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Effectivity and Cost-effectivity of the Maintenance Electroconvulsive Therapy: A mirror naturalistic analysis

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Introduction. Maintenance Electroconvulsive Therapy (mECT) is a biological long-term treatment in which patients receive ECT on periods from 2 to 4 weeks, during a variable period of time, usually for more than 6 months. Recent studies showed the efficacy of mECT in prevention of relapse and recurrences. Our study wants to demonstrate the effectivity and cost-effectivity of this therapy in the naturalistic conditions of our area.

Methodology.

Design: Retrospective longitudinal study, with mirror analysis in naturalistic conditions.

Subjects: Patients attended at the *Corporació Sanitària Parc Taulí* (Sabadell, Catalonia), and included in the mECT program during more than six months. We performed diagnostic following DSM-IV criteria, subdividing the sample in three groups: patients affected of Recurrent Major Depression, Bipolar Disorder and Schizophrenia and Related Disorders.

Measures: Number and duration of hospitalizations for the previous three years before the beginning of mECT, compared with the same data for the next three years following the beginning of mECT. Comparative analysis of direct hospitalization costs, costs of the mECT and pharmacologic costs.

Statistic: Descriptive and non- parametric tests.

Results. Sample of 35 patients (1997-2008). There is a significative reduction the number of hospitalizations and days of hospitalization in the total sample and also in each of the three subgroups. The direct total cost decreased but it

was only significant in the Bipolar Disorder subgroup, due to the increased pharmacological costs.

Conclusions. mECT in our area is an effective and cost-effective treatment with a great impact on the reduction of clinical decline and hospitalizations.

Keywords: Electroconvulsive Therapy, Maintenance, Bipolar Disorder, Effectivity, Cost

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Efectividad y Coste-Efectividad de la Terapia Electroconvulsiva de Mantenimiento: un análisis naturalístico en espejo

Introducción. La Terapia Electroconvulsiva de Mantenimiento (TECM) es un régimen de tratamiento biológico a largo plazo en el cual los pacientes reciben TEC en intervalos habitualmente de 2 a 4 semanas y a lo largo de un periodo variable según los casos y normalmente de más de seis meses. Estudios recientes han demostrado la eficacia de TECM en la prevención de recaídas y recurrencias. Nuestro estudio pretende averiguar su efectividad y coste-efectividad en nuestro medio.

Metodología.

Diseño: Estudio retrospectivo longitudinal, con análisis en espejo en condiciones naturalísticas.

Sujetos: Pacientes atendidos en la *Corporació Sanitària Parc Taulí* (Sabadell, Cataluña), en programa de TECM durante más de seis meses. Realizamos los diagnósticos según criterios DSM-IV, subdividiendo la muestra en tres subgrupos: Depresión Mayor Recurrente, Trastorno Bipolar y Esquizofrenia y trastornos Relacionados.

Medidas: Análisis comparativo respecto al número de ingresos y duración en los tres años previos al inicio de la TECM y los 3 años posteriores. Análisis comparativo paralelo

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de los costes directos: ingresos hospitalarios, TECm y costes farmacológicos.

Estadística: Descriptiva y pruebas no paramétricas.

Resultados. Muestra de 35 pacientes (1997-2008). Existe una disminución significativa de los días y número de ingresos en el total de la muestra y en cada uno de los subgrupos diagnósticos. El coste total directo disminuye, pero, debido al incremento de los costes farmacológicos, sólo es significativo en el caso del subgrupo de Trastorno Bipolar.

Conclusiones. La TECm en nuestro medio es un tratamiento efectivo y coste-efectivo con un importante impacto en la reducción de agudizaciones e ingresos hospitalarios.

Palabras clave: Terapia Electroconvulsiva, Mantenimiento, Trastorno Bipolar, Efectividad, Costes

INTRODUCTION

Electroconvulsive Therapy (ECT) is a biological treatment used effectively and safely in psychiatry. It basically consists of an induction of a tonic-clonic convulsion in a controlled manner by the application of an electrical stimulus superior to the previously detected convulsive threshold^{1,2}.

From the first years of use, observation of patients who responded to ECT during the acute phase of their disease but who relapsed, or relapsed when they were discontinued, led clinicians to include more and more patients in different application formats: periodic, continuous or maintenance format^{3,4}. Currently there is a considerable corpus of knowledge about Electroconvulsive Maintenance Therapy (mECT)⁵⁻⁸, although studies and publications in our country are scarce^{4,9-12}.

Maintenance ECT is defined as a long-term treatment regimen in which patients receive ECT at constant or variable intervals (usually between 2 and 4 weeks) and over a variable period depending on the cases^{1,13-14}, with a minimum period of six months of duration¹⁴. It is a technique mainly oriented to the prevention of the relapses (Continuation ECT) or recurrences (Maintenance ECT) and for patients resistant to other therapies^{1,3,4,14-17}. Its application follows the model of ambulatory surgery, and in general, the same precautions and steps should be followed as in the conventional ECT, but also the special ones of the ambulatory ECT^{1,14,18-19}. mECT is also a good alternative for patients who do not respond adequately to drug therapy because of resistance or intolerance, although there is a lack of detailed consensus guidelines for the use of this therapy²⁰⁻²⁴.

As we have already mentioned, in the international literature there are numerous studies about diverse aspects of the technique^{4,7,25}. In recent years, the most relevant

results come from the North American "CORE Group", *Consortium for Research on Electroconvulsive Therapy*²⁶⁻²⁸, but also from other groups²⁹⁻³⁵. In the Spanish centres, although the practice of the mECT has undergone a considerable improvement, at the moment there are few publications about the topic^{9-12,36,37}.

Regarding cost-effectivity studies, some authors suggest that in addition to reducing the number of relapses, mECT would be useful and cost-effective³⁸. It is also stated that there is a reduction of the costs in the treatment with the mECT with respect to the pharmacological treatment in pathologies like Major Depressive Disorder in the elderly²². Recently, we had the first results on cost-effectiveness of maintenance TEC in a Spanish center¹².

The objectives of our study would be, on the one hand, to determine the effectiveness and cost-effectiveness of the mECT in real conditions of assistance, and also to compare its effectivity and cost-effectivity according to the different diagnostic subgroups.

Our initial hypothesis, supported by different previous studies and our own clinical experience, would lead to a reduction in the number of admissions and the days of admission after initiating the mECT pattern, with the consequent reduction of associated direct costs.

METHODS

It is a descriptive and longitudinal study, with retrospective data collection. The subjects of the study were patients who started ECT at the *Corporació Sanitària Parc Taulí* in Sabadell (Barcelona) between January 1997 and January 2008 and with a duration of ECT treatment equal to or greater than 6 months.

The *Corporació Sanitària Parc Taulí* belongs to the Public Health Care Network of Catalonia. It serves a population of 430,000 inhabitants and is the only hospital Centre that treats major mental disorders in the area. It has an Electroconvulsive Therapy Program since 1997. Since then, the mECT technique is also usually performed. Although rates may vary each year, the total average ECTs performed is over 600 applications per year.¹²

Population

We included all patients who started mECT in this period. Patients were divided into three subgroups according to DSM-IV (APA, 2000) criteria for Recurrent Major Depression (Subgroup 1), Bipolar Disorder Type I (Subgroup 2) or Schizophrenia and Related Disorders (Subgroup 3), which included patients with Schizoaffective Disorder Type

Table 1	Description of the sample (n=35)				
	All the sample	MD Subgroup	BD Subgroup	SQZ Subgroup	Signification
N (%)	35 (100%)	15 (42.9%)	9 (25.7%)	7 SAD (20%) 4 PSQZ (11.4%)	-
Gender					
Man (%)	18 (51.4%)	6 (40%)	5 (55.6%)	7 (63.6%)	X ² =0.29/p=0.49
Women (%)	17 (48.6%)	9 (60%)	4 (44.4%)	4 (36.4%)	
Age at the start of the mECT (years) (mean, s.d., range maximum-minimum)	51.1 ± 13.9 (25 to 76)	55.0 ± 12.7 (25 to 76)	51.1 ± 15.9 (28 to 72)	45.8 ± 13.0 (30 to 66)	(a) K-W 0.531 (b) K-W 0.255 (c) K-W 0.494
Number of ECT applications (in the following next three years) (mean, s.d., range maximum-minimum)	37.5 ± 23.5 (8 to 108) Total: 1.313	33.2 ± 15.5 (8 to 63)	37.2 ± 20.7 (15 to 68)	43.5 ± 33.5 (9 to 108)	(a) K-W 0.835 (b) K-W 0.878 (c) K-W 0.939
Frequency / number of ECT by month (mean, s.d., range maximum-minimum)	2.1 ± 1.0 (0.8 to 5.2)	2.2 ± 1.1 (0.9 to 5.2)	1.8 ± 1.1 (0.8 to 4.8)	2.0 ± 0.8 (0.8 to 3.6)	(a) K-W 0.200 (b) K-W 0.429 (c) K-W 0.342
Total duration of mECT (in months) DUR (mean, s.d., range maximum-minimum)	27.8 ± 29.0 (6.0 to 146.5) Total: 975.07	26.9 ± 36.5 (6.0 to 146.5)	30 ± 28 (11.5 to 96.0)	25.7 ± 18.9 (6.0 to 67.6)	(a) K-W 0.079 (b) K-W 0.340 (c) K-W 0.849
MD: Recurrent Major Depression Disorder Subgroup. BD: Bipolar Disorder Type I Subgroup. SQZ: Schizophrenia and Related Disorders Subgroup. s.d.: Standard deviation. DUR: Duration of the period considered from the start of the mECT application until the end of the study or until the end of the study follow-up (the period may be longer or shorter than three years, but always longer than 6 months). SAD: Schizoaffective Disorder. PSQZ: Paranoid Schizophrenia. X ² : Chi Square test. p: significance. Comparison between diagnostic subgroups: (a) MD vs BD, (b) MD vs SQZ and (c) BD vs SQZ. K-W: Kruskal-Wallis test.					

Bipolar and Paranoid Schizophrenia) diagnosed by their reference specialists (Table 1).

Only those patients who received mECT for less than 6 months were excluded. All patients, except for two cases, also continued pharmacological maintenance treatment during the application of the technique. All patients were treated with various intervals and energies using a Thymatron® device from Somatics, in bifrontal application and under general anesthesia by sodium thiopentate and succinylcholine at different doses. All the patients signed the corresponding informed consent for the practice of the Electroconvulsive Therapy of our Hospital.

Method

We initially performed a descriptive analysis of the basic sociodemographic and clinical characteristics, which included gender, age, frequency, duration and number of sessions of the ECT. Subsequently, we performed an analysis of effectivity between between the previous three years and three

years after following the start of the mECM in the study subjects, as well as a cost-effectivity analysis and a comparative analysis between diagnostic subgroups. The main variables we studied in the effectivity analysis were the number of income and the number of days of hospitalization.

For the cost-effectivity analysis, we performed a direct cost analysis between the three previous years and three years after the start of the mECT, and also performed a comparative cost analysis between the three diagnostic subgroups. The main variables of direct cost included the cost in days of hospitalization, the cost in psychiatric medication and the cost of realizing the ECT itself. The previous direct total cost was calculated by the sum of the total costs in days of hospitalization and the cost of psychiatric medication in the three years prior to starting the mECT. The subsequent direct total cost was calculated by the sum of the total costs in days of hospitalization and the cost of psychiatric medication three years after starting the mECT and also the cost of the mECT itself. We include the calculation of the savings (if any) in the different costs pre-

and post start of the mECT. The direct costs are obtained by excluding the TECs realized during the acute phase, which in turn are included in the direct costs by day of hospitalization.

Data collection was performed using the patient's medical history and Therapy records. All data were conveniently anonymised.

For the calculation of the costs of admission days, we used the 2013 CatSalut (Catalan Health Public Organization) direct costs scales in our Hospital. An estimated unit of 183.31 Euros per day of hospital admission and 150.71 Euros per ambulatory Electroconvulsive Therapy was considered.

The costs of psychiatric medicaments (pre- and post) were calculated individually, including the actual Spanish total costs in Euros of the 2013 retail price of each psychiatric medication, without considering the possible differential discount of members of the Social Security or other characteristics of each patient.

Statistical analysis

An *ad hoc* database was designed using the Microsoft Excel program and the results were then analyzed using the SPSS version 21 program. Due to the small sample size, the statistics were descriptive (means, standard deviations, ranks) and data were compared using nonparametric tests (Z of Wilcoxon, Chi Square, Kruskal-Wallis and U of Mann-Whitney). When making repeated comparisons, we used the Bonferroni correction.

RESULTS

Description of the sample

We analysed 35 mECT periods corresponding to 35 patients seen between January 1997 and January 2008 (Table 1). The sample is made up of 51.4% of males, with a mean age of 51.1 years. Fifteen patients (42.9%) were included in Subgroup 1 with Recurrent Major Depressive Disorder, nine cases (25.7%) affected by Bipolar Disorder Type I in Subgroup 2, and finally, eleven cases (31.4%) in the Schizophrenia Subgroup 3 and Related Disorders (seven affects of Schizoaffective Disorder and four of Paranoid Schizophrenia). We found no significant baseline differences between the diagnostic subgroups in terms of age or gender.

Patients received an average of 37.5 sessions, which monthly includes 2.1 electro-stimulations for 27.8 months of mean duration of each mECT period (Table 1).

Analysis of effectivity

The cumulative mean hospitalizations for the three years prior to the start of the mECT was 1.9 hospitalizations *versus* 0.5 hospitalizations for the three subsequent years (Table 2). There was a total decrease of 73.5%, that is, a change from 68 hospitalizations before the start of the mECT to 18 hospitalizations (Figure 1). The number of days of hospitalizations was also significantly reduced (Table 2). We found a total of 2,210 days of hospitalizations in the three years prior, changing to 499 days of hospitalizations in the three years thereafter, with a saving of 1,711 days of hospitalization. Analysing the mean number of days of admission per patient, we found that it was significantly reduced from an average of 63.1 days of hospitalization before the start of ECT at 14.2 days of median admission three years after the start of the mECT. This represented a reduction of 77.5% in the total of days of hospitalization in the whole sample, which resulted in an average saving of 48.8 days per patient. The mean duration of each hospitalization was also reduced from the mean 32.5 days of hospitalization for the 3 years prior to the start of the mECT, to 27.7 days of average hospitalization for the 3 years following the beginning of the mECT.

Data by diagnosis subgroups

Patients in Subgroup 2 (Bipolar Disorder Type I) had a higher number of days of hospitalization and a higher number of previous hospitalization in the previous three years. Nevertheless, after initiating mECT, there was a greater decrease than detected in the other two diagnostic subgroups (Table 2).

If we take into account the patient's diagnosis, there are certain differences in the reduction of the number of hospitalizations (Table 2), although all of them are significant. This represents a reduction in the average number of hospitalizations of 83.4% (three hospitalizations less per patient) in Subgroup 2 affected by Bipolar Disorder, 70% in Subgroup 1 of Major Depressive Disorder (0.7 less hospitalizations per patient) and 64.7% in Subgroup 3 of Schizophrenia and Related Disorders (1 hospitalization less per patient).

By diagnosis subgroups, significant reductions are also observed on the days of admission (Table 2). In Subgroup 2 affected by Bipolar Disorder, a reduction of 84.9% of the days of hospitalizations was observed. In Subgroup 1 (Recurrent Major Depressive Disorder) the reduction is 63.3% after the onset of mECT, and finally in Subgroup 3 (Schizophrenia and Related Disorders), the reduction entails an average saving of 76.6% less days of hospitalizations per patient after initiating mECT.

Tabla 2	Effectivity Analysis								
	All the sample (n=35)	Z / p	MD Subgroup (n=15)	Z / p	BD Subgroup (n=9)	Z / p	SQZ Subgroup (n=11)	Z / p	Comparative (U/p)
Pre-ECT hospitalizations days in previous three years (mean, s.d., range maximum-minimum)	63.1 ± 49.7 (0 to 214) Total: 2,210		33.2 ± 25.6 (0 to 84)		115.1 ± 52.9 (39 to 214)		61.4 ± 38.6 (0 to 132)		(a) K-W: 0.001 U/p: 7.0/0.001 (b) K-W: 0.001 U/p: 48.5/0.077 (c) K-W: 0.020 U/p: 19.0/0.020
Post-ECT hospitalizations days in next three years (mean, s.d., range maximum-minimum)	14.2 ± 25.6* (0 to 91) Total: 499	-4.429 / 0.001	12.2 ± 24.3* (0 to 73)	-2.158 / 0.031	17.4 ± 28.8* (0 to 86)	-2.666 / 0.008	14.4 ± 26.8* (0 to 91)	-2.599 / 0.009	(a) K-W: 0.434 (b) K-W: 0.639 (c) K-W: 0.868
Savings in hospitalizations days (mean, s.d., range maximum-minimum)	48.8 ± 52.3 (-36 to 214) Total: 1,711		21.0 ± 31.8 (-36 to 84)		97.6 ± 57.4 (39 to 214)		47.0 ± 44.0 (-24 to 132)		(a) K-W: 0.001 U/p: 9.0/0.001 (b) K-W: 0.002 U/p: 53.5/0.134 (c) K-W: 0.033 U/p: 21.5/0.031
Total number of admissions in the previous three years (mean, s.d., range maximum-minimum)	1.9 ± 1.4 (0 to 6) Total: 68		1.0 ± 0.7 (0 to 3)		3.6 ± 1.4 (2 to 6)		1.7 ± 1.1 (0 to 4)		(a) K-W: 0.001 U/p: 5.5/0.001 (b) K-W: 0.001 U/p: 52.0/0.121 (c) K-W: 0.005 U/p: 13.0/0.004
Total number of admissions in the next three years (mean, s.d., range maximum-minimum)	0.5 ± 0.8* (0 to 3) Total: 18	-4.352 / 0.001	0.3 ± 0.6* (0 to 2)	-2.636 / 0.008	0.6 ± 1.0* (0 to 3)	-2.682 / 0.007	0.6 ± 0.9* (0 to 3)	-2.326 / 0.020	(a) K-W: 0.369 (b) K-W: 0.550 (c) K-W: 1.000
Savings in number of hospitalizations (mean, s.d., range maximum-minimum)	1.4 ± 1.5 (-1 to 5) Total: 50		0.7 ± 0.8 (0 to 3)		3.0 ± 1.6 (1 to 5)		1.0 ± 1.3 (-1 to 4)		(a) K-W: 0.001 U/p: 14.0/0.001 (b) K-W: 0.002 U/p: 66.0/0.413 (c) K-W: 0.011 U/p: 17.0/0.012

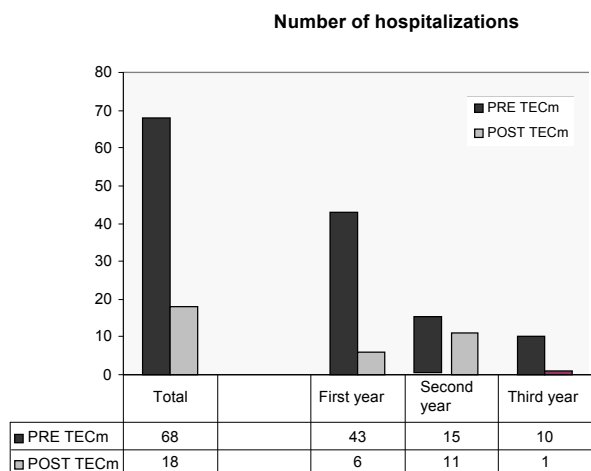
MD: Recurrent Major Depression Disorder Subgroup. BD: Bipolar Disorder Type I Subgroup. SQZ: Schizophrenia and Related Disorders Subgroup. s.d.: Standard deviation. Pre and post Z comparisons / p: Wilcoxon Z / significance. * 0.001. Comparison between diagnostic subgroups: (a) MD vs BD, (b) MD vs SQZ and (c) BD vs SQZ. K-W: Kruskal-Wallis. U / p: Mann-Whitney U / significance (p significant <0.016, after Bonferroni correction).

When we compared the three diagnostic subgroups among themselves, we observed that the patients in Subgroup 2 (Bipolar Disorder Type I) had a different previous evolution (Table 2). Probably in relation to this starting point, the saving of Subgroup 2 with Bipolar I Disorder on days of hospitalizations was also significantly higher than Subgroup 1 with Major Depressive Disorder and the saving in total number of hospitalizations was also significantly higher in the subgroup with Bipolar I disorder than in the subgroups with Major Depressive Disorder and with

Schizophrenia and Related Disorders (Table 2). However, we did not find significant differences between the three subgroups with respect to total days of subsequent hospitalizations or the number of total subsequent hospitalizations (Table 2).

Influence of gender and age

Regarding gender, it is noteworthy that, although in both genders the numbers of hospitalizations from the Pre-



The dark columns represent the number of admissions made during this time period before starting the mECT. The gray columns the number of admissions made later. Total columns include summation of admissions, while columns separated by year (first, second, or third year), only include the admissions performed in that time (year) period.

Figure 1 Evolution in the number of hospitalizations before and after starting the mECT

mECT to the Post-mECT significantly decrease, it is higher in men (80.5%) than in women (56.3%). In the period prior to the onset of mECT, males accrued 1,308 days of admission versus 983 days in females. After the onset of mECT, males only accumulated 252 days versus 334 females. Anyway, these differences were not significant.

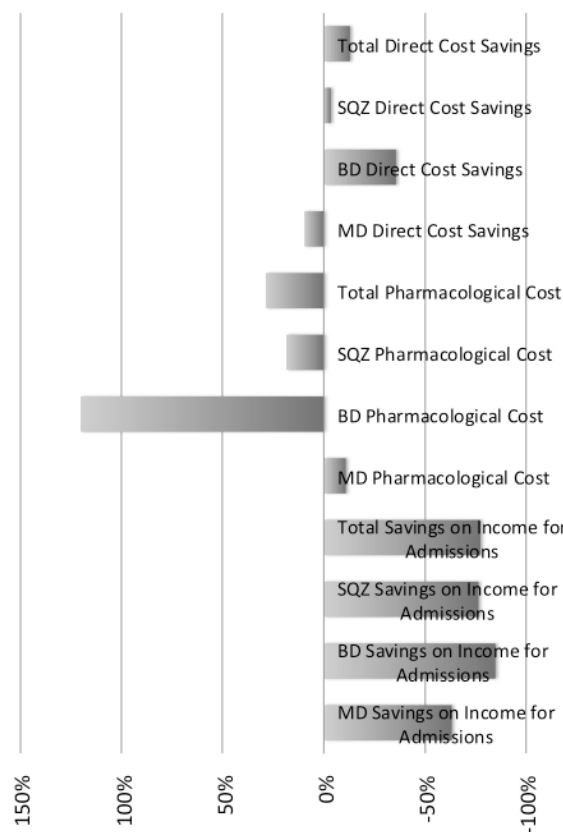
The age of the patients did not significantly influence the results, and even older patients appear to respond better to mECT. Considering the median of the sample, we divided the patients into two subgroups, above and below 52 years old. The first subgroup would consist of patients of ≥52 years old and the second by those over 52 years of age (19 cases vs 18). Although the number of hospitalizations before the onset of ECM was practically equal in both age subgroups, the decrease in hospitalizations was more remarkable in the subgroup over 52 years, but not significant.

Cost / Effectivity Analysis

In a second phase, we performed a cost / effectiveness analysis also considering the three years prior to the start of the mECT and the 3 years following the start of the mECT, including the total direct cost (days of entry and cost of psychiatric medication) in both periods (Table 3). In the case of the direct total post-start cost of the mECT, we added the cost of the mECT. We also considered the possible savings in all these aspects in the 3 years following the start of the mECT.

The three diagnostic subgroups start from somewhat different prior costs. Specifically, patients with Type I Bipolar Disorder had significantly higher costs than patients with Recurrent Major Depressive Disorder, due to a higher number of previous days of hospitalization. There were no significant differences between the subgroups regarding total cost and cost of previous psychiatric medication (Table 3). In Figure 2 we show the percentage changes (increases and percentage reductions obtained) and by diagnostic subgroups.

With the data obtained, both in the total sample and among all diagnostic subgroups, we observed a decrease that is significant in terms of the costs per day of hospitalization after mECT onset (Table 3). At the same time, we also observed that there is an increase in the total cost of post-start ECT psychiatric medication in the total sample and between Subgroups 2 and 3 (Bipolar I Disorder and Schizophrenia and Related Disorders). This increase is significant only in Subgroup 2 (Type I Bipolar Disorder). In



MD: Recurrent Major Depression Disorder Subgroup. BD: Bipolar Disorder Type I Subgroup. SQZ: Schizophrenia and Related Disorders Subgroup

Figure 2 Evolution of the costs percentages

Table 3 Cost-Effectivity Analysis

	All the sample (n=35)	MD Subgroup (n=15)	Z/p	BD Subgroup (n=9)	Z/p	SOZ Subgroup (n=11)	Z/p	Signification
Total Cost of the hospitalizations Days (in the previous three years) (mean, s.d., range maximum-minimum)	11,574.7 ± 9,127.6 (0 to 39,228.3)	6,085.9 ± 4,696.1 (0 to 15,398.0)		21,101.0 ± 9,699.2 (7,149.1 to 39,228.3)		11,265.2 ± 7,082.7 (0 to 24,196.9)		(a) K-W: 0.001 U/p: 7.0/0.001 (b) K-W: 0.001 U/p: 48.5/0.077 (c) K-W: 0.020 U/p: 19.0/0.020
Total Cost of the hospitalization Days (in the three subsequent years) (mean, s.d., range maximum-minimum)	2,613.4 ± 4,696.5 (0 to 16,681.2)	2,236.4 ± 4,469.9 (0 to 13,381.6)	-4.429 / 0.001	3,197.7 ± 5,285.2 (0 to 15,764.7)	-2.666 / 0.008	2,649.7 ± 4,914.9 (0 to 16,681.2)	-2.599 / 0.009	(a) K-W: 0.434 (b) K-W: 0.639 (c) K-W: 0.868
Savings in hospitalizations Days (mean, s.d., range maximum-minimum)	8,961.2 ± 9,596.2 (-6,599.2 to 39,228.3)	3,849.5 ± 5,846.6 (-6,599.2 to 15,398.0)		17,903.3 ± 10,530.7 (7,149.1 to 39,228.3)		8,615.6 ± 8,076.9 (-4,399.4 to 24,196.9)		(a) K-W: 0.001 U/p: 9.0/0.001 (b) K-W: 0.002 U/p: 53.5/0.134 (c) K-W: 0.033 U/p: 21.5/0.031
Cost of the ECT (in the three subsequent years) (mean, s.d., range maximum-minimum)	5,653.7 ± 3,541.5 (12,05.7 to 16,276.7)	5,013.6 ± 2,348.3 (1,205.7 to 9,494.7)		5,609.7 ± 3,132.2 (2,260.6 to 10,248.3)		6,562.7 ± 5,054.7 (1,356.4 to 16,276.7)		(a) K-W: 0.835 (b) K-W: 0.878 (c) K-W: 0.939
Total Cost of Psychiatric Medicaments (in the previous three years) (mean, s.d., range maximum-minimum)	4,353.1 ± 4,845.5 (401.3-19,316.5)	2,828.9 ± 2,733.7 (401.3 to 9,606.6)		3,059.1 ± 2,502.7 (780.2 to 8,774.0)		7,490.4 ± 6,966.9 (519.7 to 19,316.5)		(a) K-W: 0.612 (b) K-W: 0.159 (c) K-W: 0.239
Total Cost of Psychiatric Medicaments (in three years thereafter start the mECT) (mean, s.d., range maximum-minimum)	5,601.3 ± 6,889.4 (0 to 35,578.3)	2,520.9 ± 2,765.7 (0 to 9,348.7)	-1.212 / 0.225	6,732.7 ± 4,992.1 (2,470.2 to 15,061.8)	-2.073 / 0.038	8,876.3 ± 10,175.9 (0 to 35,578.3)	-0.622 / 0.534	(a) K-W: 0.007 U/p: 22.0/0.005 (b) K-W: 0.008 U/p: 35.5/0.013 (c) K-W: 0.970
Savings in Cost of Psychiatric Medicaments (mean, s.d., range maximum-minimum)	-1,248.2 ± 4,752.5 (-16,261.8 to 8,341.0)	307.9 ± 3,589.8 (-4,353.2 to 6,274.9)		-3,673.6 ± 4,033.3 (-10,867.6 to 1,324.4)		-1,385.9 ± 6,741.1 (-16,261.8 to 8,341.0)		(a) K-W: 0.013 U/p: 26.0/0.012 (b) K-W: 0.071 (c) K-W: 0.239
Previous Total Direct Cost (in three years) (mean, s.d., range maximum-minimum)	15,927.8 ± 10,199.8 (2,222.6-43,422.5)	8,914.8 ± 3,521.9 (2,645.9 to 15,815.7)		24,160.1 ± 9,860.2 (11,311.8 to 43,422.5)		18,755.6 ± 10,724.4 (2,222.6 to 40,213.8)		(a) K-W: 0.001 U/p: 3.0/0.001 (b) K-W: 0.001 U/p: 31.0/0.006 (c) K-W: 0.184

Continuation		All the sample (n=35)	MD Subgroup (n=15)	BD Subgroup (n=9)	SOZ Subgroup (n=11)	Signification
Table 3		Z/p	Z/p	Z/p	Z/p	
Subsequent Total Direct Cost (in three years) (mean, s.d., range maximum-minimum)	13,868.6 ± 9,869.3 (1,356.4-56,071.1)	-0.901 / 0.368	9,770.9 ± 5,183.8 (1,500.5 to 18,503.5)	15,540.2 ± 5,472.0 (5,118.3 to 22,513.3)	18,088.7 ± 14,909.8 (-1,356.4 to 56,071.1)	(a) K-W: 0.025 U/p: 30.0/0.025 (b) K-W: 0.059 (c) K-W: 0.732
Savings in subsequent Direct Cost (in three years) (mean, s.d., range maximum-minimum)	2,059.2_10,201.4 (-15,857.2 to 25,985.2)		-856.2 ± 7174.8 (-10,904.7 to 9,746.4)	8,619.9 ± 9,582.3 (-4,980.3 to 25,195.7)	666.9 ± 12,437.4 (-15,857.2 to 25,985.2)	(a) K-W: 0.025 U/p: 30.0/0.025 (b) K-W: 0.088 (c) K-W: 0.119

MD: Recurrent Major Depression Disorder Subgroup. BD: Bipolar Disorder Type I Subgroup. SOZ: Schizophrenia and Related Disorders Subgroup. s.d.: Standard deviation. Previous Total Direct Cost: Total Cost of the hospitalizations Days (in the previous three years) + Total Cost of Psychiatric Medicaments (in the previous three years). Subsequent Total Direct Costs (in the next three years): Total Costs of subsequent ECT + Total Cost of the hospitalization Days (in the three subsequent years) + Total Cost of Psychiatric Medicaments (in three years thereafter start the mECT). Cifers in current euros. Pre and post Z comparisons / p: Wilcoxon Z / significance. * 0.001. Comparison between diagnostic subgroups: (a) MD vs BD, (b) MD vs SOZ and (c) BD vs SOZ. K-W: Kruskal-Wallis. U / p: Mann-Whitney U / significance (p significant <0.016, after Bonferroni correction).

Major Depressive Disorder, on the other hand, a certain saving in psychiatric medication is obtained, not significant in itself, but in relation to the other two diagnostic subgroups. Figure 2 shows the economic "savings" in terms of days of income and "losses" in terms of pharmacological costs increases.

Despite this increase in the cost of psychiatric medication in Subgroup 2 (Bipolar I Disorder), paradoxically, direct costs are only reduced significantly in this same subgroup. There is also direct but not significant cost reduction in the total sample and in Subgroup 3 (Schizophrenia and Related Disorders). In Subgroup 1 (Recurrent Major Depressive Disorder) there is even a certain increase in direct total cost (Table 3).

The relative increase in pharmacological direct costs is mainly due to the high cost of some depot treatments with atypical antipsychotics that were introduced in certain cases after initiating the ECT (data not shown).

DISCUSSION

As the main results in our sample, we observed a clear overall reduction in the number of hospitalizations and the total number of days of admission following the initiation of an mECT pattern, in all diagnostic subgroups (Table 2). This result is in line with the different previous studies^{3,4,7,9,10,25,31,35}.

Although there are no significant baseline differences in terms of age, gender, number of ECT performed, ECT frequency and total ECT duration, due to diagnosis (Table 1), we have to underline the final good results in the subgroup of patients affected Type I Bipolar Disorder.

The economic aspects of cost-effectivity of ECT have been poorly studied in the different previous studies. However, both early analyses by Steffens and collaborators³⁹, of Bonds and collaborators⁴⁰, and the review by Rabheru and Persad³, detect a significant cost benefit to be determined, especially in older people affected by mood disorders. Moreover, few naturalistic studies have studied the impact of added pharmacological cost.

The review by Greenhalgh and collaborators²¹ models the economic impact of acute phase ECT on different populations. According to this analysis, although ECT shows a greater effectivity than pharmacotherapy in the initial periods, there are many doubts about its effectivity in the long term. The authors conclude that further studies are needed in the area examining the long-term effectivity of ECT as well as pharmacological treatments following a successful intervention with ECT, the short- or long-term cognitive effects of ECT, as well as the impact of the TEC on suicide and other causes of mortality. There is also a report

from the NICE Advisory Committee⁴¹ on the effectivity and cost of ECT in depression, catatonic schizophrenia and mania, as well as a NICE Guidebook⁴² (NICE, 2003–2009), with controversial results.

The results of the NICE Guideline^{41,42} and the Greenhalgh review²¹, have been debated and criticized by different authors. In particular, William McDonald²³, from the University of Atlanta has highlighted the lack of studies on the subject and the methodological problems they suffer. For example, it cites how the direct costs of treating depression (hospitalization, outpatient care and pharmaceutical costs) may be only one quarter of the indirect costs such as lost productivity, absenteeism or the enormous costs of consumed suicides. This criticism is an important point of reflection; it highlights the lack of attention to these problems of costs and cost-effectivity in therapies otherwise universally used and with a very high effectivity.

In fact, the study by Mohamed Aziz and colleagues at the University of Cincinnati²², uses a model of cost-effectivity of treatments after the application of ECT in acute phase in elderly patients with recurrent depression. Maintenance ECT proves to be more effective and cost-effective than pharmacological treatment alone.

A subsequent study in depression⁴³ compares the cost-effectiveness of acute ECT with the cost-effectiveness of repetitive transcranial magnetic stimulation (rTMS). Although the treatment itself was equally expensive in both subgroups, rTMS was less effective than ECT in this sample and costs were higher in the subgroup receiving rTMS, mainly due to the increase in direct costs of the service and cost for informal caregivers. We are not aware of similar studies with other therapeutic techniques.

We also have a study on the economic implications of the ECT continuation / maintenance in a Spanish Hospital¹². In a sample of 8 cases included in their ECT continuation / maintenance program, the results show a significant reduction in days of hospital admission, direct costs of hospital stay and visits to the emergency room, as well as a notable subjective improvement from the patients.

Our data provide interesting results for diagnostic subgroups, as well as added new data those reviewed by Greenhalgh and collaborators²¹, who do not study ECT or the specific case of ECT in Bipolar Disorder.

We have to take into account that our analysis has not considered the indirect costs. There is a debate about the indirect costs of mental illnesses, which include very relevant aspects in public health and that have generated a major call of attention from the main experts. About 14% of the global impact of diseases is due to chronic neuropsychiatric pathologies, which also lead to significant loss of sur-

vival, quality of life, absenteeism, loss of opportunities, marginalization, etc. Often, this impact is underestimated by the difficulties of linking the impacts of mental health on other diseases and socio-occupational aspects⁴⁴. In any case, the indirect costs are hardly estimable, and even more difficult to calculate for special populations as is our case of very severe and resistant patients. Our hypothesis is that costs, as they are usually measured, may not sufficiently reflect their complexity in these very serious and special populations, and that we should include quality of life and survival measures, as well as the impact on the family environment and caregivers.

We should also mention that for the calculation of the costs per hospital admission days, an estimated unit of 183.31 Euros was considered - which included ECT on a global basis during admission - while for the costs of the ambulatory Electroconvulsive Therapy performed later, a specific cost was considered in a differentiated way. This can influence the main outcome variable. In future prospective cost-effectiveness studies, all direct and indirect costs incurred with each patient, including the costs (and benefits) incurred by the disease (or the technique), could be accounted for in much more detail, for the families (and caregivers) and the health system.

Above and beyond the macroeconomic figures, it is worth noting the great benefit to the patient and his family, the significant reduction in the number of days of hospitalization and in the total hospitalization, with less suffering and distortion of everyday life associated with the illness. This aspect is relevant by itself and supposes the main success of the mECT.

The limitations of the analysis include, first and foremost, those of sample size and retrospective and uncontrolled naturalistic analysis. Likewise, the results show only those patients who have required more than six months of mECT. The cost-effectiveness analyses of our sample do not include data from outpatient and/or emergency visits, which may influence the final results of direct costs. Another of the main limitations of the study, similar to previous studies, is due to the problem of the phenomenon of regression to the mean.

The mirror analysis and its natural characteristics imply an effort of ecological validity of the results. With regard to the few previous studies, our work provides a vision of the costs and benefits of the technique based on real data, without estimates and from an extensive experience with the technique in an organizational structure prepared to assume this application. At the level of global effectiveness, our results, although with smaller samples than other previous studies in our environment, bring a new reinforcement to its implementation in future therapeutic guidelines.

As a reflection for future studies, we could consider the need to study the differences in the seizure threshold, controlling possible confounding variables or the type of application (bilateral vs. unilateral), energy, or different ECT programs.

CONCLUSIONS

Our analysis shows that there is a significant reduction, both in the global sample and in the three diagnostic subgroups, regarding the number of hospitalizations and the total number of days of hospitalizations after the start of the mECT. By diagnostic subgroups, this saving is more significant in the subgroup of Bipolar Disorder.

The economic aspects of cost-effectivity are also relevant, but when we analyse the total direct savings, it is only significant in the subgroup with Bipolar Disorder. Our data are in the same line as the different results found in the international bibliography, which allows us to affirm that Maintenance ECT is an efficient, safe and relatively cost-effective technique in the medium and long-term maintenance treatment of patients affected by a severe mental disorder that do not respond to other therapeutic strategies.

Finally, more controlled studies with prospective methodologies are needed to deepen the influence of mECT on patient outcomes, along with the study of other factors that may influence these results and with key aspects of safety and cost-benefit of the technique.

Declaration of interest

None for the purpose of this work.

Declaration of transparency

The main author, Jesús Cobo*, states that this manuscript is an honest, accurate, and transparent account of the study being presented, that some important aspect of the study has not been omitted, and that the differences with the study initially planned have been explained (and whether Are relevant, recorded.) *Guarantor of the manuscript.

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