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Research Article

Are the Prescriptions of Psychiatric Patients Who Repeatedly Attempt Suicide Distinctive? A Study Based on a Survey of Prescription Drug Overdose Patients Admitted for Emergency Medical Care

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ABSTRACT

Objectives: Examining the pharmacotherapy of patients who have attempted suicide by overdose could be useful in developing treatment and suicide prevention plans. We surveyed the drugs taken by psychiatric prescription overdose patients who received inpatient treatment and sought to determine the characteristics of patients who repeatedly attempt suicide.

Methods: Subjects were 116 patients who attempted suicide by overdose with prescription psychiatric drugs and received inpatient treatment at the Intensive Care Unit of the Emergency and Critical Care Center of Teikyo University Hospital from August 2009 to July 2010. We retrospectively surveyed clinical characteristics, including prescriptions prior to hospitalization and psychiatric diagnosis, divided subjects into a first-admission (FA) and repeat-admission (RA) groups, and compared their clinical characteristics.

Results: All subjects were prescribed benzodiazepine-receptor agonists (BZDRAs), whereas antidepressants and antipsychotics were prescribed to 58.6% and 49.1% of subjects, respectively. Emotionally unstable personality disorder, borderline-type (EUPD-B) was found to be significantly more common in the RA group. Comparing prescriptions in the FA and RA groups indicated that the prescribed dosage and prescription rate for antipsychotics were significantly higher for RA group patients.

Conclusion: This study revealed that repeat-admission attempted suicide patients had a significantly higher rate of EUPD-B and were more frequently using antipsychotic prescription drugs. Further, in these patients, more frequent use of antipsychotics is believed to correspond to patient impulsivity. The excessive prescription of BZDRAs is a serious problem requiring urgent measures. Research on the prescriptions for overdose patients may lead to clinically significant findings and should be promoted in the future.

Keywords: Suicide attempt; Overdosing; Benzodiazepine; Antidepressant; Antipsychotic; Emergency medical service; Psychiatric pharmacotherapy

INTRODUCTION

Enhancing our clinical understanding of individuals who attempt suicide and providing appropriate treatment are indispensable tasks in promoting suicide prevention measures [1,2]. Emergency medical services, responsible for treating many individuals who attempt suicide attempt, have an important opportunity to commence or reevaluate the treatment psychiatric patients [3,4]. According to a metanalysis of suicide attempt patients admitted to emergency medical services in Japan [5], these patients comprised 4.7% of all emergency admissions and 52% were overdose patients. This rate indicates that, similar to the U.S. (68%) and the U.K. (78%), overdose is the most common method used by suicidal patients treated by

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the emergency medical services in Japan [5]. However, unlike in the West where opioids are known to be the drugs most commonly used for overdosing, benzodiazepines (BZDs) are reportedly the most frequently used in Japan, accounting for 40.4% of overdoses [6].

There are three clinical points concerning the pharmacotherapy for those who overdose on prescribed drugs. The first relates to whether prescription drugs contribute to the goal of preventing suicide/suicide attempts [7]. Although, barring a small number of cases, there remains insufficient evidence for the suicide prevention effects of pharmacotherapy, it is argued that providing the appropriate pharmacotherapy with a sufficient dosage of antidepressants is useful in preventing suicide [8]. The second point concerns the need to consider the adverse effects of pharmacotherapy, which might heighten the risk of suicide or suicide attempts. For example, it has been indicated that the possibility of an increased risk of suicide should be considered when selective serotonin reuptake inhibitors (SSRIs) are used in young patients [9]. The third point is related to considerations for minimizing the risks in cases where prescription drugs are used to overdose. Overdose with tricyclic antidepressants (TCAs), for example, is frequently seen in individuals who commit suicide [10]. Thus, it is necessary to combat the dangers associated with overdose by all available means, including avoiding the use of drugs with certain toxicity and reducing the amount of prescribed medicine for patients considered to be at high risk of suicide [7].

Although there are many arguments regarding the value of pharmacotherapy for overdose patients such as these, it remains true that an insufficient number of detailed studies are being carried out on the drugs prescribed to patients who attempt suicide by overdose in the setting of the emergency medical services. We surveyed the pre-admission prescriptions of patients who attempted suicide by overdose and were brought to Teikyo University Hospital by emergency transport and received treatment in the Intensive Care Unit and found that the prescribed dosages of benzodiazepine-receptor agonists (BZDRAs) used as anxiolytics and hypnotics by their previous physician were markedly high; moreover, patients who attempt suicide by overdose had high rates of depressive disorder and emotionally unstable personality disorder, borderline-type (EUPD-B) [11]. Further, based on statistics compiled in a nationwide medical database, Okumura et al. [12] indicated that the higher the prescribed dosage of BZDs, the higher is the rate of suicide attempts.

Our goal in this study was to examine the correlations between prescriptions, suicide attempts, and repeated suicide attempts. To this end, we surveyed the prescriptions and suicide attempt histories of overdose patients who received inpatient treatment after emergency transport to the Emergency and Critical Care Center of our hospital and investigated the correlations between these factors. Our findings may prove beneficial in identifying the factors contributing to suicide attempts by overdose with prescription psychiatric drugs and the measures that can be used to reduce the number and severity of such attempts.

SUBJECTS AND METHODS

Subjects

One hundred and eighty-five patients who had attempted suicide by overdose were brought to Teikyo University Hospital by emergency transport in the 1-year period between August 2009 and July 2010. Of these, 169 patients used psychiatric prescription drugs to overdose. The selected subjects assessed in this study were the 116 patients among these who were admitted to the Emergency and Critical Care Center's Intensive Care Unit due to severe disturbance of consciousness or physical complications caused by overdosing. Three of the admitted suicidal patients were excluded from analyses due to our inability to obtain information regarding prescription drugs from their previous physicians.

Teikyo University Hospital is a leading emergency medical facility in the Tokyo metropolitan area, which sees over 12,000 emergency cases each year, including emergency room walk-in patients. Approximately 2,300 patients were admitted to Teikyo University Hospital's Emergency and Critical Care Center during the study period.

Methods

The sex, age, and clinical features [diagnosis (ICD-10), suicide attempt history, and attempt method] of the selected patients were retrospectively surveyed based on medical records. Whether the patient was prescribed medication, including BZDRAs, antidepressants, and antipsychotics, and the respective prescribed dosages, were surveyed from prescription information obtained through medical records sent by fax from the patient's previous physician subsequent to admission. Using this information, the dosages of BZDRAs, antidepressants, and antipsychotics were converted into their equivalents in diazepam, clomipramine, and chlorpromazine, respectively, based on the dose equivalence table presented by Inagaki and Inada [13], and these converted values were used in analyses. In this study, BZDs and non-benzodiazepine benzodiazepine-receptor agonists (non-BZD BZDRAs) were both regarded as BZDRAs. Psychiatric diagnoses were decided in accordance with the WHO International Classification of Diseases (ICD-10) [14] based on consensus among all psychiatrists in a liaison medical care team and by integrating all medical information, including the medical records faxed by the previous physicians. Only the primary diagnosis was used in the analyses performed in the present study.

We divided attempted suicide patients into a first-admission (FA) group and a repeat-admission (RA) group, based on whether there was a history of suicide attempts; then, we compared the age, sex, diagnosis, and other clinical features for each group. Self-destructive behavior for which the patient received physical medical treatment during the course of the current illness was considered a history of attempted suicide for the purposes of our survey.

For both FA and RA groups, we compared the prescription rate and prescribed dosages of BZDRAs, antidepressants, and antipsychotics, as well as for the respective subclass drugs.

For all analyses, we used the software packages of SPSS 24.000 (IBM, 2016). Two-tailed probability was used in analysis of variance (ANOVA) and the Mann – Whitney U test, with a significance level of 0.05. Residual analysis was performed if a significant difference was found for the x^2 test.

This research was carried out with approval from the Teikyo University Ethical Review Board (Approval No. 12-144).

RESULTS

Subjects' clinical features and prescriptions

Table 1 shows the clinical features of the study subjects. Women comprised the majority (76%) of the patients and had a mean age (SD) of 36.9 (12.0) years old. The mean duration of hospitalization was 2.6 (2.0) days with a range of 1–14 days. The primary diagnosis of these subjects was most frequently mood disorder (F3) at 44.8%, followed by personality disorder (F60) at 19.0%. In all cases, the type of personality disorder was EUPD-B. Furthermore, the mean age was lower in personality disorder patients than in other patients [28.0 (5.7) years old vs. 38.9 (12.3) years old ($F_{1,114}$=16.38, $p < 0.001$)].

With regards to the prescriptions obtained from previous physicians, all 116 patients had been prescribed BZDRAs. Among these, 95.7% of patients were prescribed BZDs and 39.7% were prescribed non-BZD BZDRAs. The diazepam equivalent of the daily average prescribed dosage was 27.8 (21.9) mg. Antidepressants were prescribed to 58.6% (68/116) of the patients and the clomipramine equivalent of the average prescribed dosage was 52.7 (70.5) mg. Among the antidepressant prescriptions, 28.4% (33/116) of the patients were prescribed SSRIs and 11.2% (13/116) were prescribed TCAs. For patients with depressive disorders (F32, F33), these rates were 39.1% (18/46) and 19.6% (9/46) respectively. Antipsychotics were prescribed to 49.1% (57/116) of the patients, and among these, second-generation antipsychotic (SGA) prescriptions comprised 35.3%. The chlorpromazine equivalent of the average prescribed dosage for antipsychotics was 121 (233) mg.

With regards to the relationship between diagnosis and prescription drugs, patients with mood disorders (F3) were found to have significantly higher average daily prescribed dosages of antidepressants than other patients [81.4 (80.1) mg vs. 29.4 (51.4) mg (U=794, $p < 0.001$)], whereas patients with psychotic disorders (F2) had higher average daily prescribed dosages of antipsychotics than other patients [426 (354) mg vs. 79 (176) mg (U=113.5, $p < 0.001$)].

Table 1: The sex, age, and clinical features of the patients (N=116) examined in the present study.

Variables	N	%
Sex		
Male	28	24.1
Female	88	75.9
Age		
16-29 years old	39	33.7
30-39 years old	36	31.0
40-49 years old	23	19.8
50-59 years old	11	9.5
≧ 60 years old	7	6.0
Mean age (SD)	36.9 (12.0)	
Diagnosis (ICD-10)		
Psychotic disorders (F2)	14	12.1
Mood disorders (F3)	52	44.8
Neurotic disorders (F4)	19	16.4
Personality disorders (F60)	22	19.0
Other [a]	9	7.8
Suicide attempt history		
No	60	51.7
Yes	56	48.3
Method of most recent suicide attempt		
Psychiatric prescription drug overdose	40	71.4
Psychiatric prescription drug overdose/cutting	7	12.5
Cutting	6	10.7
Jumping	1	1.8
Cold medicine overdose	1	1.8
Stab wound to the neck	1	1.8

[a]Other: Intellectual disability (F70) N=2, Substance use disorder (F1) N=6, Epilepsy (G40) N=1

Comparison of the FA and RA groups of attempted suicide patients

Table 2 shows the characteristics of patients in the FA and RA groups. There were no statistically significant differences with regards to the sex or age of patients in the two groups. Differences in the mean duration of hospitalization were also non-significant [2.6 (2.2) days vs. 2.6 (1.7) days ($F_{1,114}$=0.029, p=0.865)]. A significant correlation was, however, found for psychiatric diagnosis (x^2=20.36, df=4, $p < 0.001$). Residual analysis results indicated that there were significantly more patients with personality disorders in the RA group (adjusted standardized residual=4.4, $p < 0.01$). The method of the previous suicide attempts of patients in the RA group was

overdose with psychiatric prescription drugs for 84% (47/56). In the RA group, 48% (27/56) had previously made just a single suicide attempt, 13% (7/56) had made two past attempts, and 39% (22/56) had made three or more attempts. The period from the most recent suicide attempt to admission was less than 1 month for 37% (11/30) of patients, more than 1 month but less than 6 months for 37%, more than 6 months but less than 1 year for 13% (4/30), and more than 1 year for 13% (range: 3 days to 3 years, median 3 months).

Table 2: Comparison of the clinical features of attempted suicide patients in the first-admission and repeat-admission groups.

Variables	First-admission (FA Group) N=60	Group	Repeat-admission (RA group) N=56	Group
Sex (N, %)				
Male	18	30.0	10	17.9
Female	42	70.0	46	82.1
Age (years)				
Mean age (SD)	37.7 (10.8)		36.0 (13.1)	
Diagnosis (ICD-10) (N, %)[a]				
Psychotic disorders (F2)	8	13.3	6	10.7
Mood disorders (F3)	32	53.3	20	35.7
Neurotic disorders (F4)	13	21.7	6	10.7
Personality disorders (F60)	2[b]	3.3	20	35.7
Other	5	8.3	4	7.1
Prescription frequency, prescribed dosage (mg)				
Benzodiazepine-receptor agonists (N, %)	60	100	56	100
Diazepam equivalent average prescribed dosage (SD)	26.4 (20.2)		29.2 (23.7)	
Antidepressants (N, %)	33	55.0	35	62.5
Clomipramine equivalent average prescribed dosage (SD)	50.9 (80.0)		54.7 (59.3)	
Antipsychotics (N, %)	22	36.7[c]	35	62.5
Chlorpromazine equivalent average prescribed dosage (SD)	114 (256)[d]		128 (209)	

[a]$p < 0.001$, χ^2 test, [b]$p < 0.001$, Residual analysis, [c]$p=0.005$, χ^2 test, [d]$p=0.033$, Mann–Whitney U test

Comparison of prescription rates and prescribed doses in the FA and RA suicide attempt patient groups

As shown in Table 2, no significant differences were found between the FA and RA groups with respect to prescription rate or prescribed dosage of BZDRAs or antidepressants. Similarly, there were no significant differences between the two groups with regards to the prescription rate of BZDs and non-BZD BZDRAs [95% (57/60) vs. 96% (54/56) (χ^2=0.143, df=1, p=0.705), 45% (27/60) vs. 25% (14/56) (χ^2=1.484, df=1, p=0.223) respectively], nor in the prescription rate of SSRIs and TCAs [28% (17/60) vs. 27% (15/56) (χ^2=0.001, df=1, p=0.977)12% (7/60) vs. 11% (6/56) (χ^2=0.25, df=1, p=0.871) respectively].

Compared with the FA group, the prescription rate for antipsychotics was higher (χ^2=7.73, df=1, p=0.005) and the prescribed dosage larger (U=1320.5, p=0.033) in the RA group. The prescription rate for SGAs was also higher in the RA group [45% vs. 27% (χ^2=4.10, df=1, p=0.043)]. There was, however, no significant difference in the antipsychotic prescription rate between patients with and without personality disorders in the RA group [29% (6/21) vs. 40% (14/35), (χ^2=0.747, df=1, p=0.388)].

DISCUSSION

In this study of patients who had attempted suicide and received advanced treatment by emergency medical services due to psychiatric prescription drug overdose, our findings revealed features of the psychiatric diagnoses and prescriptions of patients admitted more than once for emergency medical treatment due to a suicide attempt compared to patients admitted for the first time.

The most common psychiatric diagnosis of subjects who overdosed on prescription medication was mood disorder, followed by EUPD-B, whereas the most common diagnosis for patients who repeatedly attempted suicide was EUPD-B. The importance of mood disorders among the mental illnesses affecting suicide attempt patients has been consistently reported for many years [5]. Further, borderline personality disorder (BPD; the equivalent of EUPD-B in the American Psychiatric Association diagnostic criteria DSM-5) has been detected at a high rate (55%) in structural diagnostic interviews with patients admitted to a psychiatric hospital in Japan as a consequence of suicidal behavior, such as attempted suicide and self-injury. Patients with this condition are reported to have a particularly high frequency of repeat suicide attempts during a 2-year follow-up period [15,16]. This can be determined from the inclusion of a series of suicidal threats or acts of self-harm in the diagnostic criteria for EUPD-B and BPD [14,17].

Apart from antipsychotic medications, we detected no differences between FA and RA patients with respect to the pharmacotherapy being received prior to emergency hospitalization. However, the finding that BZDRAs were prescribed in all cases and that the diazepam equivalent of the dosages substantially exceeded the normal maximum dose of 15 mg/d are serious problems affecting the entire nation. It has been indicated that there are numerous suicide attempts through overdosing on BZDs in Japan [6]. Further, the prescription rate for BZDRAs in Japan is extremely high at 75.3% [18] compared with that of 31.5% in the U.S. [19].

The use of BZDs has previously been linked to suicide and suicide attempts in epidemiological studies [20], and this relationship is considered to be associated with higher levels of impulsivity due to disinhibition as a side effect of BZDs, which can lead to suicide or attempted suicide [7]. Further, the excitement, hyperactivity, and emotional instability that manifest as paradoxical reactions to BZDs Mancuso et al. [21] have also been found to be correlated with acts of self-harm or suicide [22]. Several risk factors for the occurrence of these paradoxical reactions have been identified, including being under evident psychological conflict, a very hostile or aggressive personality, and poor impulse control [21]. It can accordingly be readily hypothesized that administering BZDRAs to EUPD-B or BPD patients who have these characteristics has the potential to promote suicide attempts. In a randomized controlled trial, Gardner and Cowdry [23] demonstrated that administering alprazolam induces disinhibition, suicidal behavior, violence, and excessive emotional release.

It has long been reported that recurrent suicidal behavior is a common feature of EUPD-B and BPD patients [24]. Moreover, the effectiveness of BZDRAs in the treatment of EUPD-B and BPD has been repudiated [25,26]. Thus, clinicians should make every effort to reduce prescriptions of BZDRAs for suicidal patients, particularly to EUPD-B and BPD patients.

A number of measures designed to reduce the number of psychiatric prescriptions, primarily those of BZDRAs, have also been introduced. For example, beginning in 2010, the Japanese Ministry of Health, Labor and Welfare began to issue alerts and warnings concerning the excessive prescription of psychiatric drugs; further, in 2012, a plan to deal with the subtraction of medical payments for excessive psychiatric drug prescriptions was adopted. A survey of the policies aimed at curtailing the prescription of BZDs in other countries and their effects revealed that there has been no reduction in prescriptions in the U.S. (policy introduced in 2006) [27] or in France (policy introduced in 2012) [28], although a reduction has been reported in The Netherlands (policy introduced in 2009) [29]. In order to verify the effects of Japan's policies for curtailing the prescription of BZDRAs, we plan to carry out a study comparing the present results that characterize the situation prior to the introduction of these policies, and recent data on the prescriptions of patients hospitalized for attempting suicide with an overdose of psychiatric prescription drugs.

In the present study, we found that antidepressants were prescribed significantly more often for mood disorders, which we believe reflects the efforts of physicians to remedy these disorders. However, we failed to identify any differences in the way these drugs were used among patients with or without a history of attempted suicide, although we assume that the multiple possible antidepressant effects of ameliorating depressive symptoms, including suicidal ideation or, contrary to assumed effects, triggering of suicidal behavior in some cases [7] might affect the results. Moreover, we found no evidence to suggest a decrease in the prescription rate of TCAs, which have high toxicity when taken excessively, for patients with repeated suicide attempt. In line with these findings, epidemiological research has indicated that the dose of antidepressants has no apparent effect on the recurrence of suicide attempts [12] and has been unable to confirm an adverse effect of antidepressant use on suicide rates [20].

Differences with respect to the history of suicide attempts were found in terms of the prescription rate and prescribed dosage for antipsychotics. This phenomenon is assumed to be related to the use of antipsychotics to control impulsivity in patients who have attempted suicide [7]. Further, although there is currently only limited evidence, it appears that the use of antipsychotics, particularly SGAs, is recommended for personality disorder patients with high impulsivity [25] and SGAs are used at a high frequency in BPD patients in practical clinical settings [30]. The findings regarding antipsychotics revealed by the present study are considered to reflect this situation.

Given that the present study was based on a retrospective research design, it has several limitations. Most importantly, we assume there to be bias in the clinical evaluations, including diagnoses, and thus it is necessary to consider this problem when interpreting the study's findings. Further, because this was a cross-sectional study, we cannot draw conclusions regarding

the causal relationships indicated by the findings. The potential effects of these limitations will require confirmation in future studies.

CONCLUSION

The noteworthy findings of this study regarding the prescriptions for patients who attempted suicide by overdose were that BZDRAs were prescribed in every case, and at high doses, and that patients repeatedly admitted for treatment by emergency services with a history of attempted suicide were diagnosed with EUPD-B at a high rate. Thus, clinicians should make every effort to reduce the prescription of BZDRAs for patients with a perceived high risk of committing suicide, as well as patients diagnosed with EUPD-B or BPD. Additionally, we found that repeat-admission patients with a history of attempted suicide were often using antipsychotics, presumably prescribed for the treatment of heightened impulsivity, which is considered to be a factor in attempting suicide. Investigating the effectiveness of antipsychotics needs to be the focus of future research.

The findings of this research indicate that studies on the drugs prescribed for attempted suicide patients will useful in developing new treatment approaches for overdose patients and reducing their suicidal tendencies. In the future, it will be necessary to continue research on the inter-relationships between psychiatric prescriptions and treatments for suicidal patients.

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