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Improvement of cycloid psychosis following electroconvulsive therapy

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ABSTRACT

Background: The treatment of choice for cycloid psychosis has traditionally been electroconvulsive therapy (ECT), but there is a lack of studies on its effectiveness.

Aims: The primary aim of this register study was to determine the rates of remission and response after ECT for cycloid psychosis. The secondary aim was to examine possible predictors of outcome.

Methods: Data were obtained from the National Quality Register for ECT in Sweden. The study population was patients ($n = 42$) who received ECT for acute polymorphic psychotic disorder without symptoms of schizophrenia or for cycloid psychosis between 2011–2015 in 13 hospitals. Remission and response rates were calculated using Clinical Global Impression-Severity (CGI-S) and -Improvement scores, respectively. Variables with possible predictive value were tested using Chi-square and Fisher's exact test.

Results: The response rate was 90.5%. The remission rate was 45.2%. Of 42 patients, 40 improved their CGI-S score after ECT ($p < 0.001$). The mean number of ECT treatments was 2.5 for non-responders and 7.0 for responders ($p = 0.010$). The mean number of ECT treatments did not differ significantly between remitters and non-remitters (7.2 vs 6.1, $p = 0.31$). None of the other investigated potential predictors was statistically significantly associated with outcome.

Conclusions: ECT is an effective treatment for cycloid psychosis. Future studies need to compare the outcome of ECT to that of other treatment strategies. *Clinical implications*: The high response rate with ECT indicates that cycloid psychosis is a clinically useful diagnosis.

Background

Electroconvulsive therapy (ECT) was first used in a human in 1938 by Cerletti and Bini. In the two decades following its introduction, ECT was the primary treatment for schizophrenia. The use of ECT gradually decreased after antipsychotic and antidepressant medications were introduced. However, the antidepressant medications were not as effective as predicted, and, in the 1980s, the use of ECT as a treatment for depression increased (1,2).

Today, there are global differences in indications for ECT and treatment techniques. In Asian countries, ECT is used primarily for schizophrenia, whereas, in Western countries, depression is the main indication. This difference means that ECT is most commonly used in younger men in Asian countries, and older women in Western countries. With regard to technique, electrode placement differs across countries, but brief pulse-wave stimulus is standard in most countries (3).

The concept of cycloid psychosis was developed in Europe during the last century. Wernicke (4) found that Kraepelin's dichotomy of endogenous psychoses resulted in classifications that were too comprehensive, and sub-classified endogenous psychoses based on the symptomatology. The concept was further developed by Kleist (5,6), who created a system based on Wernicke's work and was able to find examples of patients that did not fit the older classifications. In 1926, he was the first to mention 'zycloiden psychosen', and described two types of the disorder: confusional insanity and motility psychoses. With the ambition of creating criteria for cycloid psychoses, Leonhard (7) added a third category, anxiety-elation psychosis, and described patient cases displaying symptoms from all three categories. He defined cycloid psychosis as acute and recoverable psychoses that were not schizophrenic or manic depressive (8).

In 1974, Perris (9) reported a study of 60 patients that were difficult to classify according to Leonhard's sub-types, as most displayed a mixture of symptoms from all three categories. Based on these observations, Perris and Brockington (10) developed operational diagnostic criteria for cycloid psychosis (which are still used today) that disregard sub-

Table 1. Brockington and Perris criteria for cycloid psychosis published in 1981 [10].

1. An acute psychotic condition, not related to the administration or the misuse of any drug, or to brain injury, occurring for the first time in subjects aged 15–50 years.
2. The condition has a sudden onset with a rapid change from a state of health to a full-blown psychotic condition within a few hours, at the most a few days.
3. At least four of the following must be present:
   (a) Confusion of some degree, mostly expressed as perplexity or puzzlement.
   (b) Mood-incongruent delusions of any kind, mostly with a persecutory content.
   (c) Hallucinatory experiences of any kind, often related to themes of death.
   (d) An overwhelming, frightening experience of anxiety, not bound to particular situations or circumstances (pan-anxiety).
   (e) Deeper feelings of happiness or ecstasy, most often with a religious colouring.
   (f) Motility disturbances of an akinetic or hyperkinetic type, which are mostly expressional.
   (g) A particular concern with death.
   (h) Mood swings in the background, and so pronounced as to justify a diagnosis of affective disorder.
4. There is no fixed combination of symptoms; in contrast, the symptoms may change frequently during an episode and show bipolar characteristics.

types. These criteria also differ from Leonhard's [7] by omitting the criteria of a good outcome. According to Perris [8], the most distinctive characteristic of cycloid psychosis is the acute onset and rarity of prodromal symptoms. He also found the occurrence of the disorder to be independent of season, and mentioned that all symptoms displayed simultaneously and that the predominant symptom could change from one hour to the next, making cycloid psychosis hard to classify [11].

Diagnostic criteria for cycloid psychosis are absent in the tenth revision of the International Classification of Diseases and Related Health Problems (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [12,13]. The closest-matching diagnoses in ICD-10 are sub-groups of acute and transient psychotic disorders: acute polymorphic disorder without symptoms of schizophrenia (APPD) (F23.0), and acute polymorphic disorder with symptoms of schizophrenia (F23.1). In DSM-5, brief psychotic disorder is the best corresponding diagnosis. The lack of nosological concordance of cycloid psychosis in the DSM-IV and ICD-10 diagnostic systems was highlighted by Peralta and Cuesta [11]. The Perris and Brockington [10] criteria for cycloid psychosis are shown in Table 1. Using these criteria, Garcia-Andrade et al. [14] investigated the presence of cycloid psychosis in a broad sample of first psychotic episodes, and found that it might represent a well-defined clinical entity.

The Working Group on the Classification of Psychotic Disorders has suggested changes to the criteria for acute and transient psychotic disorders for ICD-11, whereby the sub-categories with schizophrenic and delusional symptoms are moved to the F2 section [15]. Castagnini and Foldager [16] evaluated the concept of acute and transient psychotic disorders and reported that APPD seemed distinct from the sub-categories with schizophrenic symptoms in various ways, suggesting that a revision is needed.

The treatment of choice for cycloid psychosis has been ECT [17]. However, it is suggested that second-generation antipsychotics combined with benzodiazepines could also be an effective treatment [18]. In a study published in 1974 of 60 patients in Sweden, Perris [9] observed that patients with cycloid psychosis often showed a dramatic improvement after three-to-four treatments with ECT. However, Perris [9] concluded that a response after only a few ECT treatments seemed to increase the risk of a quick relapse, requiring additional treatment to maintain a healthy state. The 60 patients in this study had 215 episodes of acute cycloid psychosis, and the treatment of choice for these episodes was ECT (46%), medication (43%), or insulin coma (6%).

There are a lack of controlled studies on the treatment of cycloid psychosis in general, including treatment with ECT. The existing studies are case reports. Little et al. [17] presented a case of a 39-year-old man who fulfilled Leonhard's [7] definition of cycloid psychosis, where combined antipsychotic and benzodiazepine medication had failed. The patient quickly recovered after receiving ECT. Suzuki et al. [19] reported similar results in a 59-year-old woman who also matched Leonhard's [7] criteria for cycloid psychosis. She was first treated with antipsychotics and antidepressants, but her condition did not improve. When ECT was used, the patient improved. She later relapsed despite olanzapine and paroxetine medication. Eventually, continuous ECT combined with lithium and paroxetine medication was used successfully to prevent recurrence.

Aims

The primary aim of this register study was to determine the rates of remission and response after ECT for cycloid psychosis. The secondary aim was to examine possible predictors of outcome.

Methods

Subjects

This was a population-based register study. Sixty-one patients were treated for cycloid psychosis or acute polymorphic psychotic disorder without symptoms of schizophrenia (F23.0) with ECT in Sweden between 2011–2015. Of those, 42 had available data for the Clinical Global Impression-Severity (CGI-S) scale before and after ECT, and the Clinical Global Impression-Improvement (CGI-I) scale after ECT [20]. The characteristics of the included subjects are presented in Table 2, stratified by sex. There were 30 women and 12 men. The patients included were treated at 13 different hospitals; 39 were inpatients, and three were outpatients. Twenty-one patients were involuntarily hospitalized, and 21 were voluntarily hospitalized (Table 2).

ECT treatment

ECT was administered using either a Mecta Spectrum 5000Q device (Mecta Corp, Lake Oswego, OR) or a Thymatron system IV (Somatics Inc., Lake Bluff, IL), depending on which hospital the patient was treated in. Both are brief pulse devices that use a bidirectional constant current. The mean number of ECT sessions was 6.6 ± 3.4. Right-sided unilateral

Table 2. Study population characteristics, stratified by sex.

	Women	Men	Whole sample
Number	30 (71.4)	12 (28.6)	42 (100.0)
Age			
18–44 years	12 (40.0)	9 (75.0)	21 (50.0)
45–84 years	18 (60.0)	3 (25.0)	21 (50.0)
Antipsychotics			
Yes	27 (90.0)	10 (16.7)	37 (88.1)
No	3 (10.0)	2 (83.3)	5 (11.9)
Number of ECT treatments	6.50 ± 3.30	6.75 ± 3.75	6.57 ± 3.39
Comorbid anxiety disorder			
Yes	6 (20.0)	2 (16.7)	8 (19.0)
No	24 (80.0)	10 (83.3)	34 (81.0)
Comorbid substance dependence			
Yes	2 (6.7)	1 (8.3)	3 (7.1)
No	28 (93.3)	11 (91.7)	39 (92.9)
Type of care			
Inpatient	27 (90.0)	12 (100.0)	39 (92.9)
Outpatient	3 (10.0)	0 (0.0)	3 (7.1)
Compulsory treatment			
Yes	16 (53.3)	5 (41.7)	21 (50.0)
No	14 (46.7)	7 (58.3)	21 (50.0)

Values are n (%) or mean ± standard deviation.

electrode placement according to d'Elia was used in 81% of the treatments (21). The mean dosage at the last treatment (if unilateral) was 0.48 ± 0.10 ms, 66 ± 20 Hz, 6.8 ± 1.1 s, 836 ± 47 mA, and 359 ± 127 mC. The mean EEG seizure duration was 45 ± 22 s. Propofol or thiopental was used as anaesthetic. Data on previous treatment with ECT were not available for four patients. Of the remaining 38 patients, 22 had previously received ECT.

Quality register

All data were extracted from the National Quality Register for ECT in Sweden. The register has been used nationally since 2011. The purpose is to enable monitoring of ECT guidelines and research. ECT is provided by 56 hospitals in Sweden, and all hospitals report to the register. The register includes information on the indication for therapy, severity of symptoms (CGI-S, CGI-I), pharmacotherapy, treatment technique, and side-effects. In 2013, the coverage for the register was 85% (22).

Measures

The CGI-S measures the severity of the patient's illness on a seven-step scale, ranging from 'normal, not at all ill' to 'among the most extremely ill' (20). It was completed once immediately before the first ECT treatment and within 1 week of the last ECT treatment. The CGI-S score after ECT was dichotomized as 'remission' and 'no remission', with the two categories that represent the healthiest state ('normal, not at all ill' and 'borderline mentally ill') classified as remission, and all other categories classified as no remission.

The CGI-I is also a seven-step scale, and records the clinically assessed improvement of the patient after ECT (20). Similarly, the CGI-I score after ECT was dichotomized as 'response' and 'no response', with the top two categories ('very much improved' and 'much improved') categorized as 'response', and all other categories classified as 'no response'.

Statistics

Sex, age, use of antipsychotic medication, number of ECT treatments, and the presence of comorbid psychiatric conditions were used as possible predictors of remission and response. For categorical variables, Chi-square tests were used to test frequency distributions when assumptions were met; otherwise, Fisher's exact test was used. For continuous variables, a t-test was used to test differences between means. A Wilcoxon signed-ranked test was used to compare CGI-S before and after ECT. A p-value of 0.05 or less was considered statistically significant. SPSS version 23 (SPSS Inc., Chicago, IL) was used for statistical analyses.

Ethics

The Regional Ethical Vetting board in Uppsala approved this study. Inclusion in the ECT quality register is non-mandatory, and patients were informed of the register, and had the option to decline participation.

Results

Remission and response rates

Thirty-eight patients were classified as responders based on the CGI-I. This gives an overall response rate of 90.5% (95% confidence interval = 81.2–99.7%). Nineteen patients achieved remission based on the CGI-S. This gives an overall remission rate of 45.2% (95% confidence interval = 39.1–70.5%; Table 3).

Forty patients (95.2%) improved their CGI-S score from pre- to post-ECT, and the remaining two patients had the same score pre- and post-ECT. There was a statistically significant improvement in CGI-S score from pre- to post-ECT ($p < 0.001$).

Age and sex

There was no statistically significant difference in remission or response rate between men and women. The remission

Table 3. Remission rates with possible predictors.

	Remission	No remission	p-value
Number	19 (45.2)	23 (54.8)	
Sex			0.33
Women	15 (50.0)	15 (50.0)	
Men	4 (33.3)	8 (66.7)	
Age			0.12
18–44 years	7 (33.3)	14 (66.7)	
45–84 years	12 (57.1)	9 (42.9)	
Antipsychotics			1.00
Yes	17 (45.9)	20 (54.1)	
No	2 (40.0)	3 (60.0)	
Number of ECT treatments	7.16 ± 3.24	6.09 ± 3.50	0.31
Comorbidity			
Anxiety disorder			0.71
Yes	3 (37.5)	5 (62.5)	
No	16 (47.1)	18 (52.9)	
Substance dependence			1.00
Yes	1 (33.3)	2 (66.7)	
No	18 (46.2)	21 (53.8)	

Values are n (%) or mean ± standard deviation.

rate was 50% for women and 33.3% for men ($p = 0.33$; Table 3), and the response rate was 93.3% for women and 83.3% for men ($p = 0.57$).

There was no statistically significant difference in remission or response rate between age groups. The remission rate was 33.3% for patients aged 18–44 years and 57.1% for patients aged 45–84 years ($p = 0.12$; Table 3). The response rate was 85.7% for patients aged 18–45 years and 95.2% for patients aged 45–84 years ($p = 0.61$).

Medication

There was no statistically significant difference in remission or response rate between patients who did and did not use antipsychotic medication at the end of ECT. The remission rate was 45.9% for patients who used antipsychotic medication at the end of ECT, and 40.0% for patients who did not use antipsychotic medication at the end of ECT ($p = 1.000$; Table 3). The response rate was 89.2% for patients who used antipsychotic medication at the end of ECT, and 100% for patients who did not use antipsychotic medication at the end of ECT ($p = 1.000$).

Number of ECT treatments

The mean number of ECT treatments was 7.16 in patients who achieved remission, and 6.09 in patients who did not achieve remission ($p = 0.31$; Table 3). The mean number of ECT treatments statistically differed between responders and non-responders (7.00 compared with 2.50, $p = 0.010$). None of the four non-responders received more than five ECT treatments. One non-responder improved after the first two ECT treatments, but then had a reaction that caused the suspicion of organic pathogenesis of the medical state and ECT was stopped. Medical examinations including blood examination, a brain scan, and an electroencephalogram did not reveal any pathology. Another non-responder slept and ate better and was less aggressive and psychotic after the first two ECT treatments, but had remaining symptoms. Medical therapy was prescribed and ECT stopped. The two other

patients withdrew consent, and one of these patients experienced subjective memory disturbance.

Comorbidity

There was no statistically significant difference in remission or response rate between patients with and without comorbid anxiety or substance dependence. The remission rate was 37.5% for patients with comorbid anxiety and 47.1% for patients without comorbid anxiety ($p = 0.709$; Table 3), and 33.3% for patients with comorbid substance dependence and 46.2% for patients without comorbid substance dependence ($p = 1.000$; Table 3). The response rate was 75.0% for patients with comorbid anxiety and 94.1% for patients without comorbid anxiety ($p = 0.158$), and 66.7% for patients with comorbid substance dependence and 92.3% for patients without comorbid substance dependence ($p = 0.265$).

Discussion

Remission and response rates

To our knowledge, this is the largest study to date of ECT for cycloid psychosis. We found a high response rate and modest remission rate.

In the current study, the rate of response was 90.5% (95% confidence interval = 81.2–99.7%), as assessed with CGI-I. Neither Perris [9] nor Garcia-Andrade and Lopez-Ibor [18] reported remission or response rates, which makes it difficult to compare their experiences with the current results. However, our results are in line with Perris's [9] opinion about ECT as a treatment for cycloid psychosis. When evaluating medical treatment, Garcia-Andrade and Lopez-Ibor's [18] results indicated that cycloid psychosis patients had a better response than non-cycloid patients. The results of the present study are in line with their finding of a good outcome after treatment for the disorder.

The fact that the four patients who did not show a response in the present study had a mean of only 2.5 ECT treatments suggests that they did not receive enough treatments. The response rate may have been even higher if these patients had received an adequate number of treatments.

Age and sex

Previous studies on ECT treatment for depression report that older patients tend to have a better response than younger patients [23]. Although not statistically significant, our results suggested higher rates of remission and response in the 45–84 year age group than in the 18–44 year age group. Women tended to have higher remission and response rates than men. Although these differences were not statistically significant, this could have been influenced by differences in the primary disorder. Some studies report that men have a higher tendency to have their diagnosis converted from APPD to schizophrenia-related disorders than women [24–27].

Comorbidity

Patients with comorbid conditions are often excluded from clinical trials of depression, and it is suggested that this contributes to the superior remission rate with ECT in clinical trials, as compared with the rates observed in community settings (28). Heikman et al. (29) found that a homogenous group of patients with depression as the only indication for ECT responded better to ECT than a group of patients with comorbidities. In line with that study, our results suggest that patients without comorbid anxiety or substance dependence tended to have higher response rates than patients with these comorbidities, although the differences were not statistically significant, possibly due to the small number of participants.

Limitations

One limitation of the present study is the small study population, which makes it difficult to reach statistical significance in the search for predictors of the outcome. Another limitation is the lack of a control group, which would be needed to compare different treatment strategies. Although unlikely, we cannot rule out the possibility that patients who did not receive any treatment would have had as good a rate of remission as the treated patients. The lack of follow-up information is also a limitation, as we have no data on conversion to schizophrenia or other diagnoses and later events. Moreover, the clinical assessments and diagnoses were made by different clinicians at different hospitals, and were not standardized according to a structured interview.

Implications

This study implies that the concept of cycloid psychosis is clinically useful and that ECT is an effective treatment. In the absence of controlled studies, the present study offers some support for guidelines recommending ECT for cycloid psychosis (22,30). It is important for future studies to compare the effectiveness of ECT and medical treatment, to evaluate which treatment strategy offers patients the best outcome. Future studies also need to incorporate measures of patient satisfaction (31). Randomized clinical trials would offer the best evidence, but are difficult to conduct, because cycloid psychosis is a rare disorder (32).

Conclusions

ECT is an effective treatment for cycloid psychosis. The response rate was high. However, the study population was too small to make firm conclusions on predictors of treatment outcome. Future studies need to compare the outcome of ECT to that of other treatment strategies.

Acknowledgements

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