

Maximal Response to Electroconvulsive Therapy for the Treatment of Catatonic Symptoms

Kotaro Hatta, MD, PhD,* Koichi Miyakawa, MD,* Tsuneyoshi Ota, MD,* Chie Usui, MD, PhD,* Hiroyuki Nakamura, MD, PhD,† and Heii Arai, MD, PhD*

Objectives: Because the number of medical lawsuits has recently increased in Japan, doses of medication above the upper limits have recently been avoided, even when treating catatonic patients. We treated catatonic symptoms with drugs within the upper limit of dosage and electroconvulsive therapy (ECT) to determine the maximal response.

Methods: We examined 50 consecutive patients with catatonic symptoms admitted to a university hospital during a 32-month period who were treated with either drugs within the upper limit or ECT.

Results: Response rates were as follows: ECT, 100%; chlorpromazine, 68%; risperidone, 26%; haloperidol, 16%; and benzodiazepines, 2%.

Conclusions: The findings indicated that ECT is the treatment of choice for catatonic symptoms.

Key Words: chlorpromazine, risperidone, haloperidol, benzodiazepine, stupor

(*J ECT* 2007;23:233–235)

Relatively high doses of benzodiazepines and electroconvulsive therapy (ECT) have been recommended for treating catatonic symptoms.^{1,2} However, medication with doses above the upper limit has recently been avoided in Japan, even for catatonic patients, because the number of medical lawsuits has increased. We compared the effects of treating catatonic symptoms with drugs within the upper dosage limits and ECT.

METHODS

Clinical Setting

The present study was conducted between January 2003 and August 2005 at the 15-bed psychiatric intensive care unit (PICU) of Juntendo University Hospital, Tokyo, Japan. Most patients were involuntarily admitted according to the 1995 Law Concerning Mental Health and Welfare for the Mentally Disabled. Patients were typically examined a few hours before admission to the PICU, and the tests included laboratory

parameters, electrocardiograms, chest and abdominal X-ray, head computed tomography or magnetic resonance imaging, and electroencephalography. Physicians completed involuntary admission forms, which were submitted to the Governor of Tokyo. Patients with severe complications were not admitted to the PICU but to the intensive care unit of our university hospital. Therefore, patients with severe complications were systematically excluded. Some patients with catatonic symptoms were transferred from psychiatric clinics and hospitals near the university hospital to receive ECT.

Assessment Procedure

Catatonic symptoms were defined according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* criteria for catatonic features specifier, including (1) motor immobility or stupor; (2) excessive motor activity; (3) extreme negativism or mutism; (4) peculiarities of voluntary movement as evidenced by posturing, stereotyped movement, prominent mannerism, or prominent grimacing; and (5) echolalia or echopraxia.³

“Partial response” was defined as the disappearance of one or more of catatonic symptoms, and “complete response” was defined as the disappearance of all catatonic symptoms. All patients were assessed by the first author. The criteria of “ineffectiveness” of each of the first 3 courses of drug treatments were no or partial response within 3 or 4 days. The reason for decision making in such a short term was that catatonia predisposes the patients to life-threatening conditions, such as the lack of water and food intake and the risk of thromboembolism.

Treatment

According to the recommendation,^{1,2} the first treatment strategy was administration of either benzodiazepines or ECT. The treatment decision took into account choices not only by a patient but also by the patient’s family. We used the following benzodiazepines: intravenous flunitrazepam (FZP) or diazepam (DZP) for patients who refused oral medication, and oral lorazepam (LZP) for those who agreed to oral medication. All doses were within the upper limits (intravenous FZP: up to 0.03 mg/kg, a second dose of up to 0.03 mg/kg; intravenous DZP: up to 10 mg, repeated doses every 3–4 hours; oral LZP: up to 3 mg/d), which is regulated by the Ministry of Health, Labour and Welfare of Japan.

Electroconvulsive therapy proceeded as follows. Patients received intramuscularly 0.5 mg of atropine sulfate, 30 minutes before ECT. They were induced with thiopental 2 to 2.5 mg/kg and paralyzed with suxamethonium 1 mg/kg. After manual ventilation, they were treated with bilateral ECT

From the *Department of Psychiatry, Juntendo University School of Medicine, Tokyo and †Department of Environmental and Preventive Medicine, Kanazawa University Graduate School of Medical Science, Kanazawa, Japan.

Received for publication May 1, 2007; accepted August 15, 2007.

Reprints: Kotaro Hatta, MD, PhD, Department of Psychiatry, Juntendo University School of Medicine, Hongo 2-1-1, Bunkyo-ku, Tokyo 113-8421, Japan (e-mail: khatta@med.juntendo.ac.jp).

Copyright © 2007 by Lippincott Williams & Wilkins

using a Thymatron System IV (Somatics Inc, Lake Bluff, Ill) set at a current of 0.9 A and a brief pulse square wave with a pulse width of 0.5 milliseconds. Electrode placement was bitemporal. The half-age method was used to determine the energy level. The therapeutic quality of elicited seizures was evaluated by looking for a synchronous electroencephalographic seizure pattern with high amplitude relative to the baseline, well-developed polyspike and spike-and-wave phases, and a clear ictal end point with pronounced postictal suppression. Psychotropic medication was discontinued during ECT, which was applied 3 times per week.

When the first treatment was ineffective, the second treatment was either ECT or antipsychotics, considering the choices preferred not only by the patient but also by the patient's family. We administered the following antipsychotics used: intravenous haloperidol (HAL) for patients who refused oral medication and oral risperidone (RIS) for patients who agreed to oral medication. All administered doses were within the upper limits (intravenous HAL, up to 10 mg/d; oral RIS, up to 12 mg/d).

When the second treatment was ineffective, the third treatment was either ECT or chlorpromazine (CPZ), considering the choices preferred not only by the patient but also by the patient's family. All administered doses were within the upper limits (oral CPZ, up to 450 mg/d).

When the third treatment was ineffective, the fourth treatment was ECT. Although antipsychotics, regardless of their pharmacological properties, have been considered of no value or dangerous for the treatment of catatonic symptoms, these claims appear to have arisen from a review of case reports.⁴⁻⁸ In contrast, some patients have responded quite well to RIS.^{9,10} We have noted that quite a few patients with catatonic stupor gradually improve and fully recover within several days of oral CPZ administration. Haloperidol is only an intravenous antipsychotic drug, except benzodiazepines, in Japan. Therefore, we included these antipsychotics among the choices.

Differences were statistically analyzed by 1-way analysis of variance. The Human Studies Committee of Juntendo University Hospital approved the study protocol, which did not require written informed consent from patients because of its naturalistic design and standard treatment.

RESULTS

During the study period, 586 patients were admitted to the PICU, of which 52 (8.9%) met the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* criteria for catatonic features specifier. Of these, 2 patients were admitted twice, so the second episode for each patient was excluded. The mean age of the 50 patients was 50.0 years (SD, 17.9 years), and diagnoses at discharge were distributed among the patients as follows: mental disorders due to a general medical condition, 10 (20%); schizophrenia and other psychotic disorders, 23 (46%); and mood disorders, 17 (34%). Details of catatonic symptoms were as follows: (1) motor immobility or stupor, 100%; (2) excessive motor activity, 44%; (3) extreme negativism or mutism, 96%; (4) peculiarities of voluntary movement evidenced by posturing, stereotyped movement, prominent mannerisms, or prominent grimacing, 68%; and (5) echolalia or echopraxia, 18%.

Two of 10 patients diagnosed with organic mental disorders were surgically treated because their catatonic symptoms resulted from continuous hypoglycemia due to insulinoma in one and from Cushing syndrome resulting from adrenal tumor in the other.

Response to First Treatment

All 7 patients who received ECT achieved remission. The remaining 41 patients received benzodiazepines with doses within the upper limits. The responses of the patients were distributed as follows: complete, 1; partial, 19; and none, 21.

Response to Second Treatment

Forty patients whose catatonic symptoms continued underwent a second treatment. Two patients received ECT, and both of them achieved remission. Nineteen patients who partially responded to benzodiazepines received oral RIS, to which 5 completely responded. Nineteen patients who were unresponsive to benzodiazepines received intravenous HAL (due to refusal of oral medication), and 3 of those responded completely.

Response to Third Treatment

Thirty patients whose catatonic symptoms continued underwent a third treatment. Two patients who received ECT achieved remission. The remaining 28 patients received CPZ, and 19 of those responded completely.

Response to Fourth Treatment

Nine patients remained catatonic after the third treatment. Of these, 6 patients who underwent ECT achieved remission. The remaining 3 patients, who responded partially to CPZ, were transferred to a psychiatric hospital, because either the patient themselves or their families refused ECT. However, because they had responded partially to CPZ, their condition was no longer life-threatening.

Response Rates to Treatments

Response rates, defined as the number of patients who responded completely divided by the total (cumulative) number of patients who received the treatment, were as follows: ECT, 100% (17/17 patients); CPZ, 68% (19/28 patients); RIS, 26% (5/19 patients); HAL, 16% (3/19 patients); and benzodiazepines, 2% (1/41 patients).

Mean duration until the start of improvement after each treatment was as follows (in days): ECT, 3.2 (SD, 2.9); CPZ, 2.9 (SD, 1.6); RIS, 2.4 (SD, 1.5); and HAL, 3.7 (SD, 0.6). The time to response with different treatments did not significantly differ among treatments ($F = 0.266, P = 0.849$). Mean duration until the disappearance of catatonic symptoms for each treatment was as follows (in days): ECT, 10.2 (SD, 5.9); CPZ, 8.9 (SD, 4.4); RIS, 5.6 (SD, 3.8); and HAL, 8.0 (SD, 2.0). The time to response with different treatments did not significantly differ among treatments ($F = 1.204, P = 0.321$).

Mean doses (SD) of DZP, LZP, FZP, HAL, RIS, and CPZ were 11.4 (3.8), 1.8 (0.3), 1.5 (0.6), 9.4 (3.9), 5.5 (3.1), and 158 (85) mg/d, respectively. The patients underwent a mean of 8.8 (SD, 1.8) ECT treatments.

Side Effects

One patient administered with HAL developed an acute laryngeal dystonic reaction. Acute liver dysfunction developed in 1 patient who received CPZ. Serum creatine kinase became elevated in 1 patient receiving RIS, which did not result in neuroleptic malignant syndrome after RIS was stopped. Although tremor and rigidity occurred in most patients, these symptoms were evident before starting treatment, and they disappeared, coincidentally, with the appearance of treatment effects. Accordingly, such symptoms resulted from catatonic symptoms rather than from the extrapyramidal side effects of antipsychotics. No patients exhibited oversedation.

DISCUSSION

Although benzodiazepines are generally recommended^{1,5} based on case series,^{11,12} the rate of a complete response to these drugs in the present study was extremely low. Three factors might account for this. First, the dosage might have been insufficient. The generally recommended doses of benzodiazepines are much higher than those applied within the upper limit in the present study. Fink and Taylor¹³ have recommended that 3 to 4 mg LZP should be given on the first day and then increased up to 16 mg as required for catatonic stupor and that a first dose of 1 to 2 mg LZP or 5 mg DZP should be increased up to 10 or 40 mg within several hours, respectively, for catatonic excitement. In contrast, the mean doses of LZP and DZP in the present study were 1.8 mg (SD, 0.3 mg) and 11.4 mg (SD, 3.8 mg), respectively. Second, the effects of benzodiazepines were transient and partial. Ungvari et al¹⁴ also documented that the effect of benzodiazepines on catatonic symptoms was not necessarily continuous, resulting in 9 of 18 patients requiring ECT. Rosebush et al¹⁵ reported that not every sign or symptom of an acute catatonic stupor responded well to benzodiazepines.

Another factor was that the psychopathology of our patients tended to be severe due to the high rate of schizophrenic patients. Ungvari et al¹⁴ also reported that patients with schizophrenia were less responsive to benzodiazepines. Beckmann et al¹⁶ noted that even a protracted course of benzodiazepine does not improve catatonic symptoms in chronic schizophrenics.

The low response to HAL in the present study is consistent with the findings of one review that high-potency antipsychotics are not very effective.⁵ Although some patients respond well to RIS,^{9,10} evidence of the effectiveness of RIS remains insufficient. The result that only 26% of patients treated with RIS achieved the remission of catatonic symptoms is a new finding. Similarly, the effects of low-potency antipsychotics on catatonic symptoms have not been sufficiently evaluated. So far, reports describe only 3 patients who have been treated with a low-potency antipsychotic. One was given intramuscularly 1 dose of CPZ during a progressive catatonic state,⁸ and another received intramuscularly 3 doses of CPZ over a 1-week period¹⁷; however, the CPZ dose was too infrequently administered to these 2 patients to evaluate its effectiveness. The remaining patient had been receiving 100 mg of CPZ orally for 1 week, but died when symptoms started

to improve.¹⁸ The present result that catatonic symptoms disappeared in 68% of patients treated with CPZ is also remarkable. Thus, the response to high- and low-potency antipsychotics might differ among catatonic patients.

The high rate of response to ECT is consistent with previous findings.^{1,5} In particular, the 100% response suggests that ECT should be the first choice of treatment for catatonic symptoms. Fink and Taylor¹³ have recommended the benzodiazepine challenge test in the algorithm for treating malignant catatonia/neuroleptic malignant syndrome before applying ECT. However, this method requires a high dose of benzodiazepine. Therefore, ECT might be the first choice when doses of drugs above the upper limits cannot be applied.

Although the noncomparative study design is a methodological limitation, it has the advantage of reality in practice by allowing the inclusion of patients who usually refuse to participate in clinical trials, such as those with catatonic symptoms. Despite this limitation, we can conservatively claim that ECT should play a more important role in the treatment of catatonic symptoms.

REFERENCES

1. Bush G, Fink M, Petrides G, et al. Catatonia II. Treatment with lorazepam and electroconvulsive therapy. *Acta Psychiatr Scand*. 1996;93:137-143.
2. Taylor M-A, Fink M. Catatonia in psychiatric classification: a home of its own. *Am J Psychiatry*. 2003;160:1233-1241.
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. Fourth Edition, Text Revision; DSM-IV-TR. Washington, DC: American Psychiatric Association; 2000.
4. Ahuja N. Organic catatonia: a review. *Ind J Psychiatry*. 2000;42:327-346.
5. Hawkins J-M, Archer K-J, Strowski S-M, et al. Somatic treatment of catatonia. *Int J Psychiatry Med*. 1995;25:345-369.
6. Hermesh H, Aizenberg D, Weizman A, et al. Risk for definite neuroleptic malignant syndrome. A prospective study in 223 consecutive in-patients. *Br J Psychiatry*. 1992;161:254-257.
7. Keck P-E, Pope H-G, Cohen B-M, et al. Risk factors for neuroleptic malignant syndrome. A case-control study. *Arch Gen Psychiatry*. 1989;46:914-918.
8. White D-A-C, Robins A-H. Catatonia: harbinger of the neuroleptic malignant syndrome. *Br J Psychiatry*. 1991;158:419-421.
9. Cook E-H, Olson K, Pliskin N. Response of organic catatonia to risperidone. *Arch Gen Psychiatry*. 1996;53:82-83.
10. Hesslinger B, Walden J, Normann C. Acute and long-term treatment of catatonia with risperidone. *Pharmacopsychiatry*. 2001;34:25-26.
11. Marneros A, Jager A. Treatment of catatonic stupor with oral lorazepam in 14-year-old psychotic boy. *Pharmacopsychiatry*. 1993;26:259-260.
12. Ungvari G-S, Leung H-C, Lee T-S. Benzodiazepines and the psychopathology of catatonia. *Pharmacopsychiatry*. 1994;27:242-245.
13. Fink M, Taylor MA. *Catatonia: A Clinician's Guide to Diagnosis, and Treatment*. Cambridge, UK: Cambridge University Press; 2003.
14. Ungvari G-S, Kau L-S, Wai-Kwong T, et al. The pharmacological treatment of catatonia: an overview. *Eur Arch Psychiatry Clin Neurosci*. 2001;251:(suppl 1):31-34.
15. Rosebush P-I, Hildebrand A-M, Furlong B-G, et al. Catatonic syndrome in a general psychiatric inpatient population: frequency, clinical presentation, and response to lorazepam. *J Clin Psychiatry*. 1990;51:357-362.
16. Beckmann H, Fritze J, Franzek E. The influence of neuroleptics on specific syndromes and symptoms in schizophrenics with unfavourable long-term course. *Neuropsychobiology*. 1992;26:50-58.
17. De Pauw K-W, Szulecka T-K. Lucid intervals in catatonia: a neuropsychiatric snare for the unwary. *Br J Psychiatry*. 1987;151:561-562.
18. Ainaworth P. A case of 'lethal catatonia' in a 14-year-old girl. *Br J Psychiatry*. 1987;150:110-112.