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Abnormal physiological conditions in acute schizophrenic patients on emergency admission: dehydration, hypokalemia, leukocytosis and elevated serum muscle enzymes

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Abstract This study investigated varieties and incidence of abnormal physiological conditions in acute schizophrenic patients on emergency. Laboratory data obtained prior to treatment from patients, admitted on an emergency basis during an 18-month period, were evaluated retrospectively, as well as demographics and clinical characteristics. Of 259 male acute schizophrenic patients (ICD-10: F2), 6.9% revealed dehydration, a third had hypokalemia and leukocytosis, and two thirds showed elevated serum muscle enzymes. These percentages were statistically significant compared with those of outpatients. In addition, the former three of these conditions in the F2 group were as frequent as those in alcohol and/or psychoactive substance abusers (ICD-10: F1) on emergency admission, although elevated serum muscle enzymes in the F2 group was less frequent than that in the F1 group. In order to prevent these abnormal physiological conditions from worsening and becoming life-threatening, one fourth of the F2 group [dehydration, 6.9%, severe hypokalemia (< 3.0 mEq/l), 2.3%, and markedly elevated serum muscle enzymes (creatine phosphokinase > 1000 IU/l), 16.5%] required medical management such as fluid therapy and various types of monitoring. In cases of a behavioral emergency, laboratory screening and monitoring of urinary output were essential. Due to their lack of cooperation, case history, physical examination, and initial vital signs did not contribute to detection of their medical condition.

Key words Schizophrenia · Emergency · Dehydration · Potassium · Creatine phosphokinase

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Introduction

Acute psychotic patients often have physical difficulties, in addition to obvious complications. These underlying medical issues have not been discussed sufficiently, except elevated muscle enzymes [8–10]. Among psychiatric emergency patients, alcohol or psychoactive substance abusers with psychoses, delirium tremens, or severe withdrawel often have profuse sweating due to excessive sympathetic activity [2, 14]. It follows that clinicians pay attention to abnormal physiological conditions such as dehydration and electrolyte disturbances in alcohol or psychoactive substance abusers. In contrast, fewer concerns are noted about these underlying abnormal physiological conditions in acute schizophrenic patients, although acute schizophrenic patients are also exhausted physically, probably due to severe psychotic excitement, incessant wandering, delusions of poisoning, or stupor.

The present study was undertaken to answer the following questions: (a) What are the underlying abnormal physiological conditions, in addition to obvious complications, among acute schizophrenic patients on emergency admission? (b) What is the severity of the abnormal physiological conditions? For instance, are there any differences in the incidence of the abnormal physiological conditions between acute schizophrenic patients and acute psychotic patients related with alcohol or psychoactive substance? In order to evaluate these, we conducted a historical cohort study [7] of psychiatric emergency patients who were admitted on an emergency basis to a psychiatric intensive care unit (PICU) in Japan.

Methods

Psychiatric intensive care unit

All patients presenting an immediate danger to themselves or to others during the night are admitted to Tokyo Metropolitan Bokuto General Hospital in the catchment area of eastern Tokyo (approximately 3,500,000 inhabitants) according to the 1995 Law Concerning Mental Health and Welfare for the Mentally Disabled. Therefore, patients are not selected, but all are severely disturbed with respect to violent behavior and are generally accompanied by policemen at the time of admission to the PICU. All patients who were admitted to the PICU were examined by a psychiatrist trained in involuntary admission from the Ministry of Health and Welfare of the Japanese Government. The examination usually took place a few hours before the patient's admission to the PICU. The physician filled out a form concerning involuntary admission, which was submitted to the Governor of Tokyo. In case of severe complications, the patient was admitted not to the PICU but to the Critical Care Center of our general hospital; therefore, patients who were accompanied with severe complications were systematically excluded.

Data collection

With this approach we did not select a sample group from the general group, but analyzed all subjects. A computerized search of the database for Tokyo Metropolitan Bokuto General Hospital was performed to identify all patients admitted to the PICU between June 1994 and November 1995. Only the first admission of each of the patients was used in this study. A total of 419 male and 240 female patients were identified by the computer survey. The data for the study were taken from or based on the medical records, including the form of involuntary admission, mental and physical examinations, laboratory data, and nurses' reports. Laboratory data, including routine blood chemistry and complete blood count before treatment, were obtained. Diagnoses were made with ICD-10 [22] at admission. Diagnoses of the 419 men were distributed as follows: organic, including symptomatic, mental disorders (F0), 16 patients; mental and behavioral disorders due to psychoactive substance use (F1), 93 patients; schizophrenia, schizotypal, and delusional disorders (F2), 259 patients; mood disorders (F3), 22 patients; neurotic, stress-related and somatoform disorders (F4), 5 patients; disorders of adult personality and behavior (F6), 15 patients; mental retardation (F7), 7 patients. Diagnoses of the 240 women were distributed as follows: F0, 15 patients; F1, 22 patients; F2, 162 patients; F3, 15 patients; F4, 6 patients; F6, 16 patients; F7, 4 patients. Of the 93 male patients who met the criteria for F1, 46, 36 and 7 patients were acute psychotic patients using alcohol, amphetamines and volatile solvents, respectively.

Our hospital treats approximately 1000 psychiatric outpatients. Laboratory examinations were performed every year in all psychiatric outpatients. Initial screening data from all psychiatric outpatients during the same period were used as control data. A total of 397 male and 475 female outpatients were identified by computer survey; approximately two thirds were schizophrenic, a quarter had mood disorders, and the rest were organic, neurotic, or personality disorders. There was no alcohol or psychoactive substance abuser because they enforced special programs for abusers in other special hospitals or clinics. The population of schizophrenia was high because there is a tendency in Japan for severe cases to be treated in public hospitals.

Statistics

To control for the effect of age on laboratory data, patients were divided into three age categories, i.e., 10–29, 30–49, and 50–69 years. There was no psychiatric emergency patient less than 10 years of age, and there were only 5 male and 2 female psychiatric emergency patients 70 years or older. Mantel-Haenszel's method was used to test the difference in the numbers with abnormal values between the two groups.

Results

Varieties of abnormal physiological conditions in acute schizophrenic patients on emergency admission

Dehydration

As shown in Table 1, 18 of 259 schizophrenic patients (6.9%) were dehydrated. Of these 18 dehydrated patients, 12 patients (67%) were without family. In addition, 17 patients (94%) were uncooperative on the initial interview and physical examination. Furthermore, in 14 patients (79%) the most recent food or water intake was unclear. These results indicate that it is difficult for physicians in a behavioral emergency situation to predict dehydration based on case history.

On physical examination, decrease of turgor or dry tongue were detected in only 7 patients (39%). This suggests that it is difficult to detect dehydration only from physical examinations, because behavioral emergency cases are uncooperative with regard to physical examination.

Rao et al. [19] reported the daily mean vital signs of drug-free schizophrenic cases, i.e., heart rate, 77.72 ± 9.47/min; systolic blood pressure, 118.9 ± 12.8 mm Hg; diastolic blood pressure 74.5 ± 9.02 mm Hg; body temperature, 36.49 ± 0.310° C, and the mean amplitudes of vital signs, i.e., heart rate, 7.33 ± 4.17/min; systolic blood pressure, 8.22 ± 4.78 mm Hg; diastolic blood pressure, 5.55 ± 3.19 mm Hg; body temperature, 0.307 ± 0.177° C. Considering the circadian fluctuation of vital signs, dehydration was detected from vital signs in 12 patients (cases 1–11, 15; 67%). However, there were only 4 cases (cases 3, 4, 10, 11; 22%) whose initial vital signs contributed to an initial diagnosis of dehydration.

There were 13 patients (72%) whose laboratory findings on admission revealed high values of hemoglobin, total protein, and blood nitrogen urea. In particular, in 6 patients (cases 1, 6, 8, 9, 16, 17; 33%) laboratory findings were essential to detect dehydration.

There were 13 patients (72%) with oliguria. In case 15 measurement of urinary output was very important because physical examination, initial vital signs, or laboratory finding failed to detect dehydration.

Thus, the rank order of usefulness to detect dehydration was as follows: laboratory findings (72%) = measurement of urinary output (72%) > changes of vital signs (67%) > physical examination (39%) > basic history.

Dehydration in the 18 patients was recognized by physical examination alone in 39%, by physical examination plus initial vital signs in 61%, by physical examination plus initial vital signs plus laboratory findings in 94%, and by physical examination plus initial vital signs

Table 1 The list of psychiatric emergency patients who met the ICD-10 criteria for F2 who were dehydrated (*ND* not detected; *BUN* blood urea nitrogen; *WBC* white blood cell count; *CPK* creatine phosphokinase)

Case no.	Age (years)	Turgor/ dry tongue	Blood pressure (systolic/diastolic; mm Hg)		Pulse (per min)		Body temperature (°C)		Urinary output (ml/h)	Hemoglobin (13.9–15.1 g/dl)		Total protein (6.0–8.3 g/dl)		Albumin (3.6–5.1 g/dl)	
			Time course(h)							Time course (h)					
			0	8	0	8	0	8		0	8	0	8	0	8
1	26	ND	110/ 90	130/108	118	66	37	36.3	40	20.9	16.8	8.4	7.5	4.9	3.8
2	51	+	90/ 62	120/ 72	108	96	36.9	36.5	25	17.4	15.3	8.2	7	5	4.3
3	50	ND	94/ 70	100/ 58	115	90	37.5	36.1	50	16.8	15.7	9.3	8.5	5.3	5.1
4	51	ND	98/ 50	142/ 88	120	96	37.9	36.9	29	16.2	15.3	8.4	7.3	5.1	4.4
5	31	+	110/ 70	150/ 70	106	97	36.6	37.3	31	16.1	15.3	7.8	6.8	4.9	4.2
6	29	ND	120/ 90	124/ 72	132	72	37.5	36.4	31	16	15.4	7.6	7.2	4.8	4.3
7	29	+	132/102	142/ 94	132	74	38.2	36.5	75	15.9	14.5	7.9	6.6	4.6	3.8
8	27	ND	100/ 70	100/ 76	80	66	36.8	35.4	17	15.8	14.8	7.8	7.4	4.8	4.2
9	24	ND	116/ 78	114/ 85	84	67	37.4	36.5	25	15.6	14.6	8.9	7.1	5.2	4.6
10	36	ND	94/ 68	130/ 70	90	80	37.8	36	25	15.3	14.6	7.1	6	4.3	3.5
11	32	ND	98/ 62	104/ 66	100	90	37.3	36.8	75	15.2	14.1	9.4	7.9	4.8	4.2
12	26	+	136/ 84	130/ 62	98	88	37.1	36.8	23	14.7	14	6.6	6.5	3.7	3.5
13	38	+	120/ 90	120/ 80	90	72	36.8	35.8	38	14.1	14	8.3	7.5	4.7	4.2
14	40	+	114/ 86	120/ 80	90	88	36.6	36.6	10	13.8	13.7	7	6.9	4.1	3.8
15	53	ND	106/ 80	100/ 50	108	55	36.8	36.6	17	14.5	13	7.2	6.3	4.2	3.6
16	59	ND	88/ 30	90/ 60	66	64	37.4	36.7	35	15.6	14.9	8.4	7.6	4.4	4
17	40	ND	114/ 88	144/ 80	84	84	37.1	36	26	15.5	14.7	8.1	7.6	4.3	3.9
18	38	+	110/ 70	108/ 66	60	64	37.3	36.7	55	13.9	13.7	8.1	7.5	4.8	4.4

Sodium (135–147/ mEq/l)		Potassium (3.6–5.1 mEq/l)		Chlorum (98–108 mEq/l)		BUN (7–22 mg/dl)		Creatinine (0.4–1.3 mg/dl)		WBC (2.7–10.3 $10^3/mm^3$)		CRP (0.0–0.3 mg/dl)		CPK (0–170 IU/l)		Dark urine
Time course (h)																
0	8	0	8	0	8	0	8	0	8	0	8	0	8	0	8	
146	140	4.7	4.5	99	102	43	35	1.2	1	14.2	8.1	0.2	1.3	4020	4550	–
142	140	3.8	3.6	103	106	30	27	0.9	0.7	7.1	5.5	0	0	177	572	–
143	142	3.5	4.1	99	103	82	65	2.4	1	16.4	14.4	1.7	2	1214	1431	–
150	149	3.7	3.5	112	112	34	33	1.1	0.9	17.2	10.9	0.8	1.5	1098	2040	–
141	141	3.8	3.8	102	104	26	26	0.9	0.8	19.5	11.1	0.2	0.8	584	853	–
139	139	3.2	3.5	100	101	32	25	1	0.9	19.5	13.9	0	0.4	1261	3340	–
147	141	4.2	3.7	113	103	23	11	0.8	0.8	8.8	8.4	1.7	1.2	10180	2770	–
145	144	5.1	4.8	107	108	24	16	0.9	0.8	12.6	7.9	0	0	121	99	–
149	147	4	3.9	113	107	25	17	1	0.7	6.6	6	0.2	0.3	748	365	–
145	147	3.3	3.1	105	109	23	20	0.8	0.8	9.2	7	6.6	4.5	17060	8020	–
132	134	6.6	4.5	95	99	33	20	0.7	0.7	28.4	21.3	3	8.3	301	293	+
141	141	3.1	3.6	98	100	29	22	1.9	0.8	11.8	10	0	0	357	301	–
149	147	3.5	3.7	112	108	29	21	0.9	0.6	8.3	7.7	0.2	0.2	644	592	–
139	140	3.8	3.8	106	106	24	12	0.7	0.5	9.2	7.5	0	0.2	931	488	–
146	146	4.6	4.3	108	110	45	34	0.8	0.8	12.3	7.1	0.1	0.2	141	152	–
137	138	5.1	4.9	100	103	28	22	1	0.9	11.7	9.2	1	0.9	3070	1120	–
141	142	3.8	3.7	100	101	24	18	0.9	0.7	13.6	8.4	0.5	0.3	563	314	–
139	140	4.3	4.1	100	104	39	25	1	0.8	6.5	6.6	0.1	0.1	267	177	–
143	142	3.5	3.8	104	104	26	20	0.9	0.6	14	9.5	1	0.8	2990	1816	–

plus laboratory findings plus measurement of urinary output in 100%, showing a cumulative effect selected to examinations performed with the passage of time after admission on an emergency basis.

Hypokalemia

As shown in Table 2, almost one third of subjects (90 patients, 34.7%) had hypokalemia. Of 90 hypokalemic patients, 24 (26.7%) ate nothing within 24 h prior to admis-

Table 2 Percentage of abnormal laboratory values in male acute schizophrenic patients who met the ICD-10 criteria for F2 (*TP* total protein; *Alb* albumin; *Na* sodium; *Cl* chlorum; *BUN* blood urea nitrogen; *Hct* hematocrit; *K* potassium; *ALP* alkaline phosphokinase; *GOT* glutamic oxaloacetic transaminase; *LDH* lactate dehydrogenase; *CPK* creatine phosphokinase; *WBC* white blood cell count; *Cr* creatinine; *GPT* glutamic pyruvic transaminase; *Amy* amylase; *BG* blood glucose)

No. of subjects	Percentage of patients showing abnormal values														
	TP > 8.3 g/dl	Alb > 5.1 g/dl	Na > 147 mEq/l	Cl > 108 mEq/l	BUN > 22 mg/dl	Hct > 50.1%	K < 3.6 mEq/l	ALP > 280 IU/l	GOT > 40 IU/l	LDH > 480 IU/l	CPK > 170 IU/l	WBC > 10 300/mm^3	Cr > 1.3 mg/dl	GPT > 40 IU/l	Amy > 220 IU/l	BG > 110 mg/dl
259	8.5	3.9	2.3	15.1	11.6	3.9	34.7	2.7	27.4	55.6	68.3	31.0	1.9	18.5	4.6	37.4

sion. In addition, 38 patients (42.2%) lived without other persons, and 84 patients (93.3%) were uncooperative; therefore, in 55 patients (61.1%) the latest time of food intake prior to admission was unclear.

Diabetes mellitus and its treatment can have effect on electrolytes and hydration; however, there was only 1 patient with diabetes mellitus in the F2 group. In addition, there was only 1 patient with concomitant vomiting, and no patients with diarrhea or who were under treatment with diuretics during 2 weeks prior to admission. Therefore, the high frequency of hypokalemia must be due to other causes. It is remarkable that percentages of hyperglycemia and leukocytosis were similar to that of hypokalemia (Table 2), although most of these conditions were mild in nature (data not shown).

The percentage of marked hypokalemia below 3.0 mEq/l was 2.3% (Table 3). In contrast to the F1 group, hypokalemia was the only finding, except for slight fever, in all 6 patients in the F2 group showing hypokalemia below 3.0 mEq/l. They received neither neuroleptic nor diuretic medication. They had no complications including endocrine and metabolic abnormalities. Hypokalemia in these patients were only identified by laboratory screening. After fluid therapy for 8 h, hypokalemia in the F2 group tended to normalize, but that in the F1 group did not (data not shown).

Elevated muscle enzymes

Approximately two thirds of subjects showed elevated muscle enzymes (Table 2). The percentage of cases with marked elevation of serum creatine phosphokinase (CPK) 1000 IU/l or more was 16.5%.

There were 9 patients of 259 in the F2 group with overt complications, 4 with fractures and one each with foot injury, burn, hepatitis type C, water intoxication, and arrhythmia. These small numbers of patients with complications may not have affected the high frequency of abnormal values in the F2 group. In addition, the presence of only two alcohol abusers and two amphetamine abusers in the F2 group could not be a major cause for the high frequency of abnormal values in the F2 group.

Nineteen patients were under treatment with antipsychotic medication within 2 weeks prior to admission; however, none of them showed neuroleptic malignant syndrome; therefore, the high frequency of elevated serum muscle enzymes must have resulted from other causes.

Leukocytosis

Eighty-one patients in the F2 group (31.0%) showed leukocytosis (Table 2). Thirty-six of 81 patients with leukocytosis showed increases of C-reactive protein above 1.0 mg/dl. Of these, 8 patients showed body temperature above 37° C, but there was only 1 patient with high fever above 38° C. This patient had moderate pneumonia. The other 7 patients had leukocytosis and in-

Table 3 The list of psychiatric male emergency patients who showed marked hypokalemia (3.0 mEq/l>) (*NP* nothing particular; *BG* (blood glucose): normal 60–110 mg/dl; *CRP* (C-reactive protein): normal, 0.3 > mg/dl; *WBC* (white blood cell count): normal, 2.7–10.3 × 10^3/mm^3; *HCT* (hematocrit): normal, 39.9–50.1%; *PLT* (platelet): normal, 13–35 × 10^4; *TP* (total protein): normal 6.0–8.3 g/dl; *Alb* (albumin): 3.6–5.1 g/dl; *T.bil* (total bilirubin): normal, 0.2–1.1 mg/dl; *Na* (sodium): normal, 135–147 mEq/l; *K* (potassium): 3.6–5.1 mEq/l; *Cl* (chlorum): normal, 98–108 mEq/l; *BUN* (blood nitrogen urea): normal, 6–22 mg/dl; *Cr* (creatinine): normal, 0.6–1.3 mg/dl; *Ca* (calcium): normal, 8.0–11.0 mg/dl; *GOT* (glutamic oxaloacetic transaminase): normal, 40 > IU/l; *GPT* (glutamic pyruvic transaminase): normal, 40 > IU/l; *LDH* (lactate dehydrogenase): normal, 140–480 IU/l; *ALP* (alkaline phosphatase): normal, 50–280 IU/l; *CPK* (creatine phosphokinase): normal, 30–170 IU/l; *Amy* (amylase): normal, 55–220 IU/l

	Age (years)	No. of previous episodes	Neuroleptic medication[a]	Psychiatric symptoms	Physical examination	BG	CRP	WBC	HCT	PLT
Emergency patients who met the ICD-10 criteria for F1										
Case 1	25	2	None	Auditory hallucinations Delusions of reference	NP	117	0.2	8.3	41.7	9.1
Case 2	39	1	None	Delirium	Vomiting	230	1.4	7.1	30.0	3.9
Case 3	46	3	None	Visual hallucinations Auditory hallucinations	Pretibial Edema	94	2.1	7.5	42.8	23.8
Case 4	52	1	None	Auditory hallucinations Delusions of reference	NP	83		4.5	38.5	20.0
Case 5	53	0	None	Auditory hallucinations Delusions of reference	NP	93	0.9	5.9	41.3	33.9
Case 6	54	0	Haloperidol	Delirium tremens	Hematemesis	87	0.02	7.6	43.0	13.9
Case 7	58	0	None	Delirium tremens	NP	88	0.02	18.8	46.9	18.8
Emergency patients who met the ICD-10 criteria for F2										
Case 1	32	3	None	Psychomotor excitement	NP	101	0.3	9.0	44.9	22.2
Case 2	35	0	None	Psychomotor excitement	NP	97	0.5	8.4	34.4	23.2
Case 3	37	2	None	Auditory hallucinations Delusions of reference	37.2° C	83	0.9	10.4	43.1	15.9
Case 4	37	0	None	Stupor	37.3° C	205	0.9	6.1	34.2	44.3
Case 5	43	1	None	Auditory hallucinations Delusions of reference	NP	121	1.2	6.9	38.1	35.8
Case 6	49	1	None	Auditory hallucinations Delusions of poisoning	NP	149	1.8	13.7	41.2	25.4

TP	Alb	T.Bil	Na	K	Cl	BUN	Cr	Ca	GOT	GPT	LDH	ALP	CPK	AMY
Emergency patients who met the ICD-10 criteria for F1														
8.8	4.7	1.4	120	2.8	61	52	2.0	8.7	34	13	735	185	540	347
6.6	3.2	0.8	137	2.8	103	8	0.5	8.2	94	63	588	204	582	105
7.4	3.0	3.5	143	2.7	102	15	1.0	9.4	104	42	722	207	660	708
8.0	4.1	3.2	150	2.5	112	54	0.7	9.7	109	53	1048	241	3030	61
7.2	4.4	0.7	138	2.5	100	8	0.9	9.7	47	55	685	136	578	59
8.0	4.1	0.8	141	2.4	104	8	1.2	9.6	49	60	564	154	171	207
7.3	3.4	1.8	137	2.9	99	16	0.7	9.1	84	35	884	221	513	360
Emergency patients who met the ICD-10 criteria for F2														
6.7	4.0	0.5	140	2.8	108	11	0.9	9.1	20	29	505	167	182	83
7.0	4.0	1.1	144	2.9	111	9	0.8	9.0	14	3	328	85	115	120
7.7	4.5	0.6	143	2.9	107	11	0.7	9.5	28	17	671	187	153	130
8.0	4.2	0.4	141	2.8	103	14	0.9	9.8	54	30	791	130	553	84
7.4	4.3	1.5	145	2.9	107	26	1.0	9.5	27	14	424	76	332	158
6.8	4.3	1.1	142	2.6	104	10	0.7	9.1	29	18	412	145	371	122

[a] Within the 4 weeks prior to admission

creased CRP as well as body temperature above 37° C, and were included in the group with other complications described above, excluding the patients with arrhythmia and water intoxication. There were no other patients with acute infectious disease. As mentioned in Methods, patients with severe complications were admitted not to the PICU, but to the Critical Care Center of our general hospital; therefore, cases accompanied with severe complications were systematically excluded. There was no patient with intoxications, acute hemorrhage, acute hemolysis, or malignant neoplasm. In addition, there was only 1 patient under treatment with lithium salts within 2 weeks prior to admission. All patients with leukocytosis, except for 8 patients with overt infectious disease, revealed a tendency toward normalization in white blood cell count (WBC) by 8 h after admission. These clinical and follow-up data

Table 4 Comparisons of percentage of abnormal laboratory values between psychiatric male outpatients and emergency patients who met the ICD-10 criteria for F1 or F2 according to age (*TP* total protein; *Alb* albumin; *Na* sodium; *Cl* chlorum; *BUN* blood urea nitrogen; *Hct* hematocrit; *K* potassium; *GOT* glutamic oxaloacetic transaminase; *LDH* lactate dehydrogenase; *CPK* creatine phosphokinase; *WBC* white blood cell count; *Cr* creatinine; *GPT* glutamic pyruvic transaminase)

Group	Age (years)	No. of subjects	Percentage of patients showing abnormal values												
			TP > 8.3 g/dl	Alb > 5.1 g/dl	Na > 147 mEq/l	Cl > 108 mEq/l	BUN > 22 mg/dl	Hct > 50.1%	K < 3.6 mEq/l	GOT > 40 IU/l	LDH > 480 IU/l	CPK > 170 IU/l	WBC > 10 300/mm^3	Cr > 1.3 mg/dl	GPT > 40 IU/l
Outpatients															
	10–29	89	0	0	0	2.2	0	7.9	0	10.1	4.5	12.4	10.1	1.1	24.7
	30–49	167	0.6	0	0	6.6	0	4.8	0	10.2	7.2	18.0	13.8	0.6	24.0
	50–69	120	0	0	1.7	9.2	8.3	1.7	4.2	10.8	13.3	19.2	9.2	3.3	12.5
Emergency patients who met the ICD-10 criteria for F1															
	10–29	16	18.8	0	0	6.3	12.5	0	31.3	43.8	62.5	68.8	18.8	12.5	31.3
	30–49	56	16.1	5.4	0	7.1	23.2	3.6	30.4	57.1	71.4	82.1	37.5	12.5	48.2
	50–69	21	4.8	4.8	4.8	14.3	19.0	4.8	47.6	95.2	90.5	90.5	28.6	9.5	61.9
Emergency patients who met the ICD-10 criteria for F2															
	10–29	96	10.4	5.2	2.1	13.5	9.3	3.1	36.5	20.8	51.0	68.8	26.0	3.1	12.5
	30–49	124	7.3	4.2	1.6	16.9	8.9	4.0	37.1	28.2	58.9	66.1	31.5	0	25.8
	50–69	39	7.7	2.6	5.1	12.8	25.6	5.1	23.1	41.0	56.4	74.4	35.9	5.1	10.3
χ^2 value by Mantel-Haenszel's method															
	Outpatients vs F1		6.50***	3.74***	0.90	2.15*	6.52***	0.59	10.7***	11.3***	13.8***	12.0***	4.62***	4.77***	5.25***
	Outpatients vs F2		5.14***	3.73***	2.39*	3.62***	5.56***	0.69	11.2***	5.82***	13.0***	13.0***	5.82***	0.67	1.03
	F1 vs F2		1.72	0.06	0.83	2.79**	1.77	0.42	0.01	5.62***	2.81**	2.31*	0.09	3.94***	5.04***

Statistically significant differences in the numbers with abnormal values between the outpatients and emergency patients met the ICD-10 criteria for F1 or F2 were calculated using Mantel-Haenszel's method; *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$

suggest that the main etiology of leukocytosis on emergency admission in the F2 group was not due to infections or certain pathological conditions, but probably to physiological neutrophilia.

The incidence of the abnormal physiological conditions in the F2 group compared with controls in the F1 group

The percentage of cases with abnormal values of total protein, albumin, sodium, chlorum, and BUN in the male F2 group were significantly higher than those of male outpatients after adjusting for age (Table 4). These results may have been associated with dehydration or tendency towards dehydration in the F2 group. Table 4 also shows that the percentage of abnormal values of potassium, glutamic oxaloacetic transaminase (GOT), lactate dehydrogenase (LDH), CPK, and WBC in the male F2 group were significantly higher than those of male outpatients after adjusting for age. This suggests the significantly high frequency of hypokalemia, elevated serum muscle enzymes, and leukocytosis in the F2 group compared with controls.

Also, the percentage of abnormal values of total protein, albumin, chlorum, and BUN in the F1 group were significantly higher than those of male outpatients after adjusting for age (Table 4). These results may have been associated with dehydration or tendency towards dehydration in the F1 group as well as the F2 group. The significantly high frequency of hypokalemia, elevated muscle enzymes, and leukocytosis in the F1 group, compared with outpatients, were also revealed. Dehydration and elevated muscle enzymes are frequently observed in the delirious or psychotic state induced by alcohol or psychoactive substances. The reasons for the high frequency of hypokalemia and leukocytosis may be complex. There was only 1 patient with diabetes mellitus in the F1 group. In addition, there was only 1 patient under treatment with diuretics in the F1 group within 2 weeks prior to admission. There was no F1 patient with injury or infectious disease. Moreover, there was no patient in this group receiving treatment with lithium salts within 2 weeks prior to admission. Thus, other reasons may be major causes for the high frequency of hypokalemia and leukocytosis in the F1 group.

The percentage of cases with abnormal values of GOT, LDH, CPK, Cr, and GPT in the F1 group were larger than those of the F2 group, respectively, after adjusting for age (Table 2). This suggests a significantly high frequency of elevated muscle enzymes, renal dysfunction, and liver dysfunction in the F1 group as compared with the F2 group. Although there were only 9 patients (3.5%) showing a GPT value of 100 IU/l or more in the F2 group, there were 13 patients (14.0%) in the F1 group. Furthermore, there were 7 patients (7.5%) showing both 100 IU/l or more GPT and 1.1 mg/dl or more total bilirubin in the F1 group, whereas there were only 4 (1.5%) in the F2 group. Interestingly, there were no significant differences in total protein, albumin, sodium, BUN, potassium, and WBC between the F1 and F2 groups. This suggests no significant differences in the frequency of dehydration, hypokalemia, and leukocytosis between the two groups. Frequencies were not affected by issues including obvious complications, medication prior to admission, or the coexistence of alcohol and/or psychoactive substance abusers in the F2 group as mentioned previously. Therefore, some issues are raised about other possible causes for dehydration, hypokalemia, and leukocytosis, such as physical agitation, decrease of water and food intake, and psychological distress, which may be common to acute psychotic patients. Results in women were similar to those in men (data not shown).

Discussion

Acute schizophrenic patients requiring emergency admission who are uncooperative frequently present problems in assessing their physical conditions and medical requirements. The present study revealed relatively high frequency of conditions including dehydration, hypokalemia, elevated muscle enzyme, and leukocytosis in the F2 group as well as the F1 group. Sixty patients (23.2%) in the F2 group, including 18 patients with dehydration (7 patients of 18 with 1000 IU/l or more CPK), 6 with hypokalemia below 3.0 mEq/l, and 36 with high value of 1000 IU/l or more CPK, needed optional medical care such as fluid therapy. In order to detect these conditions, laboratory screening was the most contributive factor. Psychiatric emergency patients were so uncooperative and excited, that a basic history, initial vital signs, or physical examination were less useful than laboratory screening. Recently, Olshaker et al. reported that the vast majority of medical problems and substance abuse in emergency department psychiatric patients can be identified by initial vital signs, a basic history, and physical examination [16]. However, the rank order of usefulness to detect dehydration in the present study was as follows: laboratory findings (72%) = measurement of urinary output (72%) > course of vital signs (67%) > physical examination (39%) ≫ basic history, as mentioned in the Results. Furthermore, hypokalemia below 3.0 mEq/l in the F2 patients was identified only by laboratory screening. Thus, the present results suggest that medical problems described here cannot necessarily be identified by a basic history, initial vital signs, or physical examination in people who need involuntary and emergency admission, and that laboratory screening is the most contributive factor in such cases.

Dehydration

The finding that 6.9% of acute schizophrenic patients were dehydrated is remarkable, especially because there seems to be no previous report on the frequency of dehydration in such cases. Physical agitation may increase water loss and accelerate dehydration, whereas decrease of water and food intake may also have resulted in dehydration and electrolyte disturbances. In emergency situations,

intravenous and/or intramuscular injections of antipsychotics and/or benzodiazepines are often used, and patients require relatively high doses [20]. During such initial medication, serious dehydration can develop rapidly. Dehydration is a contributing factor leading to and/or enhancing the incidence or severity of neuroleptic malignant syndrome [21] or rhabdomyolysis [11]. Thus, serious consideration must be given to dehydration in acute schizophrenic patients as well as alcohol and/or psychoactive substance abusers.

In order to detect dehydration, laboratory screening was the most effective in the F2 group, as mentioned previously. However, in the F1 group urinary output contributed to detection of dehydration more than laboratory screening, as 5 dehydrated patients of 13 (38%) in the F1 group also had anemia (data not shown). Although measurement of urinary output in the F2 group was also needed, it contributed to follow-up rather than the detection of dehydration, because dehydration in this group had been detected when urinary output was evaluated. Vital signs were also needed, not to detect dehydration but for follow-up, because initial vital signs were modified by physical agitation and psychological distress.

Hypokalemia

One third of acute schizophrenic patients had hypokalemia. In particular, the finding that 2.3% of acute schizophrenic patients were below 3.0 mEq/l is clinically important. Furthermore, the finding that there was no significant difference in the frequency of hypokalemia between the F1 and the F2 groups suggests etiologies common to acute psychotic patients, irrespective of psychiatric diagnosis.

Increased endogenous catecholamine levels due to anxiety cause a decrease in plasma potassium [18]. Administration of adrenaline to animals produces a biphasic response of the plasma potassium, consisting of transient hyperkalemia followed by a prolonged period of hypokalemia [18]. Recent studies have demonstrated conclusively that the hypokalemic action of the catecholamines is mediated solely by beta-2 receptors [3, 5]. This action is independent of, and does not require changes in, plasma insulin, aldosterone, glucagon, glucose, or urinary potassium excretion. Although insulin clearly has the best-defined and quantitatively most important effects on potassium distribution as well as catecholamines, it may not have additional major contribution to hypokalemia in the present results due to the finding of similar frequency of hyperglycemia, despite the small number of diabetic patients. Catecholamines stimulate hyperglycemia [4]. The evidence of a similar percentage of leukocytosis supports the etiology of a beta-2 receptor-mediated influx of potassium into skeletal muscle induced by circulating adrenaline. Transient neutrophilia occurs in association with vigorous exercise or after the injection of adrenaline [1].

Recently, Rao et al. [19] reported the association between higher adrenergic tonus and neuroleptic medication. However, in the present study only 19 patients in the F2 group of 259 were under treatment with antipsychotics within 2 weeks prior to admission. Furthermore, only 5 outpatients of 376 showed hypokalemia, although two thirds of outpatients received neuroleptic medication; thus, neuroleptic medication did not appear to be associated with hypokalemia in this study.

Another cause may be implicated in poor nutrition, i.e., the decrease of potassium intake secondary to psychotic symptoms such as physical agitation, incessant wandering, delusions of poisoning, or stupor. Unfortunately, food intake could not be confirmed by a basic history, because patients were uncooperative. Therefore, it is unclear to what extent poor nutrition was associated with hypokalemia in the present results. Investigation of potassium balance, i.e., potassium intake and excretion, is needed to clarify the precise etiologies. Also, measurement of magnesium is needed because there is a relationship between the metabolism of potassium and magnesium ions.

Medbo and Sejersted [12] reported that the potassium concentration was 0.50 ± 0.05 mmol/l below pre-exercise values after 3 min recovery from exhausting exercise for 1 min. If this value is the limit of physiological decline, hypokalemia below 3.1 mEq/l (normal 3.6–5.1 mEq/l) in the present results may have included pathological etiologies such as poor nutrition. Although the etiology is not conclusive in this study, hypokalemia is associated with most serious arrhythmias [15], which may cause unexpected sudden death. Mehtonen et al. reported that 7 of 49 sudden unexpected deaths among psychiatric cases occurred within 4 days after admission [13], although they concluded that the association between their sudden deaths and the arrhythmogenic effects of phenothiazines or tricyclic antidepressants as well as abnormalities of hydration and/or electrolytes might have been partly implicated in their sudden deaths. For instance, dehydration and/or hypokalemia might have enhanced arrhythmogenic effects of phenothiazines or tricyclic antidepressants. Therefore, potassium replenishment should be done, if the serum potassium level shows marked decrease, especially below 3.1 mEq/l, on emergency admission.

Elevated muscle enzyme

In the present study, almost two thirds of acute schizophrenic patients showed elevated serum muscle enzymes. In particular, the percentage of marked elevation of serum CPK more than 1000 IU/l was 16.5%. Gurrera and Romeo speculated that the pathophysiology of catecholamine-associated CPK elevations involved hypoxia due to ischemia caused by vasoconstriction [10]. Hypoxia could be a toxic agent against myocytes, which may lead to either increased muscle enzyme synthesis or selective leakage of muscle enzymes. The intracellular-extracellular gradient for CPK in normal myocytes is only 300 IU/l [17], which cannot account for the marked elevation of serum CPK to more than 1000 IU/l in 16.5% of acute schizophrenic patients. Therefore, increased muscle enzyme synthesis could be involved in these cases of marked elevation of CPK. In

addition, enzymes localized in the cytoplasmic compartment, such as CPK and LDH, are readily soluble, whereas GOT found in mitochondrial and cytoplasmic compartments and ALP bound to the cell membrane are less soluble and are released when damage is very severe [17]. In the present study, the percentage of abnormal GOT value in the F2 group was significantly higher than that in the control group, although there was only 1 patient with hepatic complications and only 4 cases of alcohol or psychoactive substance abuse in the F2 group. This suggests the relatively severe damage to myocytes in acute schizophrenic patients on emergency admission.

Leukocytosis

Of these four conditions in acute schizophrenic patients on emergency admission, leukocytosis may be clinically least important because pathological causes were excluded, as mentioned in the Results. Physical agitation and psychological distress are possible causes common to such a large number of patients in the emergency situation. Although the mechanism remains controversial, exercise- and adrenaline-induced neutrophilic reactions occur within minutes of the stimulus and are of short duration [1]. In addition, glucocorticoids, which may impede the flow of neutrophils from the circulating pool into the tissues, are capable of eliciting a delayed type of acute neutrophilia with maximal response at 4–24 h following stimulation [6]. These mechanisms may be associated with the leukocytosis that was probably induced by physical agitation or psychological distress in the present results.

In conclusion, the findings of this study that dehydration, hypokalemia, elevated muscle enzymes and leukocytosis frequently exist in acute schizophrenic patients on emergency admission suggest the importance of medical management in these patients to prevent the comorbid medical disorders secondary to treatment after admission. In order to detect these conditions, laboratory screening was the most contributive factor compared with basic history, physical examination, or initial vital signs, because patients in our PICU were so excited and uncooperative. A prospective study is needed to clarify the precise etiologies for the conditions described here.

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