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The Smart-Phone Application Follow-up System for Medication Compliance in Patients with Depression

Rui CHI[1], Pengfei WANG[2], Kaili ZHAO[3], Yajuan NIU[4], Jingge DU[4], Kun WANG[5], Yuanhong CHEN[5], Qinchao HUANG[5], Shaoli WANG[4], and Wentian DONG[1,*]

[1] Peking University Sixth Hospital, Peking University, Institute of Mental Health, Key Laboratory of Mental Health, Ministry of Health (Peking University), National Clinical Research Center for Mental Disorders (Peking University Sixth Hospital), No. 51 Hua Yuan Bei Road, Haidian District, Beijing 100191, P. R. China
[2] Beijing Anding Hospital of Capital Medical University, No. 5 Ankang Hutong, Xicheng District, Beijing 100088, P. R. China
[3] Development Center for Medical Science and Technology,National Health and Family Planning commission, No. 9 Chegongzhuang Ave., Xicheng District, Beijing 100044, P. R. China
[4] Beijing Huilongguan Hospital, Changping District, Beijing 100096, P. R. China
[5] Beijing Huayi Network Technology Corp, No. 27 Nanbinhe Rd., Xicheng District, Beijing 100055, P. R. CHINA
E-mails:chrzhy@126.com; youyumushi@163.com;kailizhao@vip.sina.com; niuyajuan@126.com; dujingger@163.com; wangkun@91huayi.com; chenyuanhong@91huayi.com; huangqinchao@91huayi.com; wangshl82@sina.com; dongwentian@126.com.

* Author to whom correspondence should be addressed; Tel.: 8- 01082801939; Fax: 86-010162026310

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Abstract
Objective: To evaluate the influence of a Smart-Phone Application (APP) Follow-up System (SPAFS) on medication compliance in patients treated for depression. *Methods:* Subjects aged 16-65 years old with depressive disorder, who regularly took antidepressant medications for at least one month were recruited from the Peking University Sixth Hospital and Beijing Hui Long Guan Hospital from July 1st, 2014, to April 30th, 2015. Two groups of patients were evaluated: SPAFS group (were willing to be online anytime, who received APP) and control group (agreed to adhere to traditional psychological clinical follow-up procedures). *Results:* One hundred and twenty-one patients were investigated, 57 in the SPAFS group (intervention group) and 64 in the control group. At the end of the 6-month follow-up, 17 patients in the control group and 4 patients in the intervention group discontinued their medication; there was a statistically significant difference ($P<0.05$). In the self-assessment of medication compliance, the scores in the intervention group (8.44±1.31) were significantly higher than those in the control group (6.95±2.73). The medication discontinuation rate in the intervention group was lower than that in the control group($P<0.05$). The SDS scores in the intervention group were lower than those in the control group ($P<0.05$). The self-reported medication compliance scores in the intervention group were higher than those in the control group ($P<0.05$). The most common reasons for medication discontinuation in the control group were forgetting to take the medication, concerns about brain damage from long-term medication use, and the personal decision to discontinue medications when the medical condition appeared to improve. *Conclusion:* This study showed that the SPAFS improved medication compliance during the follow-up period in patients treated for depression.

Keywords: Smart-Phone application (APP); Depression; Medication compliance

Introduction

There are ten recommendations for the treatment of depression in the third edition of the Practice Guideline for Treatment of Major Depressive Disorders issued by the American Psychiatric Association in 2010. Four common recommendations are as follows: monitoring the patient's psychiatric status; evaluating treatment effectiveness; administering intensive therapy; and providing education to the patient and family. Above recommendations emphasize that depression has a high relapse rate, propose intensive treatment throughout the course of depression, and reinforce patient compliance to increase the cure rate, decrease the relapse rate, and improve patients' quality of life and their return to their community [1].

Currently, acute depression may be successfully cured in 6 to 8 weeks, followed by a maintenance period of 4 to 6 months with medication [2]. Studies have shown that medication compliance among these patients is poor; the medication discontinuation rates among patients taking antidepressants for the first time is 35% after one month and 65% after six months. Further, 80% -90% of patients who are effectively treated with antidepressants but fail to comply with medications relapse within three years, and 10% -20% develop chronic and refractory depression [3, 4].

Many factors influence medication compliance; however, the individual initiative of the patient is the most influential factor. For example, patients might decide to discontinue medication when their symptoms improve, or they might be averse to the medication fearing brain damage caused by long-term use [5, 6]. It has been demonstrated that a patient's medication compliance can be improved with the following strategies [7, 8]:

- extending patient management throughout the whole course of the medical condition;
- providing health education on the diagnosis of depression and the side effects of antidepressant medications to the patient and their family members;
- raising awareness of the importance and the absolute necessity of adhering to the medication regimen;
- ensuring that patients, with the support of family members, are conscious of medication time schedules.

A study by a hospital in China that provided regular telephone follow-up consultations to outpatients with depression reported a significant improvement in medication compliance, including increased medication compliance, a decreased relapse rate, and an increased rate of full recovery in those who received telephone interventions [9].

The traditional management of patients with depression is either with face-to-face interviews in clinics or telephone communication. Both procedures are acceptable and practicable, but they have the disadvantages of having low efficiency, being time consuming, and having high economic costs; moreover, it is difficult to obtain the help of a doctor when the condition fluctuates or the side effects of the drug are present. The mobile medical internet has developed rapidly, providing convenient and quick communication between medical practitioners and patients via internet technology, conserving medical resources and benefiting both doctors and patients. The Universal use of smart phones, the development of Internet have all contributed to the increase in technology-based interventions for medication adherence. Previous research has given evidence of the effectiveness of physical and mental health interventions using smart phone apps, such as mood disorders [10], coronary heart disease [11], cancer [12]. However, the development rate of apps and their ever improving quality necessitates further research in reference to reduction of symptomlogy, improving patients adhere to medication. To improve the medication compliance of patients with depression, a new application program, the Smart-Phone APP for Follow-up System(SPAFS),was designed; the SPAFS provides services including patient consultations, signs and symptoms self-assessments, and medication reminders. The APP assists patients with self-management and will hopefully effectively increase medication compliance, reduce the rate of relapse, and improve the quality of life of patients.

This study aimed to evaluate the effect of the new SPAFS on medication compliance in patients with depression.

Methods

Subjects

All outpatients and discharged patients from Peking University Sixth Hospital and Beijing Hui Long Guan Hospital were recruited between July 1st, 2014, and April 30th, 2015. The study was approved by the Ethics Committee of the Peking University Sixth Hospital (Approval Number: 2014 Audit No. 8), and a consent form was signed by each subject.

Subjects who met the criteria for the diagnosis of depressive disorder according to the International Classification of Diseases-10 (ICD-10), who were 16-65 years of age and in stable condition(those with recurrent depressive disorder who were currently in a state of remission were included), and who regularly took antidepressant medication for at least one month were eligible to participate in this study.

Subjects presenting with comorbidities or a diagnosis of intellectual disability, schizophrenia, bipolar disorder, or substance use disorders; those assessed by investigators having a worsening illness, suicidal tendencies or need for further intensive medications; and those who withdrew voluntarily were excluded from this study.

Our study had two arms, with the conventional assignment of the patients to the following groups:

Intervention Group: Patients who met the inclusion criteria, who expressed a willingness to be online anytime and who consented to participate in the SPAFS were assigned to the SPAFS group.

Control Group: Patients who met the inclusion criteria and agreed to adhere to traditional psychological clinic follow-up procedures were assigned to the control group. Patients in both of the groups were treated with the same kinds of drugs, but the follow-up procedures differed. The subjects in the control group participated in traditional psychological follow-up procedures, while the patients in the intervention group participated in follow-up with the SPAFS.

Assessment Methodology

The diagnosis and symptoms assessment questionnaires were adapted for both webpage and mobile terminals.

The Zungself-rating depression scale (SDS), a standard assessment instrument employing a four-point Likert scale that has been demonstrated to accurately reflect subjective feelings of the severity of depression, was administered to the subjects. The SDS score is calculated with a self-reported 20-item questionnaire, and each item is scored on a 4-point scale ranging from 1 (never) to 4 (always). It has been previously validated and widely used in China. Patients were classified into two groups using the SDS cutoffs for the Chinese population. The SDS was completed during treatment and can objectively reflect the severity of depression symptoms within the past week.

The self-rating anxiety scale (SAS) is a 20-item self-reported assessment to measure anxiety levels based on scores obtained in 4 sections: cognitive, autonomic, motor, and central nervous system symptoms. When answering the statements, a person indicates the level at which each statement applied to him/her within a period of one or two weeks before the test. Each question is scored with a Likert-type scale of 1-4 (based on the following responses: "a small amount of time", "sometimes", "a large amount of time", or "most of the time"). Some questions are negatively worded to avoid set response. The overall assessment is scored by summing the individual scores.

Medication adherence scores were used to assess the patients' compliance with the medication regimen adherence during the study. The scores consist of 10 points, where "10" is the highest score, indicating that patients are persistently taking medications, and "1" is the lowest score, indicating that patients discontinued their medications. The actual scores were filled out by the patients.

The duration of follow-up was six months. The study procedure can be seen as follows (Figure 1).

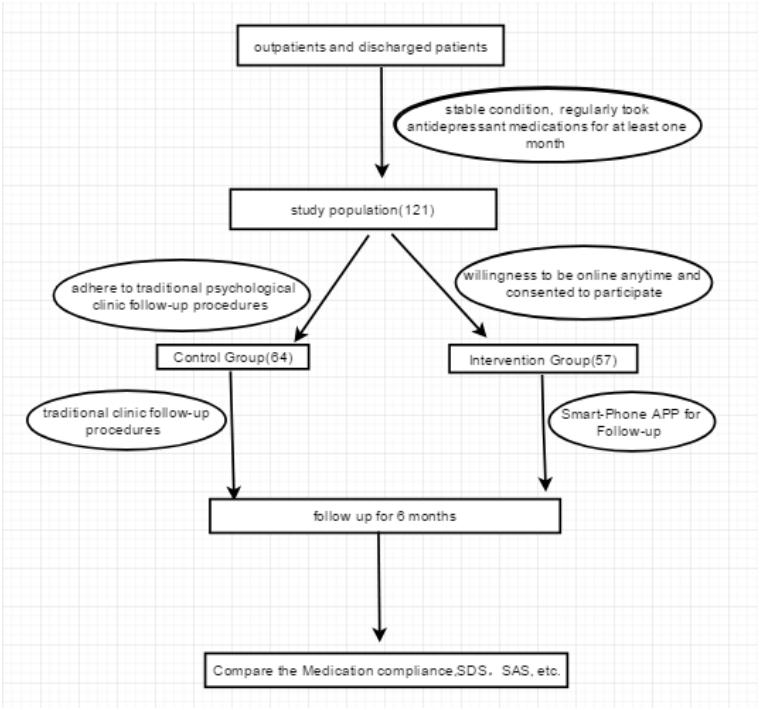

Figure 1. Study flowchart

Statistical Analysis

A database to compile participants' general information, symptom assessments, and medication adherence scores was established in EpiData 2.1. All data were double entered and verified. Data were analyzed with the Statistical Package for the Social Sciences version 17.0 (SPSS 17.0). A 2-sided alpha significance level equal to 0.05 was adopted. Independent sample t-tests and chi-square tests were applied according to the types of data.

Results

Demographic Characteristics

A total of 121 patients were enrolled in this study. A total of 57 patients, including 19 male and 38 female patients with an average age of 38.3±11.6 years, were assigned to the intervention group. A total of 64 patients, including 19 males and 45 females with an average age of 41.5±14.1 years, were assigned to the control group. No statistically significant differences in terms of gender, age, marital status, and health insurance type were observed between the two groups (see Table 1).

Table 1. Patient demographic characteristics ([a]independent sample t-test; no letter,chi-square test)

	Intervention group (n=57)	**Control group (n=64)**	***t* value or χ2 value**	***P* value**
Gender (male/female)	19/38	19/45	0.186	0.698
Age (years)	38.3±11.6	41.5±14.1	-1.368	0.174[a]
Marriage status				
Married	46	55	0.599	0.471
Single/divorces	11	9		
Health insurance type				
Medical insurance/free medical care	40	43	0.125	0.845
Self-paid	17	21		

Patients' Clinical Characteristics

No significant difference in the patient disease history between the two groups was observed (see Table 2). And no significant differences were found in the types of medications or the frequency of outpatient visits between the two groups.

Table 2. Patient clinical characteristics

	Intervention group (n=57)	**Control group (n=64)**	**t value or χ2 value**	***P* value**
Disease history (years)	32.4±11.7	36.8±14.9	-1.831	0.07[a]
Medications				
Monotherapy	31	41	1.172	0.354
Concomitant medications	26	23		
Frequency of outpatient visits				
Once a week or once a fortnight	8	4	0.872	0.281
Once a month or every 2 months	34	42		
Once every 6 months	2	11		
Irregular	13	7		

[a]independent sample t-test; no letter, chi-square test

Medication Compliance Assessment

At the end of the 6-month follow-up, 17 patients in the control group and 4 patients in the intervention group discontinued their medication; there was a statistically significant difference ($P<0.05$). In the self-assessment of medication compliance, the scores in the intervention group were (8.44±1.31) significantly higher than those in the control group (6.95±2.73). The SAS scores for anxiety and SDS scores for depressive symptoms at the end of six months were also analyzed; the SDS scores in the control group (51.21±15.41) were significantly higher than those in the intervention group (46.05±11.84). The main reason for discontinuing medication in the intervention group was concern about brain damage due to long-term medication use, whereas the main reason in the control group was the patient's personal decision when the medical condition appeared to improve.

Table 3. Medication compliance assessment scores

At the end of follow-up	**Intervention group (n=57)**	**Control group (n=64)**	**t value or χ2 value**	***P* value**
Medication compliance self-assessment score	8.44±1.31	6.95±2.73	3.883	<0.001[a]
Symptom assessment				
SDS score (Mean±SD)	46.05±11.84	51.21±15.41	2.076	0.040[a]
SAS score (Mean±SD)	43.25±10.10	41.91±13.42	0.623	0.534[a]
Medication				
Continued	53	47	8.030	0.005
Discontinued	4	17		
Reasons for discontinuation				
Symptom improvement	0	15	-	-
No symptom improvement	0	0		
Concern about brain damage	3	2		
Adverse event	1	0		

[a]independent sample t-test; no letter, chi-square test

Discussion

Our research center developed a new internet-based SPAFS for instant network communication between psychiatrists and their patients with depression, making it possible and convenient for doctors to manage patients throughout the entire course of treatment without face-to-face consultations. After six months of follow-up and management with the SPAFS, we found that the SPAFS intervention group had a significantly lower rate of medication discontinuation (26.6% vs 7.0%), a higher degree of self-assessed medication adherence, and a lower incidence of self-assessed anxiety than the traditional psychological clinical control group (Table 1-3). Consistent with relevant research results [13,14], our results have shown that mobile technologies has the potential to improve medication adherence. The current encouraging results were due to real-time interactive communication via the SPAFS, as patients could report and discuss their concerns as soon as possible with their doctors who were be able to respond instantly and resolve their worries via the internet. Furthermore, doctors were also be able to check patient records, including recent medication compliance, adverse effects and self-assessment scores at any time, and provide instructions or reminders if any problems existed. Apart from the interactive communication, the regular dissemination of electronic educational medical articles from doctors to patients also contributed to improving medication compliance. These informative articles were either authored by the doctors themselves or obtained from other sources. Their contents were professional, specifically targeted for depressive conditions and educationally beneficial to patients. Compared to the traditional psychological clinical follow-up communication methods, such as via telephones or text messages, network communication using the new SPAFS has definite advantages, especially in terms of convenience and timeliness of management. However, the effectiveness of the SPAFS is limited by the factors of patient literacy [15].

The premise of a standardized treatment protocol for depression is the establishment of an interactive alliance between doctors and patients with the common goal of achieving full recovery. Based on this alliance, doctors can educate patients and their families on the management of depression so that patients can better understand their clinical conditions and the importance of continuing medications. Doctors can also clarify the pharmacological properties of the medications, including potential side effects and measures to prevent adverse event in patients. Such a doctor-patient alliance will promote cooperation by the patients in adhering to the medication regimen in terms of time and dosage and ultimately achieve high rates of medication compliance [16, 17]. In this follow-up study, 26.6% of patients in the traditional psychological clinic control group discontinued their medication; this proportion was much higher than the 7.0% in the SPAFS intervention group. The most common reasons for medication discontinuation were concern about brain damage from long-term medication use and the patient's personal decision to discontinue the medication when the medical condition appeared to improve. Both of the reasons involve the patient's misguided subjectivity, which is mainly due to an insufficient understanding of the medical condition of depression. Hence, despite possible therapeutic improvements in the early stage, patients' lack of knowledge of a standardized treatment protocol for depression can lead to the early cessation of treatment and discontinuation of medication and thus adversely affect the overall treatment efficacy.

There are still specific problems and defects in the new SPAFS, and there is room for further improvement and optimization on the basis of the experiences of additional clinical practices. For example, follow-up via the internet system relies on written communication and therefore an affinity between doctors and patients can be lacking compared to face-to-face interviews or voice communication. Additionally, in this study, medication compliance was subjectively assessed by the patients themselves. Additional objective indicators should be employed in future studies. Additional functions, such as video communication, appointment booking, and reminders for patients to take their medications, could also be added to the SPAFS. Patients' internet behavior and users' feedback and recommendations[18]should also be taken into consideration in the design optimization of the APP to provide improved services throughout the entire course of therapy.

This study showed that the SPAFS improved medication compliance during the follow-up period in patients treated for depression.

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