Effective Factors of Non-Adherence and Admission in Bipolar Disorder

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To cite this article:
Mohammad Ebrahimzadeh Mousavi, Mercedeh Samiei, Parvaneh Mohammad Khani, Abbas Pourshahbaz, Imaneh Abbasi, Negin Ansari, Sarah Aminoroaya. Effective Factors of Non-Adherence and Admission in Bipolar Disorder. *Psychology and Behavioral Sciences*. Vol. 7, No. 6, 2018, pp. 97-103. doi: 10.11648/j.pbs.20180706.11

Abstract: Bipolar disorder is a severe mental disorder that becomes chronic in about 40% of the cases and nearly 45% of the patients experience frequent relapses. The study population included all patients with bipolar disorder with a history of admission to psychiatric hospitals. Using a nonrandom sampling method, a total of 73 patients with bipolar I disorder were selected. The study data were collected using medical records, the Structured Clinical Interview (SCID), the Scale to Assess Unawareness in Mental Disorder (SUMD), the Drug Attitude Inventory-10 (DAI-10), the Liberman's psycho-education protocol, and the checklist for patient's adherence to behavioral and medication recommendations and the reasons for temporal or permanent stopping taking medications. It was found that female patients, patients with a high school degree or higher, and patients aged older than 30 years had better treatment adherence (p<0.01). Only 3.4% of participants had good treatment adherence. According to the results of Repeated measures ANOVA, participants in the experimental and control groups had significantly different post-test and follow-up scores on drug attitude, insight, and the reasons for stopping taking medication. We can conclude that the Liberman's psycho-education protocol led to significant improvements in drug attitude, insight, and the reasons for stopping taking medication.

Keywords: Bipolar Disorder, Adherence, Non-Adherence, Psycho-Education, Readmission

1. Introduction

Bipolar disorder is a severe mental disorder, and its prevalence is estimated to be about 1-2% [1]. Several symptoms of bipolar disorder include changes in activity level, cognitive abilities, speech, and vegetative functions, such as sleep, sexual activity, aggression, irritability, impulsive behaviors, and suicide (15 times the general population), symptoms threatening both patients and those close to them [2]. Due to severity of symptoms, the first line treatment is pharmacotherapy. In fact, pharmacotherapy, in addition to reducing and controlling the symptoms and stabilizing patient's condition, helps in the maintenance of treatment gains [3]. After the acute phase of the disorder is treated and the symptoms are controlled, and following about

1 month of hospitalization (in average, 33.5 days for men and 44.7 days for women), the patient is discharged from hospital with a relatively stable condition. Bipolar disorder is a chronic disorder (it becomes chronic in 40% of cases), the patients experience frequent relapses (only about 7% of patients with bipolar 1 never experience a relapse) (45% of patients experience repeated relapses [4], and there are symptoms that threaten both the patients and people close to them. Therefore, it is necessary and important for a patient to follow and adhere to the treatment prepared and modified during hospitalization.

Treatment nonadherence is a problem that is observed in both physical and mental patients, especially those with chronic disorders. In general, 4 out of 10 patients have problems with treatment adherence [5]. Treatment adherence

is not like compliance, i.e. just using medication without any objection, but, it is a very broad concept that involves a person's medication use, having some behaviors, avoiding some behaviors, following a diet, implementing and managing life style changes, and keeping contact with clinician and treatment services and following their recommendations. Therefore, adherence refers to different aspects, including medication, behavioral, relational etc. and problem in each of these aspects is regarded as treatment non-adherence. Treatment non-adherence may represent the patient's inability to follow some or all orders from a clinician, such as adherence to prescribed medications, behaviors, and habits [4]. Non-adherence is a hidden problem, and can be intentional of unintentional. It is also something that is not usually a major focus of clinicians. Treatment non-adherence is a common and complex problem in patients with bipolar disorder, during hospitalization and after discharge from hospital.

Treatment non-adherence in patients with bipolar disorder has different forms including: 1- Full non-adherence, 2-intermittent, late adherence 3- abuse, 4- selective adherence, and 5- behavioral non-adherence [5].

Treatment non-adherence has multiple aspects, and different factors influence treatment adherence in patients including: 1-Factors related to the disorder, such as insight, drug abuse, depression, pathological factors, and continuity of symptoms. 2- Factors related to medication, such as side effects, previous drug experiences, drug dosage, drug interactions and a complex diet, drug formulation, and drug expenses. 3- Factors related to clinician and treatment centers, such as therapeutic alliance, accessibility, discharge planning, and connections between treatment services. 4- Factors related to patient, such as previous history of treatment adherence, attitude toward disorder and medication, and labels. 5- Factors related to care provider, such as attitude toward disorder and medication, capacity for monitoring and reminding the patient to take medications, labels [6].

Treatment non-adherence may have some effects on patients, clinicians, and treatment centers including: Effects of the disorder on patients and people close to them: the illness develops and becomes chronic, impairment in functioning, aggression and violence, continuity of symptoms and frequent relapses, frequent hospitalization, emergent and dangerous conditions for patients and people close to them, legal problems, high expenses, and other threats that the patient and people around them may face. Effects on clinicians and treatment centers: an increase in the number and duration of hospitalization, unnecessary changes in diagnosis and medications, wrong diagnosis of treatment resistance, emergency admissions instead of easy and danger-free admissions to the other departments of the hospital, high expenses [7].

Treatment adherence becomes more important when, after a short period of time, the patient is readmitted to the hospital with the same or even more severe symptoms, or in an emergency condition; in such a situation, the course of treatment is usually repeated. However, with identification of effective factors in treatment non-adherence, monitoring

these factors, and psychoeducation, it is possible to increase medication adherence, reduce the danger of relapse and hospitalizations, improve involvement of patients in the course of treatment, control the symptoms, help patients learn new skills, and prevent social isolation and stigmatization [8]. In fact, by considering the effective factors in treatment noncompliance in the patient, or using psychoeducational sessions, it is possible to prevent relapses to a certain extent, because the previous treatment adherence pattern in a patient does not get better automatically with time [9]. The focus of the present study is on behavioral adherence in addition to medication adherence. In addition to demographic variables, the present study is aimed at examination of three variables, including insight, attitude toward medication, and reasons for stopping taking medications in patients with bipolar disorder, and determining their effects. Moreover, in the stage of implementation of the psychoeducation protocol, we are going to test, this protocol has effects on the study variables, medication and behavioral adherence, and readmission. Therefore, examination of the effective factors in treatment non-adherence helps to identify patients with treatment non-adherence, and improve their adherence, reduce their symptoms, and prevent possible relapses and high expenses, using effective interventions.

2. Methods

This is a Longitudinal and prospective study. The study population includes all patients with bipolar disorder in Razi psychiatric hospital with a history of admission to psychiatric hospitals. A total of 73 patients with bipolar I disorder (35 women and 35 men) with psychotic symptoms who had a history of admission to psychiatric hospitals with the same diagnosis, were recruited using a purposive, nonrandom sampling method. The study was conducted from summer 2015 to spring 2016, in the departments 1 and 2 for women and Ebnesina and Aboureyhan departments for men. The study data were collected using medical records, semi-structured questionnaire (SCID), questionnaire, Liberman's psychoeducation protocol, and checklist.

2.1. Questionnaires

The Scale to Assess Unawareness in Mental Disorder (SUMD): the short form of this questionnaire has 9 different parts assessing three dimensions of insight. For the 9 sections of the SUMD, the intraclass correlation coefficient (ICC) (interrater reliability) has been reported from 0.76 to 0.99 (mean=0.89) [10]. The interrater reliability using the ICC was found to be 0.93 and 0.73. Improvements in the insight of patients during acute and remission phases indicated good content validity of the scale (p<0.01). The short form of the Persian version of the SUMD has good validity and reliability [11].

The Drug Attitude Inventory-10 (DAI-10): In a previous study, interrater reliability of 0.61 and Cronbach's alpha of 0.175 were found for the scale (p<0.001); patients with low compliance scored lower on drug attitude, and patients with moderate and high scores on compliance scored higher on

drug attitude [12]

Semi-structured interview (SCID): it has been used many times in clinical and nonclinical samples [13, 14].

Patient's adherence to behavioral and medication recommendations: it is assessed using a checklist.

The checklist of the reasons for temporal or permanent stopping taking medications: its validity was assessed by 14 experts, and a Cronbach's alpha of 0.71 was found for it.

The Liberman's Psychoeducation Protocol: it was developed by Robert Paul Liberman at the University of California, Los Angeles (UCLA) for patients with schizophrenia, bipolar and severe depression [15].

2.2. Data Analysis

The study data were analyzed using SPSS software (v. 22, IBM SPSS, Chicago, IL, USA). Descriptive statistics were used to summarize the demographic characteristics of patients. First, the internal consistency was calculated for the questionnaires, and then, participants in the experimental and control groups were matched. The independent t-test and the chi-square test were used for continuous and categorical variables, respectively, in order to examine significant differences. The means and standard deviations of the study variables for both experimental and control groups were compared at pretest, and then, the mean scores of the patients in the two groups were examined at posttest. The Chi-square test and the repeated measures ANOVA were used. The Pearson correlation coefficient was used to calculate correlations, and the multiple regression analysis with the standard method was used to examine the predictive power of variables. The level of significance was set at $p<0.05$.

2.3. Procedure

By the time that symptoms had subsided and the patient was in a relatively stable condition (usually in the second week of hospitalization), we continued with the following steps during hospitalization: first, according to the diagnosis made by a psychiatrist and patient's medical records, and then, using the SCID, the diagnosis of bipolar I disorder with psychotic features was confirmed. Then, the SCID's drug abuse and addiction criteria were considered, therefore, the use of illicit drugs, such as opiate, cannabis, heroin, crack, and methamphetamine, except cigarettes and coffee was examined. It was also considered that patients have at least one hospitalization with the same diagnosis in the previous year. The demographic variables for every patient were extracted from the patient's medical records. The SUMD that has 9 items was used to examine insight. The drug attitude was examined using the DAI-10 that has 10 items. Behavioral and medication adherence of patients were also evaluated using the checklist. Then the checklist of the reasons that, according to the patient, were behind temporal or permanent stopping taking medication was completed. Then, patients were put in different groups according to their treatment adherence, and in 8 days each comprised of two 40-minute group sessions, the Liberman's psychoeducation protocol was administered in the hospital to 30 patients who were randomly selected from treatment non-adherence subgroups. After intervention, the insight, drug attitude, and reasons for temporal or permanent stopping taking medication were examined for the second time. A 6-month follow-up after discharge was performed for patients in the intervention group (by telephone calls 2 times a week). No intervention was applied to the patients in the control group. Only those who lived with the patient were asked to call us in case of readmission of the patient to a psychiatric hospital. During or at the end of the follow-up period, in case of readmission or no readmission of the patients in both groups, the variables for diagnosis of the disorder were reexamined using medical records, SCID, insight, drug attitude, behavioral and medication adherence, and the checklist of temporal or permanent stopping taking medication. Finally, the effects of study variables on patients' treatment adherence and the impact of the psychoeducation protocol on treatment adherence and study variables, and after that, the effect of psychoeducation on relapse and readmission of the patients were determined.

2.4. Ethical Considerations

In order to follow research ethics, an approval was obtained at first from the ethics committee of University of Social Welfare and rehabilitation Sciences. In addition, the participants were given information about the goals and methodology of the study and asked to fill out and sign a form of written informed consent. The right of withdrawal from the study was explained to them in each phase as well. Before conducting the study, necessary measures were taken to minimize possible harms to participants and protect their health. In addition, without any pressure or judgment, the informed consent of participants was obtained.

3. Results

The mean age of participants was 34.25 years, ranging from 20 to 51. The education level ranged from primary school to bachelor's degree. 26.9% of the participants had jobs and 73.1% were jobless; and 46.3% were single and 34.3% were divorced. (Table 1)

Table 1. *Demographic factors are related to treatment adherence of patients with bipolar disorder.*

Variable	Treatment adherence	Type of test	significant	Df
Sex		Chi-square		
	Drug adherence		0/04	3
	Behavior adherence		0/09	4
Married		Chi-square		
	Drug adherence		0/19	2
	Behavior adherence		0/41	4
Education		Chi-square		
	Drug adherence		0/01	3
	Behavior adherence		0/14	4
Age		ANOVA		
	Drug adherence		0/00	3
	Behavior adherence		0/05	2

Patients with a high school degree or higher, compared to those with a lower education, especially primary education, had better treatment adherence. Moreover, it was found that patients aged 20 to 30 years, compared to those older than 30 years, had lower medication adherence; similar results were found for behavioral treatment adherence. We can say that patients older than 30 years, compared to those younger than that, especially patients aged 20 to 27 years, had better medication and behavioral treatment.

The results of t-test and Chi square test indicated that participants in intervention and control groups were not significantly different in gender, marriage status, education, age, drug use, and history of electroconvulsive therapy (ECT), and that participants in the two groups were matched in terms of these variables. In addition, an independent samples t-test showed no significant difference between participants in intervention and control groups in their pretest scores on drug attitude, insight, and checklist. Then, posttest and pretest scores were compared in both groups; the results indicated a significant difference between the two groups in the scores on drug attitude, insight, and checklist (p<0.001); this indicated that the intervention improved the scores on drug attitude, insight, and the checklist for participants in the intervention group.

It was found that a few participants had a good treatment adherence (only 3.4%). Due to their low number, participants with a good treatment and medication adherence were not included in the intervention and control groups. (Table 2)

Table 2. The number of patients in different adherence subgroups.

Adherence	Frequency	Percentage
Drug adherence		
Lack	11	15/2
Alternate	25	36/3
Selective	11	15/4
Abuse	20	28/9
Full	3	4/2
Behavior adherence		
Lack	39	57/1
Alternate	11	14/4
Selective	17	24/4
Full	3	4/2

A few participants had a good treatment adherence (only 3.4%). Due to their low number, participants with a good

treatment and medication adherence were not included in the intervention and control groups.

The ANOVA and Chi square tests were used and it was found that demographic variables, such as gender, education, and age had effects on treatment non-adherence of patients with bipolar disorder. It was found that female patients had better medication adherence, but no significant difference was found between men and women in behavioral treatment adherence; based on these results we can say that women have better medication adherence than men. There was also significant differences between participants with different education levels in medication adherence (p<0.01), but no significant difference was found in behavioral adherence. We can say that patients with a high school degree or higher, compared to those with a lower education, especially primary education, had better treatment adherence. Moreover, it was found that patients aged 20 to 30 years, compared to those older than 30 years, had lower medication adherence; similar results were found for behavioral treatment adherence. We can say that patients older than 30 years, compared to those younger than that, especially patients aged 20 to 27 years, had better medication and behavioral treatment.

Repeated measures ANOVA showed Participants in the intervention group, compared with controls, have higher posttest scores on drug attitude, insight, and the checklist of the reasons for stopping taking medication. a significant difference was found between participants in the intervention group and controls in posttest and follow-up scores on drug attitude, insight, and the checklist of the reasons for stopping taking medication. These results indicated that patients in the intervention group, compared with controls, had higher posttest scores on drug attitude, insight, and the checklist of the reasons for stopping taking medication, and they had also higher scores than controls in the follow-up. (Table 3)

Repeated measures ANOVA showed Participants in the intervention group, compared with controls, have higher posttest scores on drug attitude, insight, and the checklist of the reasons for stopping taking medication. a significant difference was found between participants in the intervention group and controls in posttest and follow-up scores on drug attitude, insight, and the checklist of the reasons for stopping taking medication.

Table 3. The repeated measures to compare mean on drug attitude, insight, and the checklist.

	M			F			Significant		
	Attitude	Insight	Check list	Attitude	Insight	Check list	Attitude	Insight	Check list
intervention				58/04	1/59	71/97	0/00	0/00	0/00
Pre-test	5/84	5/03	30/87						
Post-test	8/18	12/50	41/68						
Follow-up	7/90	12/28	40/28						
control				58/04	1/59	71/97	0/00	0/00	0/00
Pre-test	5/20	5/57	28/62						
Post-test	5/22	8/94	28/77						
Follow-up	5/02	4/91	28/37						

A linear regression analysis showed, Patient's treatment non-adherence in the past predicts their non-adherence in the future, the t value for treatment adherence was significant

(p<0.001). According to the regression model, patient's treatment adherence in the past predicts their non-adherence in the future. In overall, treatment adherence in the past

predicts 79% and 30% of the total variance of medication adherence and behavior adherence in the future, respectively. The Beta coefficient was also 89 and 56 for medication adherence and behavioral adherence, respectively. In overall, the results of the linear regression analysis indicated that

previous behavioral and medication adherence of the patients in the control group, significantly predicts their treatment adherence pattern in the future. their treatment adherence pattern in the future. (Table 4)

Table 4. Regression analysis for behavioral and medication adherence in the past for the control group.

Variable	Levels of test	m	SD	correlation	significant	R	Adjust R	B	Beta	t	significant
Drug adherence				0/89	0/00	0/89	0/79	0/92	0/89	11/47	0/00
	Pre-test	3/48	1/66								
	Post-test	3/57	1/71								
Behavior adherence				0/56	0/00	0/56	0/30	0/40	0/56	3/96	0/00
	Pre-test	4/17	2/14								
	Post-test	3/82	1/54								

A linear regression analysis showed, Patient's treatment non-adherence in the past predicts their non-adherence in the future, the t value for treatment adherence was significant (p<0.001). In overall, treatment adherence in the past predicts 79% and 30% of the total variance of medication adherence and behavior adherence in the future, respectively. In overall, the results of the linear regression analysis indicated that previous behavioral and medication adherence of the patients in the control group, significantly predicts their treatment adherence pattern in the future. their treatment adherence

pattern in the future.

We used the Pearson correlation coefficient showed a correlation of 0.24 between behavioral and medication treatment adherence in all participants (P<0.04), and a correlation of 0.43 in the intervention group (p<0.01). Therefore, the results indicated a positive relationship between medication and behavioral adherence. also The results indicated a significant difference between patients in the intervention and control groups in the time of readmission. (Table 5)

Table 5. Patients in the intervention group and controls in the number of readmissions.

	Admission in first 2 months	Admission in second 2 months	Admission in third 2 months	No Admission in 6 months	df	significant
intervention	1	15	4	12	3	0/00
control	15	13	0	7	3	0/00

Significant difference was found between patients in the intervention group and controls in the number of readmissions.

In addition, the results showed, drug attitude, insight, job and age have a greater role in explaining non-adherence to treatment. (Table 6)

Table 6. The role of each of the variables in explaining non-adherence to treatment.

variables	Df	f	significant	Partial eta
education	3	2/92	0/03	0/07
marred	2	1/72	0/18	0/03
Sex	3	2/85	0/05	0/04
Age	4	3/90	0/00	0/19
Insight	4	6/64	0/00	0/29
attitude	4	9/39	0/00	0/36
reasons for stopping taking medication	4	2/72	0/03	0/14
job	1	19/45	0/00	0/22

The results showed, drug attitude, insight, job and age have a greater role in explaining non-adherence to treatment.

4. Discussion

We found that a few participants had a good treatment adherence (only 3.4%). It was found that female patients, patients with a high school degree or higher and patients aged older than 30 years had better treatment adherence (p< 0.01).

The study results indicated an increase in posttest scores on drug attitude, insight and the checklist for participants in the intervention group relative to those for controls. In the next step, in a third assessment using the repeated measures ANOVA, significant differences were found between participants in the intervention group and controls in the scores on drug attitude, insight and checklist; this indicated that the effects of the psychoeducation protocol for participants in the intervention group were maintained through the 6-month follow-up, and patients in the intervention group, compared to controls, gained higher scores on drug attitude, insight and the checklist. In other words, the Liberman's psychoeducation protocol had positive effects on the three variables scores, and this effect was maintained through the 6-month follow-up. This finding is consistent with the results of the studies by D'souza et al. (2010), Harvey & Peet (1991), Colom et al. (2003), and Atri et al. (2007). [16, 17, 18].

Another effective factor in the improvement of the patients' scores and their medication and behavioral treatment adherence, and also in the reduction of readmission rate was performing a telephone follow-up (two phone calls a week), and encouraging the patients to have at least one visit per month. This is in line with the some findings [19].

It was found that patients in the intervention group, compared to controls, had a significant reduction in duration of hospitalization. In other words, the protocol led to a longer

remission time, better treatment adherence, and lower number of readmissions, and during the 6-month follow-up, patients in the intervention group were readmitted later than controls. This can also be attributed to attentional effect and a positive expectation about the intervention method.

The results indicated a significant difference between patients in the intervention and control groups in the time of readmission; patients in the intervention group were readmitted later than controls. In fact, during the 6-month follow-up, most readmissions in the intervention group occurred in the 4th to 6th months, but, most readmissions in the control group were in the first three months. this indicates that our psychoeducational intervention led to an improvement in the medication and behavioral adherence of the patients with bipolar disorder, improved their remission, increased the time period between discharge and readmission, and led to less severe symptoms in case of readmission. These results are in line with the findings of Berk et al. (2010) [9], Haddad, Brain, Scott, 2008) [7]. So there were significant difference between patients in the intervention group and controls in admission and their condition at the time of readmission, i.e. variables like insight level, presence of dangerous or severe symptoms, and patients' and their relatives' level of satisfaction. In fact, at the time of readmission, patients in the intervention group were in a better condition than controls who had severe symptoms and were often in need of stronger medications and ECT. Therefore, there was a significant difference between the two groups in patient's condition at the time of readmission.

It was also found that previous treatment adherence of the patients in the control group (those who did not receive any intervention) could significantly predict their treatment adherence in the future; this means that, most probably, a patient's medication and behavioral adherence pattern in the past (whether readmission occurs in the first month or in the first year) would not change automatically. Because patients usually do not develop a better medication or behavioral adherence automatically, and they will have usually the same adherence pattern in the future. The results of the studies by willigan et al. (2010) [20], Colom et al. (2000) [21], are consisted with this finding.

A significant relationship was found between medication and behavioral adherence (p=0.05), but after intervention, a significant relationship was found between the two variables at 0.01 level; this indicates that our intervention led to an improvement in both types of adherence, however, medication treatment was still higher than behavioral treatment. After administering the protocol and the follow-up period, correlation between medication and behavioral adherence, that was lower before the intervention, increased. In other words, adherence to one aspect of treatment has impact on adherence to other aspects of treatment. It was also found that medication adherence was more significant than behavioral adherence, and some patients who faced with these behavioral recommendations for the first time wondered why, despite taking their medications, got sick

again and readmitted to the hospital. But after the intervention, correlation between medication and behavioral treatment increased, and the relationship became significant at 0.01 level, that is, the patients had behavioral adherence in addition to medication adherence, and this led to an improvement in both medication and behavioral adherence, increased the impact of the two types of adherence on each other, and brought the patients closer to the main objective, i.e. remission.

5. Conclusion

The study results indicated the positive effect of drug attitude, insight, and the checklist of the reasons for stopping taking medication on treatment adherence. After administering the psychoeducation protocol to the patients, an increase was found in the scores on drug attitude, insight, and the checklist of the reasons for stopping taking medication, and the improvement was maintained through a 6-month follow-up period. An improvement was also found in patients' adherence patterns in both medication and behavioral adherence; this had positive effects on the number of readmissions. But higher improvements were found in medication treatment adherence relative to behavioral treatment adherence, and this can be attributed to the fact that this protocol is more focused on medication treatment adherence. Based on the findings of the present study, we can conclude that the Liberman's psychoeducation protocol led to significant improvements in drug attitude, insight, and the reasons for stopping taking medication, enhanced treatment adherence, and reduced readmission rate; this conclusion is more based on theoretical grounds, and supports the previous findings.

Finally, we can conclude that using questionnaires and by having short and inexpensive sessions at the time of admission to the hospital, many factors effective in treatment non-adherence can be assessed, and by administering proper protocols to patients in several sessions, and arranging telephone follow-ups and regular monthly visits, many of the problems in terms of treatment adherence can be avoided.

6. Limitations

1. Participant attrition: Some factors, including the symptoms of the disorder, participants' intolerance, lack of motivation, and being tired of hospital condition were effective in the attrition.

2. The study sample was limited to patients of Razi psychiatric hospital.

7. Suggestions

Future studies are suggested to put more focus on behavioral adherence along with medication adherence, work with larger samples, have longer follow-ups, use home visits, and consider other variables that may be effective in treatment adherence of patients with bipolar disorder.

Participants in the present study were selected from one impatient center, therefore, we suggest other researchers to examine these variables in other treatment centers and also in outpatient centers. It is also suggested that, in addition to pharmacotherapy, psychotherapy and psychoeducation be included in the treatment programs of psychiatric hospitals.

Acknowledgements

Conflict of Interest

Chief editor of Science PG, There is no conflict of interest for any of the authors of this manuscript titled "Effective Factors of Non-Adherence and Admission in Bipolar Disorder" (2011123).

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