilton Depression Scale; HAMA: Hamilton Anxiety Scale; PSQI: Pittsburgh Sleep Quality Index scale; BSS: Beck Scale for Suicide Ideation; QSA: Suicide Attitude Questionnaire.

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Introduction

As a common emotional disorder, the main clinical features of depression are significant and long-lasting emotional withdrawal, decreasing energy, fatigue, reduced activity, or a sense of loss of interest. It is often accompanied by significant anxiety, sleep disturbances, or other physical symptoms, as well as comorbid mild cognitive impairment in the elderly [1]. Its high prevalence, recurrence, and associated suicide rates have caused significant burdens to patients, their families, and the society. The World Health Organization (WHO) has estimated the overall suicide rate for men and women aged 75 y and above to be 50/100,000 and 16/100,000, respectively [2]. Psychiatric disorders, particularly depression, increase the risk of suicide [3]. In the US, the annual prevalence of severe depression is 10% [4], and the lifetime prevalence of depression in China is 3.2-5.9%.

Sleep Disturbances in Depression (SDD) occur in up to 70% of patients with depression, and include difficulty in falling asleep, frequent awakenings during the night, and non-restorative sleep [5,6]. Persistent sleep problems might affect patients' depression and anxiety, or even lead to suicide, and thereby increase the suicide risk significantly [7]. The first clinical symptom in 61.8% of patients with depression is sleep disturbances, and at least 40% of patients meet the diagnostic criteria for chronic insomnia [8]. Polysomnography (PSG) studies on depression have shown that the main changes in sleep patterns in patients with depression are increased phase transitions during various sleep periods, waking up early, increased wake-up times, increased phase I sleep, decreased sleep efficiency and sleep maintenance rate, reduced slow-wave sleep, and shortened REM sleep latency (RL) [9].

Previous reports have considered the relationship between sleep and depression as a unidirectional causal relationship; i.e., depression led to sleep disturbances. In recent years, a large number of studies have questioned this view, and have suggested that there is a complex two-way relationship between sleep and depression [10]. However, to date, the cause-effect relationships between depression and sleep, as well as the pathological mechanisms of SDD, are still not well understood.

The aim of this study was to understand the risk factors of SDD and to observe the improvements after anti-depressant treatment.

Materials and Methods

Subjects

Patients with initial and recurrent depression, who were treated in the Jining Psychiatric Hospital, Jining, China, from October 2011 to October 2012 were selected. Patients were included if they met the following criteria: (1) The diagnostic criteria for a mood disorder depressive episode and recurrent depressive disorder in the International Classification of Diseases, Tenth Edition (ICD-10; a clinical cataloging system that went into effect for the US healthcare industry on October 1, 2015, after a series of lengthy delays; http://searchhealthit.techtarget.com/definition/ICD-10). (2) Age over 18 y. (3) Chinese Han population. (4) Total score on the 17-item Hamilton Depression Scale (HAMD) ≥ 17 points. (5) Voluntary participation in this study and signing of informed consent. Exclusion criteria were as follows: a history of organic brain depression, psychotic depression, psychoactive substance-related depression, and psychogenic depression. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Jining Psychiatric Hospital. Written informed consent was obtained from all participants.

Survey tools

The Pittsburgh Sleep Quality Index Scale (PSQI) was used to assess patients' subjective sleep quality, with total scores ranging from 0 to 21 points, and with a higher score indicating poorer sleep quality [11]. The Simplified Coping Style Questionnaire (SCSQ), which included 20 items, was used to assess patients' stress levels. The questionnaire was composed of two dimensions, namely positive responses and negative responses. A higher score indicated an increased tendency to use a given coping style. The SCSQ uses a four-level scoring system, and has good reliability and validity [12]. The Hamilton Depression Scale 24 (HAMD-24) and Hamilton Anxiety Scale (HAMA) were used to evaluate patients' depression and anxiety symptoms [13,14]. The Beck Suicide Scale (BSS) was used to assess the intensity of patients' suicidal tendencies and suicidal risk levels [15]. The intensity of suicidal tendency was based on the 1st to 5th items, with a score between 0 and 100 points. A higher score indicated greater suicidal tendency intensity. The suicide risk level was based on the 6th to 19th items to assess the real suicide possibility of a subject with suicidal tendencies. A higher score indicated a greater suicidal risk [16,17]. The Suicide Attitude Questionnaire (QSA) [18] was compiled by Xiao and was used to assess patient's attitudes towards suicide. The questionnaire included 29 items and was divided into four dimensions: F1: understanding the nature of suicidal behavior (nine items), F2: attitude toward suicidal people (10 items), F3: attitude towards the families of suicidal people (five items), and F4: attitude towards euthanasia (five items). This questionnaire had good reliability and validity. Each item was scored as "fully agree," "agree," "neutral," "disagree," and "completely disagree." In order to facilitate the statistical analyses, based on the average of each dimension, 2.5 and 3.5 points were used as cut-off values. The attitude towards suicide was divided into three categories: ≤ 2.5 points: having recognition, and a positive, understanding, and tolerant attitude toward suicide; 2.5-3.5 points: having a contradictory and neutral attitude toward suicide; ≥ 3.5 points: having an oppositional, negative, rejecting, and discriminatory attitude toward suicide.

The HAMD-24 and HAMA were scored by two highly qualified psychiatrists. The PSQI, SCSQ, BSS, and QSA were assessed by patients themselves, under the guidance of physicians. The SCSQ was only used once before treatment, but other scales were used for scoring before treatment and at the end of 3 months of treatment.

Statistical analysis

The SPSS15.0 software package was used, and the t-test was used to compare changes in clinical symptoms in patients between before and after treatment. The linear correlation or variance test was used to analyse the factors related to sleep disturbances before treatment, and partial correlation analysis was used to analyse the impacts of sleep disturbances on prognosis. Differences were considered significant at an α of 0.05.

Results

General information

This study enrolled 160 patients, and excluded 14 patients that could not finish the treatment for various reasons, or for whom scales were incomplete at the end of the 3-month treatment. A total of 146 patients, including 93 men and 53 women, aged (46.38 ± 11.52 y) met the inclusion criteria and completed all the items in the PSQI, SCSQ, HAMD-24, HAMA, BSS, and QSA. The overall positive response factor score in the SCSQ was 27.56 ± 8.32, and the negative response factor score was 31.12 ± 6.98.

Sleep disturbances-related factors

Table 1 shows that before treatment, the PSQI score was significantly related to sex, marital status, physical illness, premorbid personality, family history, early onset, age, educational years, positive response score, negative response score, HAMD-24 score, HAMA score, BSS score, and QSA score ($P<0.05$).

Clinical symptom changes

Table 2 shows that after treatment, the scores in the PSQI, HAMD-24, and HAMA significantly reduced ($P<0.05$), and the scores of the first three dimensions in the QSA significantly reduced ($P<0.05$), as compared to those before treatment.

Impact of sleep disturbances on prognosis

As seen in Table 3, pre-treatment sleep disturbance-related factors varied. Partial correlation analysis showed that after treatment, the PSQI score was significantly positively correlated with the scores in the HAMD, HAMA, QSA, and BSS (P<0.05), indicating that improvements in SDD had a significant impact on the prognosis of depression.

Table 1. *Analysis of sleep disturbances-related factors before treatment.*

	Factor	PSQI score	Statistical value	P
Gender	M (n=93)	15.23 ± 2.59	F=6.57	<0.05
	F (n=53)	17.63 ± 2.08		
Marital status	Married (n=98)	16.52 ± 2.54	F=0.38	>0.05
	Single, divorce, or widowhood (n=48)	17.45 ± 1.76		
On job	Yes (n=32)	16.83 ± 3.74	F=1.68	>0.05
	No/retired (n=114)	17.53 ± 2.32		
with sickness	No (n=22)	16.58 ± 2.53	F=7.23	<0.05
	Yes (n=124)	18.29 ± 2.13		
Premorbid personality	Introversive (n=80)	17.26 ± 3.01	F=3.98	<0.05
	Neutral (n=40)	17.98 ± 3.13		
	Extroversive (n=26)	16.51 ± 2.22		
Family history	Yes (n=48)	18.86 ± 2.16	F=8.47	<0.05
	No (n=98)	16.73 ± 3.41		
Initial onset	Yes (n=86)	16.16 ± 1.98	F=19.86	<0.05
	No (n=60)	18.38 ± 1.73		
Age	18~30 (n=27)	16.35 ± 3.24	F=21.35	<0.05
	30~50 (n=65)	17.53 ± 2.96		
	50~65 (n=30)	18.05 ± 2.89		
	>65 (n=24)	18.63 ± 1.97		
Education	Illiterate (n=25)	18.66 ± 3.27	F=19.23	<0.05
	Primary school (n=19)	18.52 ± 3.17		
	Middle school (n=58)	17.65 ± 3.58		
	College or higher (n=44)	16.37 ± 3.53		
Positive respond score	27.56 ± 8.32		R=15.63	<0.05
Negative response score	31.12 ± 6.98		R=2.13	<0.05
HAMD-24	26.79 ± 6.57		R=1.35	<0.05
HAMA	28.83 ± 6.95		R=1.28	<0.05
BSS	16.05 ± 4.56		R=0.98	<0.05
QSA	2.53 ± 0.46		R=0.76	<0.05

Table 2. *Clinical symptom changes before and after treatment.*

Factor	Before treatment	After treatment	t	P
PSQI	18.28 ± 2.56	8.87 ± 3.27	27.37	<0.05

HAMD-24	28.79 ± 6.57	8.98 ± 5.78	27.35	<0.05
HAMA	28.83 ± 6.95	8.76 ± 5.83	26.73	<0.05
Attitude to suicidal behavior (F1)	3.18 ± 0. 63	2.32 ± 0.68	11.21	<0.05
Attitude to suicide (F2)	2.88 ± 0.4 5	2.07 ± 0.70	11.76	<0.05
Attitude to suicide relatives (F3)	2.51 ± 0.41	1.99 ± 0.59	8.75	<0.05
Attitude to euthanasia (F4)	2.7 6 ± 0.80	2.64 ± 0.85	1.24	>0.05

Table 3. Correlation analysis of PSQI with HAMD, HAMA, QSA and BSS after treatment.

Post-treatment HAMD		Post-treatment HAMA		Post-treatment QSA		Post-treatment BSS	
R	P	R	P	R	P	R	P
0.66	<0.05	0.63	<0.05	0.65	<0.05	0.58	<0.05

Discussion

This study revealed that sex, educational years, physical illness, positive family history, early onset, and attitude towards suicide were risk factors for SDD. The reversal of sleep disturbances had a critical effect on the prognosis of depression, and was a predictor of depression prognosis. These partial risk factors have also been verified in other studies. A recent study also showed that autonomy, support, job stress, job satisfaction, and knowledge of depression were all factors related to depression [19].

Depression leads to disturbances in physiological rhythms, which would result in disturbances in circadian sleep-wake cycles, hormonal secretion patterns, and fluctuations in mood, all of which can be objectively measured [20]. The incidence and severity of SDD partially depend on the patient's sex, age, depression subtype, depression severity, and cognitive impairment [21]. Sleep disturbances can occur at any age; usually, complaints about sleep problems begin at the age of 20 to 40 y, and are rare before puberty [22]. Elderly patients with depression normally have more difficulty in maintaining sleep than younger patients, and their sleep is often lighter, shorter, and more fragmented. The most serious insomnia has been reported to occur in patients with neurotic depression and psychotic depression, and more typically affects elderly patients [23], which is consistent with the finding of this study that age is a risk factor of SDD. The co-occurrence of depression and anxiety could increase the likelihood of sleep deterioration [24].

Insomnia in severe depression is linked with suicide and responds poorly to various antidepressant treatments [25], consistent with the finding of this study that depression was related to anxiety score, attitude to suicide, and other factors. Genetic studies on depression have found that the probability of depression in first-degree relatives of patients with depression was 1.5-3 times greater than that in the general population. Previous studies have shown that the causes of affective disorder might also lead to sleep disturbances, and might involve a genetic predisposition, consistent with the finding of this study that a family history of this condition is one of the risk factors of SDD. Clinical and epidemiological studies have demonstrated that sleep disturbances could be used as one of the predictors of psychiatric disorders, and disturbed sleep is often a precursor of depression; even when no other symptom of depression has appeared clinically, insomnia might already have occurred. Simultaneously, sleep patterns could also be used to speculate on disease status. For instance, more nocturnal waking or waking up early, inability to fall asleep after waking, and morning fatigue and weakness, could indicate a more depressive phase, while shorter sleep duration and a sense of not needing sleep normally indicates a manic phase [26,27]. Experimental studies have confirmed that the first-degree relatives of patients with depression might be prone to having similar or different sleep disturbances [22]. Livingston studied the elderly in communities and found that sleep disturbance was the best predictor of depression [28]. Chang surveyed young medical school students and found that the risk of depression increased two-fold after 30 years of insomnia [29]. Perlman followed up patients with bipolar II disorder and found that patients with shorter sleep duration exhibited a significantly higher risk of depressive episodes within the subsequent 6 months, indicating that short sleep duration might be the prodromal symptom of a depressive episode [30].

Sleep disturbance is an important depression symptom and is a causative factor of suicide among patients with depression. The influence of sleep disturbances on the efficacy of antidepressants and the prognosis of depression has gained attention worldwide, and research has revealed that insomnia is not only a symptom of depression, but also has a major influence on the clinical outcomes and course of depression. In patients with chronic insomnia, about 30% of cases have at least one episode of depression in their lifetime, and the relative risk of new-onset depression is four times the risk of patients without insomnia [31]. Sleep disturbance is an independent risk factor for an increased suicide rate in patients with depression [32]. Insomnia could also predict an increased risk of depression in the future; furthermore, residual insomnia

after antidepressant treatment is associated with an increased risk of depression recurrence [10]. SDD is also influenced by recurrent disease courses; previous studies have found that abnormalities in sleep indicators might be associated with the long-term outcomes of the disease; in particular, persistent abnormal sleep indicators, such as RL shortening and slow-wave sleep reduction that remain in the remission period, might indicate a higher risk of recurrence [33]. The quality of sleep can predict the risk of developing diabetes. It is well known that chronic diseases, such as diabetes, place an emotional stress load on patients. The prognosis of diabetes can be affected by sleep quality and psychological distress and symptoms [34]. The present study showed that sleep disturbance was an important predictor of the prognosis of depression; the more serious the sleep disturbances, the less ideal was the remission of a patient's depression and anxiety symptoms, and the more serious the passive suicidal tendency, which was consistent with the findings of other studies.

In summary, SDD-related factors are diverse, and the mechanism of SDD appears to be closely related to the pathological mechanisms of depression. An in-depth study of SDD would help to reveal the pathogenesis of depression and could be of great significance in guiding clinical treatment and assessing the prognosis of depression.

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Conflict of Interest

All authors have no conflict of interest regarding this paper.

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