Observational Study

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Relationship between mental disorders, psychotropic drugs, and constipation in psychiatric outpatients

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Abstract

Constipation has been reported to be more common in patients with mental disorders than in the general population. However, its relationships with psychiatric diagnosis, medication, age, and sex have not been fully identified.

A total of 875 patients from the outpatient department were included in the study. As a retrospective observational study, the psychiatric diagnoses and psychotropic medications were examined based on the medical charts. Fecal conditions, including problems with defecation, abdominal pain, sense of incomplete evacuation, use of laxatives, frequency of defecation, and stool characteristics according to the Bristol Scale, were investigated.

The study included 368 males and 507 females, with median ages of 48 and 52 years, respectively. The most common psychiatric diagnoses were depressive disorders (33%), followed by anxiety disorders (19%). Females had significantly higher rates of problems with defecation and laxative use than males ($P < .001$, $P < .0001$, respectively). The frequency of laxative use increased significantly with age ($P < .0001$). The multivariate analyses revealed the close relationship between hypnotics and problems of defecation and that between hypnotics, antipsychotics, and laxative use.

In psychiatric outpatients, females had significantly higher rates of problems with defecation and laxative use than males. The use of laxatives significantly increased with age. Problems with defecation were significantly more common in patients taking hypnotics and laxative use was significantly more common in patients taking hypnotics and antipsychotics.

Abbreviations: DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, 5th edition, GAF = Global Assessment of Functioning, ROC = receiver operating characteristic.

Keywords: antipsychotic, bowel habit, constipation, hypnotic, mental disorder, psychotropic drug

1. Introduction

Constipation is one of the most common physical complaints and is reported to occur in about 2% of the general population in the United States[1] and 2.5% in men and 4.3% in women in Japan.[2] The frequency of constipation in patients with mental disorders is reported to be 20%[3] or 37%,[4] which is much higher than that in the general population. The causes of constipation that have been identified include decreased activity due to mental disorders, obesity, lack of dietary fiber, insufficient water intake, and taking psychotropic drugs.[5] However, the frequency of constipation due to mental disorders and the mechanism of constipation, including the relationship with the administered drugs, have not been fully investigated. Thus, to understand the actual situation of constipation, which is one of the most common physical symptoms of psychiatric outpatients, we investigated the relationship between problems of defecation, actual defecation (stool frequency and form), and the use of laxatives, and psychiatric diagnoses, the degree of social functioning, and the psychotropic drugs administered.

2. Methods

2.1. Subjects

We conducted a retrospective study of consecutive patients who visited Akebono Clinic (Ishinomaki City, Japan) between February and October 2019. Of our outpatients, 875 patients who provided general consent for their clinical information to be used for research purposes were included in the study.

2.2. Data collection

Problems with defecation, abdominal pain, sense of incomplete evacuation, use of laxatives, frequency of defecation, and stool characteristics according to the Bristol Scale (Bristol Stool Form Scale)[6] were investigated based on a self-administered questionnaire. The details of sex, age, psychiatric diagnoses, medications, and degree of social functioning were collected from the medical charts.

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Psychiatric diagnoses were determined according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5).[7] Patients with comorbid psychiatric disorders were classified under the category of their main psychiatric disease.

Antipsychotics, antianxiety drugs, antidepressants, anticholinergics, and hypnotics were distinguished as they were the most commonly prescribed medications in our clinic. The number of psychotropic drugs taken was also investigated. Social functioning was assessed according to the Global Assessment of Functioning (GAF).[8]

2.3. Statistical analyses

JMP (version 13.0; SAS Institute, Cary, NC) was used for data collation, statistics, and analyses. Student *t* test, Fisher exact test (2-sided), and the chi-square test were used for univariate analysis of each factor, and $P < .05$ was used to screen for the possible correlation factors with statistical significance under a single-factor action. Multivariate logistic regression analysis was used to screen for the possible correlation factors after univariate analysis, with $P < .05$ considered as statistically significant. The cutoff value for patient age was calculated by receiver operating characteristic (ROC) curves in which laxative use was considered a positive result.

This study was conducted in accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects and with the approval of the Japanese Association of Neuro-Psychiatric Clinics (No. 2020-2).

3. Results

The study subjects were 875 patients (368 males and 507 females), with a median age of 48 years for males and 52 years for females. Of the males, 65% were in their 30s to 50s; of the females, 49% were in their 30s to 50s and 39% were over 60.

As shown in Figure 1, the most common psychiatric diagnoses were depressive disorders, followed by anxiety disorders, trauma- and stress-related disorders, and neurodevelopmental disorders. Overall, 33% had problems with defecation and 18% used laxatives.

Table 1 shows the relationships between clinical characteristics, psychotropic medications, problems with defecation, and laxative use by univariate analyses. Females had significantly higher rates of problems with defecation and laxative use than males ($P < .001$, $P < .0001$, respectively). Laxative users were significantly older than nonusers ($P < .0001$). While the frequency of defecation problems was about 30% in all age groups, the frequency of laxative use increased significantly with age ($P < .0001$; Fig. 2).

While the frequency of defecation problems was not different among psychiatric diagnoses, the frequency of laxative use was different ($P = .045$). Problems with defecation were significantly more common among patients taking hypnotics ($P = .024$) and laxative use was significantly more common among patients taking hypnotics and antipsychotics ($P < .0001$, $P = .014$, respectively). The frequency of laxative use was 14% among patients taking <3 psychotropic drugs and 23% among patients taking 3 or more psychotropic drugs ($P = .0006$). However, there was no relationship between problems with defecation and the number of medications.

There was no significant relationship between social functioning assessed by GAF, problems with defecation, and laxative use. The stool form was reported in the range of types 3 to 5 of the Bristol Scale in 86% of the patients.

Table 2 shows the relationships between clinical characteristics, psychotropic medications, problems with defecation, and laxative use by multivariate analyses. The cutoff value for patient age was set at 53 years based on the ROC curves in which laxative use was considered a positive result. Problems with defecation were significantly more common in females and in patients taking hypnotics. Laxative use was significantly more common in females, older patients, those with neurodevelopmental disorders, those with somatic symptoms and related disorders, and those taking hypnotics or antipsychotics.

4. Discussion

The Rome Criteria for functional constipation have been widely used internationally as diagnostic criteria for constipation.[9] The 2017 Japanese Guidelines for Chronic Constipation also incorporate the Rome IV criteria, such as frequency of defecation, hard stool, straining during defecation, the persistent sense of incomplete evacuation, and the persistent sense of difficulty in defecation, as the diagnostic criteria for chronic constipation.[10] However, in actual clinical practice, the symptoms of constipation reported by patients vary, and the prevalence of constipation varies depending on the definition of constipation.[1,2] In addition, although the frequency of constipation

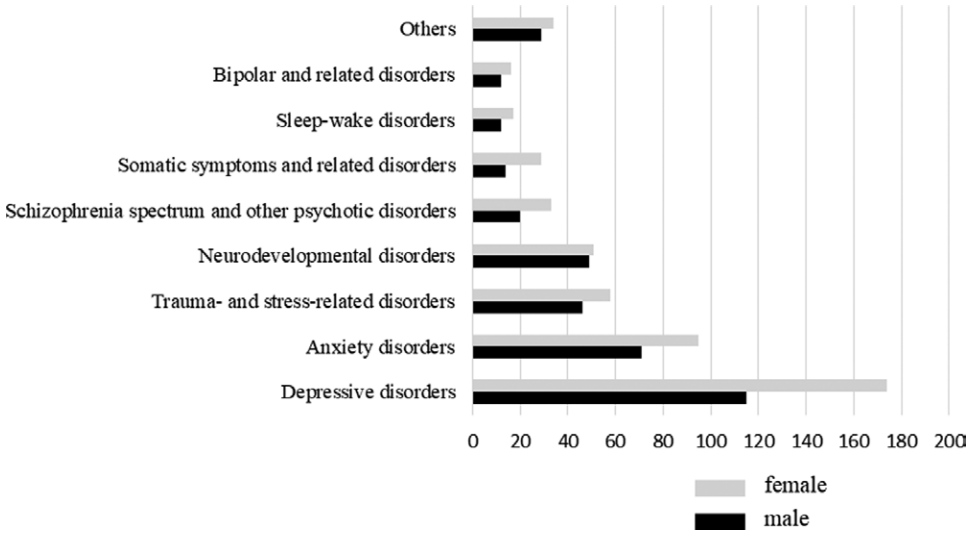

Figure 1. Patients' psychiatric disorders.

Table 1

Relationships between clinical factors and problems of defecation, laxative use by univariate analyses.

	Problems of defecation					
	Present	Absent	*P* value	Laxative users	Laxative nonusers	*P* value
Sex						
Male	88 (27%)	243 (73%)	<.001	33 (10%)	295 (90%)	<.0001
Female	175 (38%)	286 (62%)		110 (24%)	340 (76%)	
Age (yr)						
Mean ± SD	51.1 ± 17.5	50.0 ± 16.8	.8	60.7 ± 16.3	47.7 ± 16.0	<.0001
Median	–51	–48		–62	–46	
Psychiatric diagnoses						
Depressive disorders	100 (37%)	169 (63%)	0.63	56 (21%)	213 (79%)	.045
Anxiety disorders	43 (28%)	110 (72%)		23 (15%)	126 (85%)	
Trauma- and stress-related disorders	27 (29%)	66 (71%)		9 (10%)	85 (90%)	
Neurodevelopmental disorders	32 (39%)	51 (61%)		14 (17%)	67 (83%)	
Schizophrenia and other psychotic disorders	15 (29%)	36 (7%)		11 (24%)	35 (76%)	
Somatic symptoms and related disorders	14 (35%)	26 (65%)		12 (31%)	27 (69%)	
Sleep–wake disorders	8 (30%)	19 (70%)		8 (30%)	19 (70%)	
Bipolar and related disorders	8 (31%)	18 (69%)		2 (8%)	23 (92%)	
Others	12 (34%)	23 (66%)		6 (18%)	28 (82%)	
Psychotropic drugs						
Hypnotics						
Yes	139 (37%)	233(63%)	0.024	89 (24%)	275 (76%)	<.0001
No	123 (30%)	293(70%)		53 (13%)	358 (87%)	
Antipsychotics						
Yes	53 (37%)	89 (63%)	0.25	35 (26%)	101 (74%)	.014
No	209 (32%)	437 (68%)		107 (17%)	532 (83%)	
Antianxiety drugs						
Yes	149 (34%)	287 (66%)	0.54	89 (21%)	345 (79%)	.08
No	113 (32%)	239 (68%)		53 (16%)	288 (84%)	
Antidepressants						
Yes	159 (34%)	314 (66%)	0.79	92 (20%)	378 (79%)	.26
No	103 (33%)	212 (67%)		50 (16%)	255 (84%)	
Anticholinergics						
Yes	7 (32%)	15 (68%)	0.89	6 (27%)	16 (73%)	.27
No	255 (33%)	511 (67%)		136 (18%)	616 (82%)	
Antiepileptic drugs						
Yes	22 (29%)	53(71%)	0.45	10 (17%)	58 (83%)	.41
No	240 (34%)	473(66%)		132 (23%)	575 (77%)	
Number of psychotropic drugs						
≤2	129 (30%)	297 (70%)	0.068	56 (14%)	360 (86%)	.0006
≥3	132 (37%)	228 (63%)		82 (23%)	271 (77%)	
GAF						
≤30	15 (38%)	25 (62%)	0.1	11 (31%)	25 (69%)	.11
31–60	150 (36%)	266 (64%)		69 (17%)	344 (83%)	
60<	82 (29%)	205 (71%)		54 (19%)	229 (81%)	

GAF = Global Assessment of Functioning (American Psychiatric Association, 1994), SD = standard deviation.

is said to be high in patients with mental disorders,[3] it has been reported that fewer of these patients complain of constipation even when they are constipated due to the nature of the mental disease itself.[4] Thus, in order to understand the actual status of constipation in patients with mental disorders, we must keep these points in mind, including the definition of constipation.

In the present study, we used a self-administered questionnaire, which was designed to be as easy and simple as possible for patients with mental disorders to understand, and investigated problems with defecation, laxative use, and stool characteristics according to the Bristol Scale to provide as objective an assessment as possible.

The prevalence of constipation in the general population varies depending on its definition[1,2]: if chronic constipation is defined as hard stools, straining, and/or < 3 stools per week, >25% of the time, the prevalence is 17.4%.[11] The prevalence of chronic constipation according to the Rome III criteria was reported to be 24.0%, while the pooled prevalence was 15.3% in studies using Rome I criteria, 11.2% in studies that used Rome II criteria, 10.4% in those that used Rome III criteria, and 10.1% when Rome IV criteria were used.[12,13]

The male-to-female ratio was reported to be 1:2.2, and the prevalence increased in those aged 50 years and above and sharply in those aged 70 years and above.[14] In the present study, the frequency of laxative use was significantly more common in females and increased significantly with age. However, there was no association between problems with defecation and age.

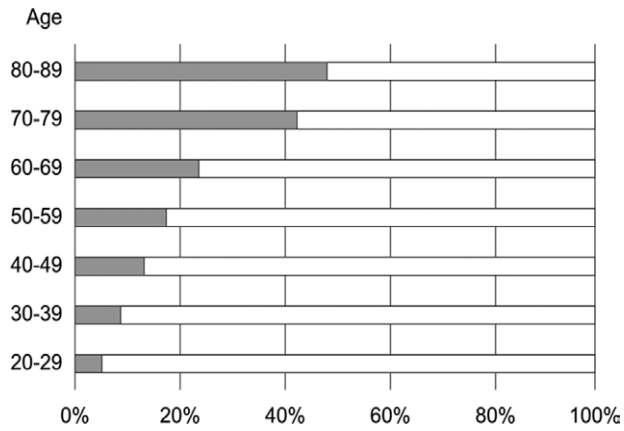

Figure 2. Frequency of laxative use by age group. Solid column: laxative users. Hollow column: laxative nonusers.The frequency increases with age ($P < .0001$). Patients in their teens and 90s were excluded due to small sample size.

It has been suggested that childbirth is one of the most common reasons for the high rate of laxative use in females, and an increase in the number of drugs taken, decreased activity, and decreased defecation urgency are reasons for the high rate of laxative use in older adults.[15,16]

Since physical inactivity has been suggested as a risk factor for constipation,[17] it is reasonable to assume that improving the severity of mental disorders and inactivity will lead to improvement in constipation. The relationship between constipation and the severity of mental disorders has been reported in autism spectrum disorders.[18] While the GAF is one of the scales to rate psychological, social, and occupational functioning of individuals with mental disorders,[19] there was no relationship between problems with defecation, laxative use, and psychological, social, and occupational functioning rated by the GAF in the present study. It is necessary to investigate the relationship between constipation and the severity of mental disorders assessed using other rating scales for depression and anxiety symptoms.

In the present study, problems with defecation were significantly more common in patients taking hypnotics and laxative use was significantly more common in patients taking hypnotics and antipsychotics. It has been reported that constipation occurs frequently as a side effect of antipsychotic medication,[20] especially in patients receiving clozapine, in which the frequency of constipation is reported to be as high as 31.2% and 54.5%.[5,21] In our study, the frequency of laxative use was significantly higher (26%) in patients on antipsychotic medication. It has

Table 2

The relationships between clinical characteristics, psychotropic medications, problems with defecation, and laxative use by multivariate analyses.

	Problems of defecation			Laxative use		
	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Sex						
Male	1.00	Reference		1.00	Reference	
Female	1.70	1.25–2.32	<.001	2.70	1.72–4.22	<.001
Age (yr)						
<53				1.00	Reference	
≧53				3.95	2.54–6.12	<.001
Psychiatric diagnoses						
Depressive disorders				4.47	0.92–21.81	.064
Anxiety disorders				4.68	0.92–23.92	.064
Trauma- and stress-related disorders				3.18	0.57–17.69	.186
Neurodevelopmental disorders				6.84	1.29–36.27	.024
Schizophrenia and other psychotic disorders				2.79	0.53–14.72	.227
Somatic symptoms and related disorders				7.67	1.36–43.46	.021
Sleep-wake disorders				5.74	0.94–35.15	.059
Bipolar and related disorders				1.00	Reference	
Others				3.58	0.59–21.58	.164
Psychotropic drugs						
Hypnotics						
Yes	1.42	1.05–1.92	.021	1.67	1.03–2.71	.038
No	1.00	Reference		1.00	Reference	
Antipsychotics						
Yes				2.27	1.25–4.14	.007
No				1.00	Reference	
Number of psychotropic drugs						
≦2				1.00	Reference	.573
≧3				1.15	0.71–1.88	

CI = confidence interval.

been reported that there is a significant association between hypnotics and constipation in inpatients with internal medicine and cardiovascular diseases,[22] suggesting that constipation may occur as an adverse effect of hypnotics. Since antianxiety drugs that belong to the same benzodiazepine class showed no significant association with laxative use, it is necessary to carry out further investigation into the difference in constipation frequency among different types of hypnotics. Sleep disturbance is one of the common symptoms found in various mental disorders. Bidirectional associations between depression, anxiety, and sleep disturbance have been reported.[23,24] Therefore, treatment of constipation may improve sleep disturbance and other mental disorders, such as depression and anxiety.

One of the limitations of the present study is that it did not take into account the effects of mental disorders because the analysis was conducted based only on the primary psychiatric diagnoses.

The present study revealed a close relationship between the laxative use and mental disorders and medications, but there are few reports investigating the mechanism and the relationship between psychiatric disorders and constipation up to now. We would like to proceed with further prospective studies on the relationship between constipation and mental disorders, including insomnia, and the effects of constipation treatment on mental disorders.

5. Conclusions

In psychiatric outpatients, females had significantly higher rates of problems with defecation and laxative use than males. Laxative use significantly increased with age. Problems with defecation were significantly more common in patients taking hypnotics and laxative use was significantly more common in patients taking hypnotics and antipsychotics.

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