Prescribing Patterns in Child and Adolescent Outpatient Psychiatry: A Retrospective Cohort Study of Prescriptions in the First Year

Keitaro KIMOTO, Kyuta HANAWA, Syunya TAKASE, Yuki TAKAHASHI, Natsuru WATANABE, Fumiaki AKAMA, Yuichi ONISHI, Katsunaka MIKAMI and Kenji YAMAMOTO

Department of Psychiatry, Tokai University School of Medicine

(Received June 13, 2023; Accepted August 14, 2023)

Objective: Recently, excessive and off-label prescribing of psychotropic drugs for children and adolescents have become a problem. Child and adolescent psychiatric patients receive treatment in many departments and department-specific psychotropic drug use has not been analyzed. We surveyed prescriptions for child and adolescent psychiatric outpatients during their first year of treatment.
Methods: The participants were 302 patients, 15 years or younger, who made their first visit to the outpatient psychiatry department of Tokai University Hospital from September 1, 2015 to September 1, 2016. Prescription details and patient profiles were retrospectively investigated using medical records.
Results: Medication was prescribed for 20.9% of patients (63/302) with the prescription rate increasing with age. Psychotropic drugs were prescribed for 15.6% of patients (48/302), with attention-deficit/hyperactivity disorder (ADHD) medications being most frequently prescribed (20 cases). Other than psychotropic drugs, iron pills (25 cases) and herbal medicines (21 cases) were prescribed frequently.
Conclusions: The pharmacotherapy and psychotropic prescription rates were low. This may be due to the use of non-pharmacological interventions and the lack of inpatient facilities. With the publication of guidelines for pharmacotherapy in child psychiatry in Japan, measuring the patterns of psychotropic drug prescription in children and adolescents is important, and would make treatment more transparent.

Key words: adolescent, child, prescribing, psychiatry, psychotropic

INTRODUCTION

In a report by Giannakopoulos *et al*. on pharmacotherapy in child and adolescent psychiatric patients, the prescription of psychotropic drugs for psychiatric patients aged 6–17 years increased dramatically between 1990 and 2010 [1], and there was a fear of overmedication. In a survey on psychotropic prescriptions for children and adolescents in Japan, which was part of a survey of outpatients aged 18 years or younger in a social medical practice, a comparison between 2002–2004 and 2008–2010 showed an increase in prescription odds for attention-deficit/hyperactivity disorder (ADHD) drugs and antipsychotic drugs [2], indicating an increasing trend in the prescription of psychotropic drugs for children and adolescents with mental illness. However, these data are not compared by department, and include the numbers of prescriptions given in pediatrics, psychosomatic medicine, and general psychiatry, in addition to specialist child and adolescent outpatient psychiatry; and therefore, do not reflect the actual prescribing practices of child and adolescent psychiatrists.

The system of medical care for patients with child and adolescent psychiatric disorders in Japan is under-developed and varies considerably from region to region. In recent years, the number of medical institutions specializing in child psychiatry and child and adolescent psychiatry have gradually increased, but there is little basic data on the type of pharmacotherapy provided in these institutions. Therefore, we conducted a survey to clarify the actual prescribing practices for first-time patients of an outpatient psychiatric department specializing in child and adolescent psychiatry.

MATERIALS AND METHODS

Overview of the outpatient clinic for children and adolescents, Department of Psychiatry, Tokai University Hospital

Tokai University Hospital is in Isehara City in the midwestern part of Kanagawa Prefecture. Isehara City, Atsugi, Hadano, and Hiratsuka are nearby cities from which the hospital receives most of its patients. Isehara City has a total population of approximately 102,000 with approximately 13,000 persons aged 0 to 15 years; Hadano City has a total population of approximately 160,000 and approximately 19,000 persons aged 0 to 15 years; Hiratsuka City has a total population of approximately 258,000 and approximately 32,000 persons aged 0 to 15 years; Atsugi City has a total population of approximately 226,000 and approximately 30,000 persons aged 0 to 15 years (all values are given as of November 2022 from each city office website).

From its inception, the psychiatry department has had two divisions, adult and child psychiatry. Since the psychiatric ward was closed in 2005 with the opening

Keitaro KIMOTO, Department of Psychiatry, Tokai University School of Medicine, 143 Shimokasuya, Isehara, Kanagawa 259-1193, Japan
Tel: +81-463-93-1121 Fax: +81-463-94-5532 E-mail: k.kimoto@tokai-u.jp

Table 1 Details of prescribed drugs

Antipsychotic drugs	**Chinese Medicine (Kampo Medicine)**
aripiprazole	Goshuyoto extract granules
quetiapine	Keishikaryukotsuboreito
risperidone	Keishikashakuyakudaioto
Antidepressants	Ninjin'yoeito granules
amitriptyline	Saikokaryukotsuboreito
trazodone	Shokenchuto granule
ADHD medication	Yokukansan granule
atomoxetine	Yokukansankachimpihange extract granules
methylphenidate	**Iron preparations**
Hypnotics/sleeping pills	ferrous fumarate
brotizolam	sodium ferrous citrate
flunitrazepam	**Antihistaminergic drugs**
ramelteon	chlorpheniramine
rilmazafone	hydroxyzine
Anxiolytics	**Others**
alprazolam	acetaminophen
bromazepam	dextromethorphan
clotiazepam	lamotrigine
	midodrine

of a new hospital, we no longer provide inpatient psychiatric care, and since 2006 we have shifted to psychiatric care centered on liaison psychiatry and outpatient treatment. In the children's department, liaison psychiatry and outpatient treatment are the main activities. In addition, the department also provides services as commissioned physicians for educational institutions, such as child guidance centers, rehabilitation facilities, and government agencies.

In the outpatient clinic for children and adolescents, initial and follow-up outpatient consultations are conducted 5 days a week for children and adolescents between the ages of 0 and 15 years, and the number of initial outpatient consultations is approximately 350 per annum. The number of first-time outpatients is approximately 350 per year. Cases that require hospitalization at the time of the first outpatient visit or that deteriorate during the outpatient program are referred to an affiliated psychiatric hospital for continued treatment.

Study design and participants

This was a retrospective cohort study. The total number of participants was 302 patients aged 15 years or younger who made their first visit to the outpatient department of psychiatry at Tokai University Hospital during the 1-year period from September 1, 2015, to September 1, 2016. Each patient's age and sex, psychiatric diagnosis at first visit, area of residence, presence or absence of a letter of referral, place of referral, outcome 1 year after the first visit, presence or absence of drug therapy during the first year after the first visit, and any prescription details, were retrospectively analyzed in the outpatient clinic records.

The reason why the survey period was set at 1 year after the initial diagnosis was because we considered 1 year to be the period during which pharmacotherapy is initiated after the pathology is understood and environmental adjustments are made. For child and adolescent psychiatric disorders other than the acute phase of the schizophrenia or severe depression, it is recommended in the guidelines that pharmacotherapy be administered after understanding the pathophysiology and making environmental adjustments [3]. If 1 year has passed since the initial diagnosis, it is considered that the pathophysiology has been understood and environmental adjustments have been made to the possible extent.

Psychotropic drugs were defined based on "Today's Therapeutics" [4] and previous studies [2] (Table 1). The three mood stabilizers, carbamazepine, lamotrigine, and sodium valproate were defined as mood stabilizers in the absence of a diagnosis of epilepsy.

For statistical purposes, when coexisting diagnoses were present, the same participant was classified into multiple diagnostic categories and the total number of diagnoses was used for statistical processing. Welch's t-test was used for age. Comparison of the ratio of the number of diagnoses to the number of cases with and without prescriptions was performed using the Fisher's direct establishment test and χ^2 test, respectively. Comparisons of the with-prescription and without-prescription groups for items other than diagnoses were made using the χ^2 test, and residuals were analyzed when the χ^2 test showed a significant difference.

Ethical considerations

Approval to conduct this clinical study was obtained from the Clinical Research Review Committee of Tokai University Hospital (Approval No. 17R-079). As this was a retrospective cohort study using only medical information, a poster about the content of the study was presented in the outpatient clinic as an opt-out procedure.

RESULTS

Patient profiles (Table 2)

Of the 302 first-time patients, 205 (67.9%) were male and 97 (32.1%) were female. The mean age (standard deviation) was 8.3 (3.8) years. When the eligible patients were divided into the following age groups: 0–5, 6–10, and 11–15 years, the highest number of patients in "all cases" and "with-prescription" were in the 6–10 year age group. Sixty-three patients (20.9% of all

Table 2 Patient profiles comparing those with and without prescriptions

Number of persons (%)	All cases 302	With prescription 63 (20.9)	No prescription 239 (79.1)	Residual analysis p value
Sex Male (%)	205 (63.8%)	36 (57.1%)	169 (70.7%)	$p < 0.05$
Age Mean (SD)	8.3 (3.8)	10.2 (3.4)	7.7 (3.8)	$p < 0.01$
Age-group				
Number of prescriptions (%)	302	63 (20.9)	239 (79.1)	
[ ] Number of psychotropic prescriptions		[48]		
prescriptions				
0～5 yrs	88	5 (5.7)	83 (94.3)	$p < 0.01$
		[5]		
6～10 yrs	156	35 (22.4)	121 (77.6)	
		[29]		
11～15 yrs	58	23 (39.7)	35 (60.3)	$p < 0.01$
		[14]		
Initial psychiatric diagnosis				
〔ICD-10*〕				
F4	81	22	59	
F8	175	26	149	
F9	35	11	24	
Other (F3, F5, F7)	6	4	7	
Total	302	63	239	
With a letter of introduction	194	42	152	
Referral source				
Other departments within this hospital	30	8	22	
Medical institutions other than this hospital	117	27	90	
Government, schools, kindergarten	47	7	40	
Total	194	42	152	
Outcome				
Out-patient clinic of this hospital	154	54	100	$p < 0.01$
End to medical care	130	6	124	$p < 0.01$
Other (hospital transfer, patient-initiated withdrawal of care)	18	3	15	
Total	302	63	239	

*) F3 indicates mood disorders; F4, neurotic disorders, stress-related and somatoform disorders; F5, behavioral syndromes associated with physiological disturbances and physical factors; F7, mental retardation; F8, disorders of psychological development; and F9, behavioural and emotional disorders with onset usually occurring in childhood and adolescence.

cases) were treated with medication during the 1-year study period from the first visit, and the number of patients prescribed psychotropic drugs (ADHD medications, antipsychotics, anxiolytics, antidepressants, mood stabilizers, and sleeping pills), excluding iron pills, anti-allergy drugs, and Chinese medicine, was 48 (15.9% of all cases).

Comparison of the "with-prescription" and "without-prescription" groups (Table 2)

Age and sex

The mean age (standard deviation) was 10.2 (3.4) years in the "with-prescription" group and 7.7 (3.8) years in the "without-prescription" group. Comparing by sex, 36 (57.1%) of the patients with prescriptions and 169 (70.7%) of the patients without prescriptions were male, and the proportion of males was significantly higher in the "without-prescription" group ($\chi^2 = 4.21$, $df = 1$, $p = 0.040$).

Age-specific

When the participants were divided into three age groups (0–5, 6–10, and 11–15 years), there was a trend toward an increase in both the total prescription rate and the psychotropic drug prescription rate during the 1-year study period from the initial visit. A significant difference was found when comparing the "with-prescription" and "without-prescription" groups (Yate's $\chi^2 = 22.825$, $df = 2$, $p = 0.000$), and the results of the residual analysis showed that a larger proportion of the 0–5-year-olds were "without-prescription" and a larger proportion of the 11–15-year-olds were "with-prescription".

In terms of prescriptions for psychotropic medications (ADHD medications, antipsychotics, antianxiety medications, antidepressants, mood stabilizers, and sleeping pills), five cases (5.7% of cases aged 0–5 years), 29 cases (18.6% of cases aged 6–10 years), and 14 cases (24.1% of cases aged 11–15 years) had pre-

Table 3 Total number of prescriptions by psychiatric diagnosis at initial visit

		F3	F4	F5	F7	F8	F9	Total
Number of cases with prescriptions		3	22	1	0	26	11	63
Total number of prescriptions (%)	ADHD medication	0	3	0	0	7	10	20 (19.2)
	Antipsychotics	0	1	1	0	6	1	9 (8.7)
	Anxiolytics	2	3	1	0	1	0	7 (6.7)
	Antidepressants	1	1	0	0	1	0	3 (2.9)
	Hypnotics	0	6	0	0	3	0	9 (8.7)
	Kampo/Chinese medicine	1	8	0	0	10	2	21 (20.2)
	Iron preparations	1	12	0	0	10	2	25 (24.0)
	Antihistaminergic drugs	0	2	0	0	2	2	6 (5.8)
	Others *	0	4	0	0	0	0	4 (3.8)
	Total number of prescriptions	5	40	2	0	40	17	104 (100)

*) Others include acetaminophen, dextromethorphan, lamotrigine, and midodrine.

scriptions.

Psychiatric diagnosis at initial visit

Initial psychiatric diagnoses were classified using the following two-digit ICD-10 codes (The ICD-10 Classification of Mental and Behavioral Disorders) [5] codes: F0, organic, including symptomatic, mental disorders; F1, mental and behavioral disorders due to psychoactive substance use; F2, schizophrenia, schizotypal, and delusional disorders; F3, mood disorders; F4, neurotic disorders, stress-related and somatoform disorders; F5, behavioral syndromes associated with physiological disturbances and physical factors; F6, disorders of adult personality and behavior; F7, mental retardation; F8, disorders of psychological development; and F9, behavioral and emotional disorders with onset usually in childhood and adolescence. The highest number of psychiatric diagnoses was F8 with 175 cases, followed by F4 with 81 cases, F9 with 35 cases, and others (F3, F5, F7). There was no significant difference between the "with-prescription" and "without-prescription" groups in terms of psychiatric diagnoses at the initial visit.

Referral letter and referral source

The number of cases with a letter of referral was 194, accounting for 64.2% of the total. The most common referral source was "medical institutions other than this hospital" (117 cases), followed by "government agencies, schools, kindergartens," etc. (47 cases). The presence or absence of a referral letter and the referral source were compared between the "with-prescription" and "without-prescription," groups but no significant differences were found.

Outcomes

Comparison of outcomes between the "with-prescription" and "without-prescription" groups showed a significant difference (Yate's $\chi^2 = 37.801$, $df = 3$, $p = 0.000$), and analysis of residuals showed more patients attended our clinic "with-prescription" and more patients attended the final examination "without-prescription".

Psychiatric diagnoses and prescribed medications at the initial visit (Table 3)

Table 2 shows the details of the drugs actually prescribed in the "with-prescription" cases. In terms of total prescriptions, 40 F4 and 40 F8 cases had prescriptions, followed by 17 F9 cases, 5 F3 cases, and 2 F5 cases.

The most common prescriptions for F4 were herbal medicines and iron pills (12 and 8 prescriptions, respectively), followed by sleeping pills (6 prescriptions); for F8, herbal medicine and iron pills were prescribed in 10 cases, followed by antipsychotic drugs in 6 cases and sleeping pills in 3 cases; for F9, ADHD medications were prescribed in 7 cases, followed by herbal medicine in 10 cases. For F3, two prescriptions were for anxiolytics, and one each for antidepressants, Chinese herbal medicine, and iron pills.

DISCUSSION

In order to clarify prescription patterns in child and adolescent psychiatric outpatient clinics, a survey was conducted regarding the content of prescriptions during the 1-year period from the time of the initial visit. The results showed that: (1) medication was prescribed for 20.9% of all patients (63/302 cases) during the 1-year period from the initial visit, with the prescription rate increasing with age, (2) psychotropic drugs were prescribed for 15.6% of all patients (48/302 cases), with ADHD medications being most frequently prescribed (20 cases), and (3) other than psychotropic drugs, iron pills (25 cases) and herbal medicines (21 cases) were frequently prescribed. There is no previous study in Japan that investigated the prescription patterns of all prescription drugs classified according to psychiatric disorders, so we are unable to compare our findings with those published to date.

Prescription patterns of psychotropic drugs

There are no reports on the prescription patterns of psychotropic medications for outpatient child and adolescent psychiatric patients at single or multiple facilities in Japan, and limited information from other countries [6–8]. Although it is difficult to compare these reports with our results due to the differences in medical systems and study design, we cite prescription rates for reference.

Turkey reported a 61.8% prescription rate for psychotropic medications (psychostimulants, antidepressants, antipsychotics, antihistamines, and mood stabilizers) among patients aged 0–18 years; Croatia reported a 50.4% prescription rate for psychotropic medications (antipsychotics, antidepressants, and anti-anxiety medications) among adolescents aged 12–18 years; and Botswana reported a 71.4% prescription rate for psychotropic medications (antipsychotics, antidepressants, psychostimulants, antiepileptics, and anti-anxiety medications) among patients 17 years and younger.

Our results showed that psychotropic medications (ADHD medications, antipsychotics, antianxiety medications, antidepressants, mood stabilizers, and sleeping pills) were prescribed in 48 of 304 patients (15.6%). Factors affecting the prescription rate at our hospital included: (1) many patients are diagnosed with F8 developmental disorders, F4 neurotic disorders, and stress disorders, many of which are difficult to treat with pharmacotherapy. They are mainly seen for evaluation, educational consultation, disease education, and psychotherapy (for the patient and family), and (2) many of them are treated with non-pharmacotherapeutic interventions that improve their symptoms, with 130 of 304 patients (42.8%) being treated within 1 year, and (3) our facility does not have inpatient psychiatric beds, so the number of severely ill patients who require inpatient care is small. The results of this study also showed an increase in the rate of psychotropic medication prescriptions as the age of the patients increased. Although the reasons for this cannot be determined from the present survey, it is possible that parents are often resistant to medication for younger children, and that patients with ADHD and autism spectrum disorder (ASD) experience maladjustment and over-adjustment in school life, increasing the need for medication.

Although the increase in prescriptions for ADHD medications has become a hot topic in recent years (2), ADHD medications were prescribed in only 20 cases, or 19.2% of the total number of prescriptions. In contrast, when looking at the psychiatric diagnosis at the initial visit, F8 and F4 cases received prescriptions in addition to F9 (Table 3), suggesting that ADHD complications became apparent within a year of the initial visit and ADHD medications were prescribed even for patients with F8 and F4 as psychiatric diagnoses at the time of the initial visit. In contrast, as shown in Table 2, 24 patients (68.6% of those diagnosed with ADHD at the initial visit) with a psychiatric diagnosis of F9 at the initial visit were followed for 1 year without prescription. In a survey of prescriptions for ADHD conducted in Japan over a 4-year period from April 1, 1997, to March 31, 2001, 14 (66.7%) of 21 patients with ADHD who visited the outpatient clinic of the Department of Psychiatry at the National Sanatorium Nishibeppu Hospital were treated with pharmacotherapy [9]. In addition, in a study of outpatients at a French university hospital, ADHD medications were prescribed for 147 of 219 (67.1%) children with ADHD [10]. Compared to the two aforementioned studies with clear prescription rates for ADHD [9, 10], we found a lower rate of ADHD medication prescribing at our hospital. One possible reason for the lower rate compared to the two studies [9, 10] is that this study investigated prescriptions within 1 year of the first visit, while the study period in Kohara *et al.* was 4 years and that of Courtabessis' study was 3 years and 3 months, which may have influenced the result. One possible explanation is that the length of the study period may have influenced the results. In addition, our clinic provides non-pharmacological interventions, such as family counseling, parent training, social skills training, and school interventions in the outpatient care of patients with ADHD, and it is possible that non-pharmacological interventions may have influenced the lower rate of prescriptions for ADHD medications.

Use of drugs other than psychotropic drugs

In examining the prescription of drugs other than psychotropic drugs, iron preparations and herbal medicines were frequently prescribed. In F4 and F8 diagnoses in particular, the number of prescriptions for iron preparations (12 and 10 cases each) and for herbal medicines (8 and 10 cases each) was high. There have already been many reports on the relationship between serum iron and ferritin levels and restless legs syndrome (RLS) and ADHD, which cause insomnia in children. Although growing children have a high demand for iron and are prone to iron deficiency, it has been reported that a decrease in ferritin, which reflects iron stores, is also related to the severity of RLS and ADHD in children [11, 12]. Since 2015, we have also focused on the relationship between ferritin and psychiatric symptoms, such as depression, anxiety, irritability, and poor concentration associated with insomnia and fatigue. We then evaluated psychiatric symptoms in children with decreased serum ferritin levels, regardless of iron deficiency anemia status, and retrospectively confirmed the efficacy and safety of iron administration in these children [13]. Regardless of the type of disease, iron preparations may be effective in treating insomnia and psychiatric symptoms in children and should continue to be considered for prescription in child and adolescent psychiatric outpatient clinics because of their minimal adverse effects.

In a report by Nawate *et al.* on the prescription of Kampo medicine (Chinese medicine) in outpatient child psychiatry, Kampo medicine was prescribed to 57 (21.7%) of a total of 263 outpatients, with Yokukansan being the most common drug [14]. Although there is little evidence for Kampo treatment for psychiatric disorders in children, recently, the effects of Yokukansan and Yokukansankachimpihange extract granules have been reported for irritability, hyperactivity, and sleep disorders in autism spectrum disorder and ADHD [15, 16], and more evidence is expected to accumulate in the future.

In recent years, the increase in the use of psychotropic drugs for child and adolescent patients has been halted in Europe and the United States, and factors such as the approval of new drugs, the expansion of indications, and the development and dissemination of treatment guidelines are considered to be contributing factors [17]. Although child psychiatric pharmacotherapy guidelines [3] have been published in Japan, it will continue to be important to understand the actual situation of how psychotropic drugs are used in children and adolescents to make treatment more transparent.

Limitations and Significance of this Study

This is a retrospective study, and the study period is short, within 1 year of the initial diagnosis. Therefore, it is difficult to examine how the diagnosis of psychiatric disorders, severity of illness, and environmental factors, including the patient's environment, affect psychotropic drug prescriptions. In addition, because the study was conducted at a single institution, there is a limitation in that patient background and the characteristics of the institution are strongly reflected in the content of prescriptions. To clarify these factors, it is necessary to conduct a prospective study based on standardized diagnostic procedures at multiple institutions. However, this study has a certain value in that it clarified the prescribing patterns in the first year after the first visit to a child and adolescent psychiatric outpatient clinic. In addition, this study was conducted before sleeping pills (melatonin) indicated for insomnia in children were marketed, and it is possible that the prescriptions of sleeping pills and other drugs are very different today.

ACKNOWLEDGMENTS

This study was supported by the "Research Incentive Support Program" of the Tokai University Research Organization.

COI DISCLOSURE

This study was supported by the "Research Incentive Support Program" of the Tokai University Research Organization. This study was not funded by any pharmaceutical companies.

REFERENCES

1) Giannakopoulos G. Trends in mental health care among children and adolescents. N Engl J Med 2015; 373: 1078–9.
2) Okumura Y, Fujita J, Matsumoto T. Secular changes in psychotropic drug prescribing for children in Japan: utilization of a survey by social medical practice from 2002 to 2010 (original article). J Neuropsychiatr 2014; 116: 921–35.
3) Nakamura K. Guidelines for the Pharmacological Treatment of Child and Adolescent Psychiatric Disorders. Tokyo, Jiho Co, 2018.
4) Urabe A, Shimada K, Kawai S. Today's Therapeutics, 2020 Edition. Commentary and Handbook. Tokyo: Nanzando, 2020.
5) World Health Organization. International statistical classification of diseases and related health problems, 10th revision, Fifth edition, 2016 [Internet] [cited 2022 May 5]. Available from: https://apps.who.int/iris/handle/10665/246208.
6) Altay M, Bozatli L, Sipka B, Görker I. Current pattern of psychiatric comorbidity and psychotropic drug prescription in child and adolescent patients. Medicina (Kaunas) 2019; 17: 159.
7) Kaštelan A, Hladnik A, Petrić D, Gudelj L, Graovac M. Prescribing patterns in adolescent psychiatric practice: an important role of antipsychotics. Psychiatr Danub 2019; 31 Supplement 2: 153–61.
8) Olashore A, Ayugi J, Opondo P. Prescribing pattern of psychotropic medications in child psychiatric practice in a mental referral hospital in Botswana. Pan Afr Med J 2017; 26: 83.
9) Kohara H, Goto E, Miyazaki H. Application of pharmacotherapy in attention deficit hyperactivity disorder (original article). Child Adolesc Psychiatry Relat Fields 2004; 45: 65–77.
10) Courtabessis E, Pupier F, Surig L, Picot MC, Nogué E, Macioce V, *et al*. Clinical factors associated with decision to recommend methylphenidate treatment for children with ADHD in France. Eur Child Adolesc Psychiatry 2018; 27: 367–76.
11) Dosman C, Witmans M, Zwaigenbaum L. Iron's role in paediatric restless legs syndrome – a review. Paediatr Child Health 2012; 17: 193–7.
12) Konofal E, Lecendreux M, Arnulf I, Mouren MC. Iron deficiency in children with attention-deficit/hyperactivity disorder. Arch Pediatr Adolesc Med 2004; 158: 1113–5.
13) Mikami K, Okazawa H, Kimoto K, Akama F, Onishi Y, Takahashi Y, *et al*. Effect of oral iron administration on mental state in children with low serum ferritin concentration. Glob Pediatr 2019; 6: 1–5.
14) Nawate M, Nihei H, Iwamoto K, *et al*. Prescription of Chinese herbal medicine in outpatient clinic for children's mental health (child psychiatry outpatient clinic) (original article). KKR Sapporo Med Cent Med J 2013; 10: 44–7.
15) Ujike T. Effects of Yokukansankachimpihange extract granules on child psychiatric disorders. Phil Kampo 2010; 32: 18–9.
16) Kawashima K. A study on the usefulness of Kampo in pervasive developmental disorders (2). Jpn J Orient Med 2007; 58: 175.
17) Lopez-Leon S, Lopez-Gomez MI, Warner B, Ruiter-Lopez L. Psychotropic medication in children and adolescents in the United States in the year 2004 vs 2014. Daru 2018; 26: 5–10.