ORIGINAL ARTICLE/ARTIGO ORIGINAL

The Effectiveness of Maintenance Electroconvulsive Therapy
A Eficácia da Eletroconvulsivoterapia de Manutenção

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Resumo

Introdução: A eletroconvulsivoterapia (ECT) é um tratamento seguro e eficaz, indicado para o tratamento de doenças mentais graves resistentes ao tratamento. No entanto, está associado a uma alta taxa de recaída após o término do curso de ECT agudos (ECT-A). É recomendado realizar tratamento de manutenção de forma a aumentar a taxa e duração da remissão. A ECT de manutenção (ECT-M) é uma opção, embora ainda pouco utilizada. O objetivo deste estudo foi avaliar a eficácia da ECT-M em reduzir o número e duração de hospitalizações, assim como custos associados, em doentes com doença mental grave.

Métodos: Foi realizado um estudo em espelho comparando o número e duração de hospitalizações antes e após iniciação de ECT-M. Foram colhidas informações relativamente a dados demográficos e técnicos, assim como dose de medicação. Foi comparado o custo médio antes e após a iniciação de ECT-M. Todos os tratamentos foram realizados com uma MECTA spECTrum 5000QÒ. A análise estatística foi realizada com o SPSS 22.

Resultados: Foram incluídos 16 doentes no estudo. O número médio de tratamentos de ECT-M eletroconvulsivoterapia foi 41, com uma duração média de 23 meses. A frequência mais comum foi mensal. Foi obtida uma diferença estatisticamente significativa quanto ao número de hospitalizações (Mdn= 2,0 antes e Mdn=0,0 após) e ao número total de dias em internamento (Mdn=86,0 antes e Mdn=14,5 após). Foram encontradas diferenças marginais na dosagem de antidepressivos, com valores superiores no período após iniciação e ECT-M. Não foram encontradas diferenças significativas na dosagem de antipsicóticos. O custo médio por doente, antes e após iniciação de ECT-M foi, respetivamente, 10 621€ e 5 653€.

Conclusão: Na amostra estudada, a ECT-M reduziu significativamente o número de internamentos e dias de hospitalização. A iniciação de ECT-M reduziu o custo por doente em 47%.

Abstract

Introduction: Electroconvulsive therapy (ECT) is a safe and effective treatment for treatment resistant severe mental disorders. However, it has a high relapse rate, following the acute course (A-ECT). Maintenance treatment is recommended to increase remission rate and duration. Maintenance ECT (M-ECT) is an option, although under-prescribed. The aim of this study was to assess M-ECT effectiveness in reducing number and duration of hospital admissions, as well as associated costs, in patients with severe mental disorders. Mirror study comparing number and duration of hospital admissions before and after first M-ECT.

Methods: Information was gathered for demographic and technical data, and drug dosing. Mean cost before and after the initiation of M-ECT was compared. All treatments were performed with a MECTA spECTrum 5000QÒ. Statistical analysis was performed using SPSS 22.

Results: A total of 16 patients were enrolled. The mean number of M-ECT treatments was 41.25 with a mean duration of 23 months. Treatment frequency was mainly once a month. A statistically significant decrease was found for number of admissions (Mdn=2.0 before and Mdn=0.0 after) and for total days in admission (Mdn=86.0 before and Mdn=14.5 after). Marginally significant results were found for antidepressive dosage, with higher dosages in the after initiation

period. No significant results were found for antipsychotic dosage variation. The mean cost per patient, before and after initiation of M-ECT, was respectively 10 621€ and 5 653€.

Conclusão: In our sample, we found that M-ECT significantly reduces number of admissions and days in admission. Initiating M-ECT treatment decreased cost per patient by 47%.

INTRODUCTION

Patients with severe mental disorders require treatment even after remission of the acute phase, in order to avoid relapses and a progressive functional deterioration. Electroconvulsive therapy (ECT)[1] is an effective and safe[2-4] treatment for severe mental disorders, most notably mood disorders[5,6] and schizophrenia.[3] However, the relapse rate is very high, with most recurrences occurring within the first 6 months after treatment.[7-9] Additional ECT sessions after acute electroconvulsive therapy (A-ECT) are successful in sustaining remission of symptoms over a long period of time[10-12] so maintenance electroconvulsive therapy (M-ECT) is recommended for patients with treatment-resistant mental disorders[13,14] and there are some guidelines on how and when to use it.[1,15,16] ECT cost is a major concern which can limit its access, mainly when compared to other available treatments. In 2003, the National Institute for Clinical Excellence published an economic analysis not favourable to the use of ECT in several situations,[17] including maintenance treatment, justified by lack of evidence on its effectiveness and also high risk for adverse effects, which was promptly criticized.[18,19] Since then, other studies demonstrated the opposite view,[16,20] stating that M-ECT is effective and cost-effective as a third line option. However there are few studies that consider the cost-effectiveness of M-ECT. The present study has the potential to support the already existing evidence that M-ECT is a maintenance treatment option for patients who have had at least a response to a course of A-ECT. Thus, our aim is to demonstrate that M-ECT is an effective option for maintenance treatment in patients with severe mental disorders and to determine its long-term cost-effectiveness.

MATERIAL AND METHODS

a. Study design

Mirror-image studies (or pre-post design studies) are those in which outcomes are compared before and after a specific event (eg. an intervention). A mirror study was designed to compare, in each patient, the number of hospital admissions and the total number of days as inpatients before and after the initiation of M-ECT. Accordingly, for each patient, 2 time intervals were used: between the initiation

of M-ECT and 31st December 2018 (after initiation group), and the homologous period of time previous to the first M-ECT treatment (before initiation group). By general agreement, M-ECT refers to all treatments done after the first six months following A-ECT. All patients were at least 18 years when they started M-EC. An informed consent according to the Portuguese Mental Health Act and our Hospital's procedure, was signed prior to the first treatment. Only patients who were on their first M-ECT programme were included, to prevent resampling from our first study.[21] Patients were referred to ECT by their consultant psychiatrist, and evaluated by the main ECT practitioner before initiating an A-ECT course. Titration was done on the first session, according to electrode placement. After conclusion, the consultant psychiatrist and main ECT practitioner discussed criteria for initiation of M-ECT, which included adequate response to the A-ECT course and absence of adverse effects.

b. Patient data

Variables such age, sex, main diagnosis, number of A-ECT and M-ECT, treatment duration, electrode placement, dosage and M-ECT frequency were gathered. Patients were diagnosed by the referring psychiatrist, according to the International Classification of Diseases, revision 9 (ICD-9) classification system which is still officially used in our institution. Patients' diagnoses were then grouped by major diagnostic categories using the International Classification of Diseases, revision 10 diagnoses (ICD-10). Data was collected for antidepressant and antipsychotic dosing in each patient to evaluate changes during the M-ECT. Fluoxetine equivalent dose for antidepressants[22] and olanzapine equivalent dose for antipsychotics[23,24] were chosen.

c. Cost calculation

The cost per day of an inpatient – excluding costs regarding diagnostic and therapeutic exams and medication - and the cost of an ECT treatment were analysed. A comparison was made between the mean cost of a patient before (cost per day x mean number of days in the ward) and after start M-ECT (cost per day x mean number of days in the ward + cost per ECT treatment x mean number of A-ECT and M-ECT). For this, we used the database of our institution, the GDH (Homogenous Diagnostic Group), and the values

from our institution's 2018 financial reports. We used mean values, as it more appropriate for cost calculation and policy making than medians.

d. Technical information

All patients were treated in our ECT unit using a constant-current (800 mA, 200 J) spECTrum 5000Q (MECTACORP, Portland, Oregon, USA), with the 2013 software upgrade (ie, using the "Optimized Dosage" dosing tables).[25] Unilateral treatments used 0.3-millisecond ultra-brief pulses with doses 6 times above the seizure threshold, and bilateral treatments 1.0-millisecond brief pulses with doses 2.5 times above the seizure threshold. Anaesthesia consisted of a combination of intravenous atropine (0.5 mg), thiopental (<6 mg/kg), and succinyl-choline (0.5 mg/kg).

e. Statistical analysis

Performed under SPSS (version 22). Descriptive statistics were presented as means (M) and standard deviations (SD) for quantitative symmetrical variables and medians with interquartile ranges otherwise. For categorical variables, frequencies (n) and percentages were presented. Before and after initiation comparisons were performed with Wilcoxon rank test for asymmetrical variables. Paired samples t-test were used in case of normally distributed variables. Shapiro-Wilk test and histogram were used for this decision. Significance was considered for $p<0.05$. We also considered marginal significant differences for $p<0.010$ when sample size was lower than 15.

RESULTS

a. Sample description

This study enrolled 9 (56%) men and 7 (44%) women in a total of 16 patients ranging from 22 to 76 years old (M=53; SD=16). The most frequent diagnosis were schizophrenia (ICD-10 F20) and mood disorders (ICD-10 F30-F35). The number of A-ECTs varied between 5 and 15 and the number of M-ECTs varied between 11 and 192. Minimum and maximum treatment duration were 6 and 57 months. Frequency of M-ECTs was mostly once a month. Electrode placement was mostly bilateral (BL) and the remaining were right unilateral (UL). Applied dosage ranged from 230 mC to 1124 mC. Further information is provided in Table 1.

Table 1. Sample characteristics

Variable	Statistic
Age (years)	53 (16)
Sex:	
Female	7 (44%)
Male	9 (56%)
Main diagnosis:	
Schizophrenia	7 (44%)
Schizoaffective disorder	2 (12%)
Mood disorder	7 (44%)
Number of A-ECT	8.81 (3.26)
Number of M-ECT	41.25 (44.84)
Treatment duration (months)	23 (16)
Electrode placement:	
Right unilateral	2 (12%)
Bilateral	14 (88%)
Dosage (mC)	572 (337)
Treatment frequency:	
Weekly	2 (12%)
Fortnight	3 (19%)
Monthly	11 (69%)

Results presented as M(SD) for quantitative and n(%) for categorical variables.

b.   Comparative analysis

Statistical differences were found for the number of admissions and days in admission, before and after M-ECT initiation. A reduction in median number of admissions and median days in hospital diminished was observed (Table 2). Also, marginally significant results were found for fluoxetine equivalence. No significant results were found for antipsychotic dosage variation ($p= 0.280$) (Table 3).

Table 2. Admissions *before* and *after* initiation of M-ECT

	Before treatment	After treatment	Wilcoxon Test (p-value)
Number of admissions	2.0 (1,2 – 2,8) [1.0 – 8.0]	0.0 (0.0 – 1.0) [0.0 – 4.0]	$p=0.003$
Days in admission	86.0 (75.0 – 118.0) [32.0 – 206.0]	14,5 (0.0 – 59.2) [0.0 – 112.0]	$p<0.001$

Results presented as Mdn ($P_{25} - P_{75}$) [min - max]

Table 3. Drug dosage before and after initiation of M-ECT

	Before initiation	After initation	Wilcoxon Test (p-value)
Fluoxetine (n=9) (mg)	37 (28)	50 (27)	$p=0.053$
Olanzapine (n=14) (mg)	10 (8)	12 (8)	$p=0.280$

Results presented as M (SD)

c.   Cost per patient

The cost per inpatient per day, considering 2018 values, was 111€ (euros) and the cost of a single ECT treatment was 46€. The mean number days before and after initiation o M-ECT was 95.69 and 31.19, respectively. Therefore, the mean cost, per patient before and after the initiation of M-ECT was, respectively, 10 621€ and 5 653€. The financial burden with these patients is 47% less after they initiate M-ECT. We used means to calculate cost because it is more appropriate for policy making studies. However, using medians would be more statistically accurate, and the reduction in costs would be 66%. This values are only approximate as inflation was not considered. To this matter we accept that the increase in cost of hospitalization and ECTs is similar over time.

DISCUSSION

a.   Reducing readmissions

M-ECT significantly reduced the number of hospital admissions and the total days in admission within the same patient. All subjects had at least one admission (Mdn= 2.0) prior to M-ECT. After beginning M-ECT, only three patients had further admissions. Number of hospital admissions was perceived as an outcome for relapses with severe symptoms. Although this is an indirect measure of clinical efficacy, these results support those of previous studies,[26-28] that propose M-ECT as an effective maintenance treatment. The authors believe this study adds evidence to the existing literature, by demonstrating the effectiveness of M-ECT in diminishing hospital admissions (and its length) in a real-world set. Due to small sample size, which is a shared issue found in studies regarding M-ECT, we were not able to control for other variables such as electrode placement or main diagnosis.

b.   Patient medication

At the beginning of M-ECT all patients were receiving at least one antipsychotic or antidepressant. Dosages of both these psychopharmacological categories increased (16% and 36%, respectively), though with no statistical significance. Therefore, these small differences are very unlikely to affect the main outcomes.

c.   Cost of maintenance treatment with M-ECT

The economic advantage of M-ECT as a maintenance treatment was evaluated. A reduction of almost 50% in cost with hospital admissions was observed after initiation of M-ECT. Most patients were undergoing M-ECT only once a month, so this cost reduction might be even superior in studies with a longer follow-up period. It is important to consider that we have a Beveridgian National Health Service in Portugal so these results can vary in countries with different Health Services and policies concerning ECT. Patients that start M-ECT have significantly less hospital admissions and spend less days in the ward which is also an indirect way of assessing functionality. Other studies display similar results which showed a significant decrease in cost of treatment after initiation of M-ECT,[21,29,30] and that M-ECT can reduce treatment cost to less than a third.[31] The authors question

the necessity for a revision on guidance on the use of electroconvulsive therapy by NICE. Since 2003, the evidence for recommendation of M-ECT as a cost-effective maintenance treatment as substantially grown, as this study add strength to that hypothesis.

d. Study limitations

Mirror-image studies, although easy and inexpensive to develop, have inherent disadvantages such as regression to the mean, time period bias, lack of a control group, and asymmetrical treatment durations. This needs to be considered when interpreting our findings. A selection bias must be considered, as only patients that had an adequate response to A-ECT underwent a M-ECT course, thus artificially selecting patient with better prognosis. Although these results indirectly imply that the decrease in hospital admissions implies clinical improvement, psychometric evaluations were not applied to these patients. We pinpoint this as one of the biggest limitation of this study. Psychometric evaluations is now being routinely applied to all patients in our facility for future studies. Lastly, we did not calculate medication costs, which would make the cost analysis more accurate, even tough there were no significant differences between the two groups.

e. Future research

More studies in this area are needed in order to provide robust data for the creation of guidelines on the use of M-ECT in different mental disorders with emphasis in a more objective evaluation of clinical efficacy and long--terms effects of M-ECT.

CONCLUSION

In our sample, initiation of M-ECT after a course of A--ECT significantly reduced the number of admissions and days in admission in the psychiatric ward. Increases in drug dosage were unlikely to affect this outcome. Furthermore, initiating M-ECT treatment decreased cost by 47%. These results are in line with previous studies.

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