Efficacy of electroconvulsive therapy: a systematic review of scientific evidence

J. M. Bertolín Guillén[a], C. Sáez Abad[a], M. E. Hernández de Pablo[a] and S. Peiró Moreno[b]

[a]*Psychiatry Unit. Consorcio Hospital General Universitario de Valencia.*
[b]*Escuela Valenciana de Estudios para la Salud (EVES). Generalidad Valenciana. Spain*

Eficacia de la terapia electroconvulsiva: revisión sistemática de las evidencias científicas

Summary

We carried out a systematic study of bibliographical review of scientific evidence provided by clinical trials that assessed the short, medium and long-term efficacy of electroconvulsive therapy (ECT) from 1965 until June 2003. The studies with the following features have been excluded: a) *those in which ECT is not the aim of the research;* b) *those that do not compare ECT with another different treatment;* c) *those in which the aim of the research is not to evaluate the efficacy of ECT, and* d) *those in which the studies are not randomized clinical trials. We have used the biomedical databases Medline, Psyclit, IME and Cochrane. On applying the corresponding search strategies on every bibliographical repertory, a total amount of 916 studies were found, which were reduced to 62 after having applied the specified exclusion criteria. The scientific evidence obtained, which compare the efficacy of ECT exclusively in depression, schizophrenia, mania and Parkinson disease, are systematized.*

Key words: *Electroconvulsive therapy. Systematic review. Depression. Schizophrenia. Mania. Parkinson's disease.*

Resumen

Realizamos un estudio sistemático de revisión bibliográfica de las evidencias científicas proporcionadas por los ensayos clínicos que evalúan la eficacia de la terapia electroconvulsiva (TEC) a corto, medio y largo plazo desde el año 1965 hasta junio de 2003. Se excluyen los trabajos en los que: a) *la TEC no es el objeto de la investigación;* b) *si no se compara la TEC con otro tratamiento distinto;* c) *cuando el objeto del estudio no es valorar la eficacia de la TEC, y* d) *cuando los estudios no son ensayos clínicos aleatorizados. Usamos las bases de datos biomédicas: Medline, Psyclit, Cochrane e IME. Al aplicar las correspondientes estrategias de búsqueda en cada uno de los repertorios se hallaron un total de 916 estudios, que se reducen a 62 tras aplicar a su vez los correspondientes criterios de exclusión especificados. Se sistematizan las evidencias científicas obtenidas, que comparan la eficacia de la TEC exclusivamente en depresión, esquizofrenia, manía y enfermedad de Parkinson.*

Palabras clave: *Terapia electroconvulsiva. Revisión sistemática. Depresión. Esquizofrenia. Manía. Enfermedad de Parkinson.*

INTRODUCTION

The use of ECT since it has been made known to the international scientific community by Cerletti and Bini in 1938[1] has undergone a growth boom in the United States and Europe, including Spain. However, in spite of more than half a century of its use, there are still information gaps about the evidence on safety, efficacy and effectiveness of short, middle and long term ECT that need to be explained. In fact, there is a vast «gray zone» in this regards formed by a large volume of medical knowledge of middle or low grade evidence.

Correspondence:
José Manuel Bertolín Guillén
Unidad de Psiquiatría
Consorcio Hospital General Universitario de Valencia
Av. Tres Cruces, s/n
46014 Valencia (Spain)
E-mail: jose.m.bertolin@uv.es

The systematic study of the bibliographic review of scientific evidence that we perform in the following agrees with the need to assess this health care technology[2,3]. Its object is to provide reliable, synthetic and clear information that facilitates decision making in relationship to the ECT in the different professional, administrative and political areas of the country. This knowledge should serve both to rationalize its use as well as to control the problem of arbitrary decisions and its consequences[4], as is advocated by the so-called «evidence based psychiatry»[5-7] and the modern public health care politics[8].

METHODS

1. Analysis and discussion of the findings on efficacy of the ECT obtained from primary sources constituted by articles published in biomedical journals (indica-

ted with an asterisk in the section corresponding to the references). Period: from 1965 to June 2003. Study selection: articles included in the bibliographic databases: Medline, Psyclit, Cochrane and IME.

2. Common general inclusion criterion: randomized clinical trials that assess the therapeutic efficacy of ECT. A screening was performed with the studies obtained according to the specified exclusion criteria applied in the order indicated. Thus, if a study fulfilled one of them, the next one was not applied. To carry out the screening, the summaries were used and, in the cases in which these did not supply enough information, the whole article was used.
3. Exclusion criteria: *a) the ECT is not the study object*: the ECT is only mentioned in the description of the patients, discussion of the results or description of the different treatments for a certain disorder; *b) the ECT is not compared with another treatment:* studies whose objective is to compare different types of ECT, with the exception of those that compare unilateral ECT with bilateral ECT, given the importance of this differentiation; *c) the object of the study is not to assess the therapeutic efficacy of ECT*: studies oriented towards the assessment of treatment procedures (anesthetics, treatment frequency, stimulus intensity, etc.), adverse effects, action mechanisms, and aspects related to the information and attitude on this treatment, and *d) studies that are not randomized clinical trials*: this includes secondary sources or reference information such as revisions, editorials, letters and others.
4. Control of possible biases: *a) interpretation bias of the studies*: it is controlled by the degree of scientific evidence evaluated according to the validated quality scale of Jadad et al.[9] in a range of 0-5, low quality being when the score ≤ 3; *b) sample bias:* by the simultaneous use of several strategies or combination of logical operations different from the search, and *c) bias of non-selection of studies*: contrast of the findings with other known revisions and meta-analyses.
5. After applying the criteria mentioned, 62 original studies were obtained, after having eliminated 6 that used all or part of the sample of some already included previous study[10-15]. All those included finally compare the efficacy of ECT in depression, schizophrenia, mania or Parkinson's disease (table 1).

RESULTS

Depression

ECT versus antidepressants

ECT has not been shown to be more effective than amitriptyline in regards to response rate. However, it can be stressed that both treatments mean better results than the use of the pharmacological placebo or simulated ECT[16]. These results are similar to those obtained by Wittenborn et al.[17], who also did not find any differences between imipramine and ECT, although both treatments were shown to be superior to the placebo. The data offered by this second study are very limited.

In the case of the melancholic subtype, there are also no differences between ECT and imipramine, although the remission rate is somewhat greater in the first case, 93 %, than in the second one, 73 %[18]. These percentages are similar to those observed in one of the first trials on ECT[19], in which 84 % response was obtained versus 72 % with imipramine. However, in the case of endogenous depressions, even though there are similar improvement rates with imipramine and with ECT[20,21], the response is faster with the latter[20].

In regards to chlorpromazine, it has been observed that adding it to the treatment with ECT does not mean any benefit in regards to therapeutic result or in the number of treatments necessary or days of hospital stay[22]. The results of this study showed that there were no differences between the patients who received ECT plus chlorpromazine and ECT plus placebo. Thus, in the first group, 86 % remitted or improved greatly versus 76.3 % in the second group. On the other hand, although the improvement rate with ECT (84 %) doubled that shown with phenelzine (38 %), we do not have data on the statistical significance[19].

In regards to the drug-resistant patients, the results obtained have to be considered carefully since the resistance is evaluated incorrectly in most of the cases. Thus, for example, in the study of Folkerts et al.[23], the treatment was not adequate in some of the patients, although drug resistance was an inclusion criteria, and they were also those who obtained the best results. In the same way, the sample was resistant to only one course of tricyclics in the Dinan and Barry study[24]. In this subgroup of patients, unilateral ECT was shown to be superior to paroxetine both in the response rate, there being 71 % with ECT versus 28 % with paroxetine, as well as in its rapidness[23], this advantage being seen after only one week of treatment.

In addition, the best efficacy of the ECT found by Davidson et al.[25] offers some restrictions. In this study, in which patients refractory to treatment with the usual psychotropes at adequate doses were included, the comparison was established with the combination of phenelzine plus amitriptyline. Due to the secondary effects caused by this combination, the doses used were very low and, thus, the study should be replicated with others that are more adequate to be able to speak of a real superiority of ECT. In contrast to these results in favor of ECT, the study performed by Dinan and Barry[24] in a sample of endogenous depressed patients resistant to a treatment course with tricyclics showed that the response rates with the adjuvancy of ECT versus lithium were similar, there even being a greater rapidness of response with lithium.

In reference to the decision to continue the antidepressive drug treatment or not during the ECT sessions, the data do not support the first option[26]. Continuing it during the ECT does not offer any additional advantage over its interruption and later reinitiation after finishing that treat-

TABLE 1. Description of the 62 clinical trials included in our review

Author	*Inclusion criteria*	*Sample*			*Quality*	*Results*
Abraham and Kulhara (1987)[64]	Schizophrenia (RDC)	N = 28	G.1 → N = 14 G.2 → N = 14	Bilateral ECT: 2/week Trifluoperazine: 20 mg/day Simulated ECT: 2/week Trifluoperazine: 20 mg/day	SEG: 1 B: DB R: ND	G.1 greater response than G.2; non-differences between groups after week 16
Abrams and Taylor (1976)[50]	Depression Endogeneity	N = 21	G.1 → N = 10 G.2 → N = 11	Bifrontal-temporal ECT: 3/week Dominant and non-dominant unilateral ECT simultaneously: 3/week	SEG: 3 B: DB R: HT	G.1 more effective than G.2
Abrams, et al. (1983)[51]	Depression (DSM III)	N = 70	G.1 → N = 33 G.2 → N = 37	Bifrontal-temporal ECT: 3/week Right unilateral ECT: 3/week	SEG: 1 B: SB R: ND	G.1 more effective than G.2
Abrams et al. (1991)[52]	Depression (DSM III) Gender: man	N = 47	G.1 → N = 18 G.2 → N = 20 G.3 → N = 9	Bilateral ECT Right unilateral ECT Left unilateral ECT	SEG: 0 B: DB R: ND	No differences between G.1 and G.2
Agarwal y Winny (1985)[66]	Schizophrenia (RDC)	N = 30	G.1 → N = 15 G.2 → N = 15	Bitemporal ECT: 3/week[a] Simulated ECT: 3/week[a]	SEG: 1 B: DB R: ND	Faster response in G.2
Andersen et al (1987)[77]	Parkinson's disease Drug resistance	N = 11	G.1 → N = 5 G.2 → N = 6	Bilateral ECT: 3/week Simulated ECT: 3/week	SEG: 2 B: DB R: ND	Increase of times *on* in G.1
Arfwidsson et al (1973)[22]	Depression Endogenous or mixed	N = 57	G.1 → N = 29 G.2 → N = 28	Bifrontal-temporal ECT: 3/week Placebo: chlorpromazine Bifrontal-temporal ECT: 3/week Chlorpromazine: 50 to 150 mg/day (mean: 100)	SEG: 3 B: DB R: ND	No difference between groups in efficacy, treatment no., hospital stay
Bagadia et al (1983)[62]	Schizophrenia (RDC)	N = 78[b]	G.1 → N = 18 G.2 → N = 20	Bitemporal ECT: 2 to 3/week Placebo: chlorpromazine Simulated ECT: 2 to 3/week Chlorpromazine: 400-600 mg/day	SEG: 2 B: D.B R: ND	No differences between groups
Brandon et al (1984)[29]	Depression (PSE)	N = 95	G.1 → N = 53 G.2 → N = 42	Bilateral ECT: 2/week Simulated: 2/week	SEG: 5 B: DB R: RN	G.1 more effective than G.2
Brandon et al (1985)[73]	Schizophrenia (PSE)	N = 19	G.1 → N = 9 G.2 → N = 10	Bilateral ECT: 2/week Simulated ECT: 2/week	SEG: 5 B: DB R: RN	G.1 more effective than G.2
Chanpattana et al (1999)[14]; Chanpattana et al (1999)[69]	Schizophrenia (DSM IV)	N = 51	G.1 → N = 15[b] G.2 → N = 15[b] G.3 → N = 15[b]	Bifrontal-temporal ECT: 2/week Bifrontal-temporal ECT: 2/week Flupenthixol: 12-24 mg/day Flupenthixol: 12-24 mg/day	SEG: 0 B: SB R: ND	Prevention of relapses: G.2 greater than G.1 and G.3. G2 less BPRS than G.1 and G.3. Without differences G.1 and G.3 in BPRS. Relapse at 6 months[c]: G.1: 93%; G.2: 40%; G.3: 93%
CPCBMRC (1965)[19]	Depression	N = 269	G.1 → N = 74 G.2 → N = 65 G.3 → N = 65 G.4 → N = 65	ECT[d]: 1 or 2/week Imipramine: 50 mg/day Phenelzine: 15 mg/day Placebo: antidepressive	SEG: 1 B: DB R: ND	Response rate[e]: G.1: 84%; G.2: 72%; G.3: 38%; G.4: 45%
Davidson et al (1978)[25]	Depression Unipolar or secondary to anxiety disorder	N = 19	G.1 → N = 9[f] G.2 → N = 8[f]	ECT[g]: 3/week Phenelzine: 15-45 mg/day Amitriptyline: 100 mg/day	SEG: 2 B: SB R: RN	G.1 more effective than G.2
D'elia et al (1977)55	Depression Endogenous and severe	N = 61	G.1 → N = 30 G.2 → N = 31	Non-dominant unilateral ECT Placebo: L-tryptophan Non-dominant unilateral ECT L-tryptophan: 6 g/day	SEG: 2 B: DB R: ND	G.1 more effective than G.2
Dinan y Barry (1989)[24]	Depression (DSM III) Endogenous	N = 30	G.1 → N = 15 G.2 → N = 15	Bilateral ECT: 3/week Lithium: 600-800 mg	SEG: 1 B: SB R: ND	No differences between groups
Fleminger et al (1970)[48]	Depression	N = 36	G.1 → N = 12 G.2 → N = 12 G.3 → N = 12	Bifrontal-temporal ECT Right temporoparietal ECT Left temporoparietal ECT	SEG: 1 B: DB R: ND	G.1 and G.3 improve
Folkerts et al (1997)[23]	Depression (ICD 10) Bipolar or unipolar Drug-resistant[h]	N = 39	G.1 → N = 21 G.2 → N = 18	Non-dominant unilateral ECT: 3/week Paroxetine: 40-50 mg/día	SEG: 0 B: ND R: ND	G.1 more effective than G.2
Flaser and Glass (1980)[46]	Depression	N = 33	G.1 → N = 16[b] G.2 → N = 13[b]	Bilateral ECT: 2/week Non-dominant unilateral ECT: 2/week	SEG: 0 B: SB R: ND	No differences between groups

TABLE 1. Description of the 62 clinical trials included in our review (continuation)

Author	*Inclusion criteria*	*Sample*			*Quality*	*Results*
Freeman et al (1978)[51]; Freeman (1978)[10]	Depression	N = 40	G.1 → N = 20 G.2 → N = 20	Bifrontal ECT: 2/week First week: simulated ECT, 2/week Following: bifrontal ECT, 2/week	SEG: 3 B: DB R: ND	After 1st week: G.1 more effective than G.2
Gangadhar et al (1982)[20]	Depression (ICD 9) Endogenous	N = 32	G.1 → N = 16 G.2 → N = 16	Bilateral ECT first 2 week: 3/week. Following: 1/week Imipramine: 75-100 mg/day	SEG: 3 B: DB R: ND	First 2 weeks of treatment: G.2 more effective than G.1
Gregory et al (1985)[28]	Depression (ICD 9)	N = 69	G.1 → N = 23 G.2 → N = 23 G.3 → N = 23	Bitemporal ECT: 2/week Right unilateral ECT, 2/week Simulated ECT: 2/week	SEG: 3 B: DB R: ND	G.1 and G.2 more effective than G.3
Grunhaus et al (2000)[59] Dannon et al (2002)[15]	Depression (DSM IV) Severe	N = 40	G.1 → N = 16 G.2 → N = 20	Right unilateral ECT[i]: 2/week Transcranial magnetic stimulation: 5/week	SEG: 2 B: SB R: AL	Psychotics: G.1 more effective than G.2 Non-psychotics: no differences betwwen groups
Grunhaus et al (2003)[60]	Depression(DSM IV) Drug-resistant Severe	N = 40	G.1 → N = 20 G.2 → N = 20	Unilateral or bilateral ECT Transcraneal magnetic stimulation: 5/week	SEG: 2 B: SB R: AL	No differences between groups
Haliday et al (1968)[41]	Depression Endogenous[j]	N = 52	G.1 → N = 18 G.2 → N = 18 G.2 → N = 16	Bilateral ECT: 2/week Right unilateral ECT: 2/week Left unilateral ECT: 2/week	SEG: 1 B: SB R: Gr 3	No differences between groups
Heikman et al (2002)[36]	Depression (DSM IV)	N = 24	G.1 → N = 8 G.2 → N = 8 G.2 → N = 8	Right unilateral ECT high doses Right unilateral ECT low doses Bifrontal ECT	SEG: 1 B: DB R: ND	No differences between groups: G.1 improves faster than G.2 and G.3
Herrington et al (1974)[54]	Depression Severe	N = 43	G.1 → N = 21 G.2 → N = 22	ECT[g]: 3/week L-Tryptophan: 6-8 g/day	SEG: 1 B: ND R: ND	G.1 more effective than G.2
Horne et al (1985)[44]	Depression[k] (DSM III)	N = 53	G.1 → N = 26 G.2 → N = 27	Bitemporal ECT: 3/week Non-dominant unilateral ECT: 3/week	SEG: 5 B: DB R: ND	No differences between groups
Jagadeesh et al (1992)[33]	Depression (RDC) Endogenous[i]	N = 25	G.1 → N = 12 G.2 → N = 13	Bifrontal-temporal ECT: 3/week First week: 1 session bifrontal-temporal ECT Following: Simulated ECT 3/week	SEG: 3 B: DB R: ND	No differences between groups, both improve
Janakiramaiah et al (1982)[67]	Schizophrenia (RDC)	N = 60	G.1 → N = 15 G.2 → N = 15 G.3 → N = 15 G.4 → N = 15	Bitemporal ECT: 3/week + clorpromazine: 300 mg/day Bitemporal ECT: 3/week + clorpromazine: 500 mg/day Chlorpromazine: 300 mg/día Chlorpromacine: 500 mg/día	SEG: 0 B: SB R: ND	G.2 and G.4 more effective than G.1 and G.3
Janakiramaiah et al (2000)[18]	Depression (DSM IV)	N = 45	G.1 → N = 15 G.2 → N = 15 G.3 → N = 15	Bilateral ECT: 3/week Imipramine: 150 mg/day Sudarshan Kriya Yoga: daily	SEG: 1 B: SB R: ND	No differences between groups, all improve
Janicak et al (1991)[45]	Depression[L] (RDC)	N = 30	G.1 → N = 9 G.2 → N = 21	Bilateral ECT: 3/week Unilateral ECT non-dominant: 3/week	SEG: 1 B: DB R: ND	No differences between groups, both improve
Janicak et al (2002)[61]	Depression (DSM IV)	N = 26	G.1 → N = 15 G.2 → N = 11	Transcranial magnetic stimulation: 5/week Bilateral ECT: 3/week	SEG: 0 B: ND R: ND	No differences between groups
Johnstone et al (1980)[32] CRCDP (1983)[11]	Endogenous depression	N = 70	G.1 → N = 35 G.2 → N = 35	Bifrontal ECT: 2/week Simulated: 2/week	SEG: 3 B: DB R: PG	G.1 better result than G.2
Lambourn y Gil (1978)[30]	Depressive psychosis	N = 32	G.1 → N = 16 G.2 → N = 16	Right unilateral ECT: 3/week Simulated ECT: 3/week	SEG: 3 B: DB R: Bd	No differences between groups
Lamy et al (1994)[43]	Severe depressive unipolar or bipolar (DSM IIIR)	N = 46	G.1 → N = 23 G.2 → N = 23	Bitemporal ECT: 3/week Parietotemporal ECT: 3/week	SEG: 3 B: DB R: AA	No differences between groups
Langer et al (1995)[57]	Depression[m] (DSM III) Severe and drug-resistant Gender: woman	N =20	G.1 → N = 10 G.2 → N = 10	Bitemporal ECT: 2/week Isoflurane narcotherapy: 2/week	SEG: 1 B: DB R: ND	Both groups improve

TABLE 1. Description of the 62 clinical trials included in our review (continuation)

Author	*Inclusion criteria*	*Sample*			*Quality*	*Results*
Letemendia et al (1993)[47] Delva et al (2001)[13]	Depression (DSM III)	N = 83	G.1 → N = 22[b] G.2 → N = 20[b] G.3 → N = 17[b]	Bitemporal ECT: 3/week Bifrontal ECT: 3/week Right unilateral ECT: 3/week	SEG: 0 B: SB R: ND	G.1 and G.2 more effective than G.3
Lisanby et al (1998)[39]	Depression (RDC and SADS) Endogenous	N = 79	G.1 → N = 23 G.2 → N = 17 G.3 → N = 19 G.4 → N = 20	Bilateral ECT high dose: 3/week Bilateral ECT low dose 3/week Right unilateral ECT high dose: 3/week Right unilateral ECT high dose: 3/week	SEG: 0 B: DB R: ND	High doses more effective than low doses
Malitz et al (1986)[40]	Depression (RDC)	N = 52	G.1 → N = 27 G.2 → N = 25	Bifrontal-temporal ECT Right unilateral ECT	SEG: 1 B: DB R: ND	G.1 therapeutic response greater than G.2
May y Tuma (1965)[63]	Schizophrenia	N = 100	G.1 → N = 20 G.2 → N = 20 G.3 → N = 20 G.4 → N = 20 G.5 → N = 20	ECT: 3/week (onset), followed by 2/week Individual psychotherapy: 2 h/week Fharmacoteraphy: Stelazine o thorazine[n] Individual psychotherapy Fharmacoteraphy[o] Routine treatment[p]	SEG: 0 B: SB R: ND	MHS and MACC: G.3 and G.4 greater improvement than G.5 and MACC: G.3 greater improvement G.1 and G.2
Mayur et al (2000)[26]	Depression (DSM IV)	N = 30	G.1 → N = 15 G.2 → N = 15	Non-dominant unilateral ECT: 3/week Antidepressive placebo Non-dominant unilateral ECT: 3/week Antidepressants	SEG: 2 B: DB R: ND	No differences between groups in response rate
McCall et al (2002)[35]	Depression	N = 77	G.2 → N = 40 G.1 → N = 37	Right unilateral ECT Bilateral ECT	SEG: 1 B: DB R: ND	No differences between groups
McDonald et al (1996)[16]	Depression	N = 30	G.1 → N = 12 G.2 → N = 10 G.3 → N = 4 G.4 → N = 4	ECT[q]: 3/week Amitriptyline: 50 mg/day Simulated ECT: 3/week Placebo: amitriptyline	SEG: 2 B: DB R: ND	No differences between groups (worse response in G.3 and G.4)
Naidoo (1956)[68]	Schizophrenia	N = 80	G.1 → N = 20 G.2 → N = 20 G.3 → N = 20 G.4 → N = 20	ECT[q] + placebo: reserpine Placebo: reserpine Reserpine: 5 mg/day TEC[q] + reserpina. 5 mg/día	SEG: 2 B: DB R: ND	No statistical analysis of the differences performed
Pridmore (2000)[58]	Depression (DSM IV) Drug-resistant	N = 22	G.1 → N = 11 G.2 → N = 11	Non-domnant unilateral ECT: 3/week 2 series of Day 1: Non-dominant unilateral ECT. Day 2, 3, 4 and 5; transcranial magnetic stimulation	SEG: 0 B: SB R: ND	No differences between groups
Reichert et al (1976)[71]	Psychiatric patient	N = 58	G.1 → N = 32 G.2 → N = 26	Bifrontal-temporal ECT: 3/week Non-dominant unilateral ECT: 3/week	SEG: 0 B: ND R: ND	Improvement in both groups
Sachs et al (1989)[56]	Depression	N = 11	G.1 → N = 6 G.2 → N = 5	Bitemporal ECT: 3/week Placebo ergoloid mesylates: 2 mg/day Bitemporal ECT: 3/week Ergoloid mesylates: 2 mg/day	SEG: 2 B: DB R: ND	G.2 more effective than G.1
Sackeim et al (1987)[38]	Depression (RDC and SADS)	N = 52	G.1 → N = 27 G.2 → N = 25	Bifrontal-temporal ECT: 3/week Right-unilateral ECT: 3/week	SEG: 3 B: DB R: ND	G.1 more effective than G.2
Sackeim et al (1993)[37]	Depression (RDC)	N = 100[b]	G.1 → N = 23[b] G.2 → N = 23[b] G.3 → N = 23[b] G.4 → N = 23[b]	Bifrontal-temporal ECT low dose: 3/week Bifrontal-temporal ECT high dose: 3/week Right unilateral ECT moderate dose: 3/week Right unilateral ECT high dose: 3/week	SEG: 0 B: DB R: Gr 20	G.3 less effective than G.4, G.1 and G.2; G.4 less effective than G.2

TABLE 1. Description of the 62 clinical trials included in our review (continuation)

Author	*Inclusion criteria*	*Sample*		*Quality*	*Results*
Sackeim et al (2000)[34]	Depression (RDC and SADS)	N = 84	G.1 → N = 20[b] Bifrontal-temporal ECT: 3/week G.2 → N = 20[b] Right unilateral ECT low dose: 3/week G.3 → N = 20[b] Right unilateral moderate dose: 3/week G.4 → N = 20[b] Right unilateral ECT low doses: 3/week	SEG: 2 B: DB R: BP	G.1 and G.4 more effective than G.2 and G.3
Sarkar et al (1994)[65]	Schizophreniform disorder (DSM IIIR)	N = 30	G.1 → N = 15 Bifrontal-temporal ECT 3/week + haloperidol: 15 mg/day G.2 → N = 15 Simulated ECT 3/week + haloperidol: 15 mg/day	SEG: 3 B: DB R: ND	No differences between groups
Sikdar et al (1994)[76]	Manic episode (DSM IIIR)	N = 30	G.1 → N = 15 Bifrontal-temporal ECT 3/week + chlorpromazine: 600[r] mg/day G.2 → N = 17 Simulated ECT 3/week + chlorpromazine: 600[r] mg/day	SEG: 3 B: DB R: ND	G.1 more effective and faster response than G.2
Small et al (1968)[53]	Psychiatric patient	N = 100	G.1 → N = 50 Bitemporal ECT: 3/day G.2 → N = 50 Flurothyl: 3 week	SEG: 4 B: DB R: ND	No differences between groups
Small et al (1986 and 1988)[75,12]	Bipolar depression (DSM III, RDC)	N = 34[s]	G.1 → N = 17 Bitemporal ECT[t]: 3/week G.2 → N = 17 Lithium: 0,6-1,5 mmol/l	SEG: 3 B: SB R: RN	G.1 more effective than G.2
Steiner et al (1978)[21]	Depression Endogeneous Gender: woman	N = 12	G.1 → N = 4 Bilateral ECT 2/week G.2 → N = 4 Imipramine: 75 mg/day + L-triiodothyronine: 25 mg/day G.3 → N = 4 Imipramine 75 mg/day + placebo L-triiodothyronine	SEG: 2 B: DB R: RN	No differences between groups
Stromgren (1973)[42]	Depression Endogeneity	N = 100	G.1 → N = 52[b] Non-dominant unilateral ECT: 2/week G.2 → N = 48[b] Bilateral ECT: 2/week	SEG: 1 B: DB R: ND	G.1: 25% do not respond to treatment G.2: 22,9% do not respond. With no differences between groups in response to treatment
Taylor and Fleminger (1980)[72]	Schizophrenia (PSE)	N = 20	G.1 → N = 10 Bilateral or unilateral ECT: 3/week G.2 → N = 10 Simulated: 3/week	SEG: 2 B: DB R: ND	G.1 more effective than G.2
Taylor and Abrams (1985)[49]	Depression (DSM III)	N = 37	G.1 → N = 15 Bifrontal-temporal ECT: 3/week G.2 → N = 22 Right unilateral ECT[u]: 3/week	SEG: 0 B: SB R: ND	G.1 more effective than G.2
Ukpong et al (2002)[74]	Schizophrenia (ICD 10)	N = 20	G.1 → N = 10 Bilateral ECT: 2/week G.2 → N = 10 Simulated: 2/week	SEG: 2 B: DB R: ND	No differences between groups
Wessels (1972)[70]	Schizophrenia (Bleuler criterion)	N = 100	G.1 → N = 49 Bifrontal-temporal ECT: 1/day Thioridazine: 200 mg/day G.2 → N = 51 Right unilateral ECT[u]: 1/day Thioridazine: 200 mg/day	SEG: 3 B: DB R: NA	G.1 and G.2 improve
West (1981)[27]	Depression	N = 25	G.1 → N = 13 Bitemporal ECT: 2/week G.2 → N = 12 Simulated ECT: 2/week	SEG: 1 B: DB R: ND	G.1 more effective than G.2
Wittenborn et al (1962)[17]	Depression Woman	N = 63	G.1 → N = 21 ECT G.2 → N = 21 Imipramine G.3 → N = 21 Placebo	SEG: 0 B: ND R: ND	G.1 and G.2 more effective than G.3

AA: alternative assignment; B: blinded; Bd: balanced by age and gender; BRPS: Brief Psychiatric Rating Scale; CIE: Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines; CPCBMRC: Clinical Psychiatry Committee of British Medical Research Council; CRCDP: Clinical Research Centre, Division of Psychiatry; DB: double blind; DSM: Diagnostic and Statistical Manual of Mental Disorder; EB: exchanged blocks with the same distribution of treatment by stratum conditions; Gr.20: assignment in groups of 20; Gr.3: group of 3, each one of the 3 to treatment group; HT: heads or tails; ND: not described; PG: prerandomization grouping by desilusions, agitation and delay; PSE: Present State Examination; R: randomize; RC: randomized code; RDC: Research Diagnostic Criteria; RN: random numbers; SADS: Schedule of Affective Disorders and Schizophrenia; SB: simple blind; SEG: scientific evidence grade; SL: according to list created a priori. a: the dose of chlorpromazine established by the investigators on month prior to onset of study is maintained; b: it is not specified to which group the losses belong; c: analysis by intention to treat; d: except 98 patients, the rest change group or another treatment is applied due to non-improvement; e: without statistical analysis or differences; f: neither the initial N per group nor to which group the losses belong are described; g: the position of the electrodes is not described; h: the drug resistant poorly assessed in some cases; i: if the patient does not improve, bilateral is applied; j: not all the patients; k: 17% psychosis congruent with the mood state and melancholia; l: bipolar and schizoaffective depression; m: 30% psychosis congruent with the mood state and 70% melancholia; n: drug and dose adapted to needs of each patient; o: drug and dose adapted to the needs of each patient, but the dose is less than in G.3; p: sedation, hydrotherapy, nursing cares and occupational therapy; q: first 6 weeks: 1/week, and the following: 1/15 days; r: after the sixth session, the dose may be adjusted by the investigator; s: initially 44, but the 10 occur during the baseline; t: some have unilateral ECT and pass to bilateral if no-response; u: all the patients G.2 are right handed.

ment. Besides not seeing an increase in the proportion of relapses, the anticholinergic effects are less with the discontinuation of the antidepressants.

Real ECT versus stimulated ECT

There is a series of studies that show that the real ECT is more effective than the simulated one, verifying that convulsion plays a main role in the effect of this technology. In a pioneer study performed to assess ECT efficacy[19], it was found that the improvement rate with real ECT (84%) was practically twice that found with its simulation (45%), however it does not supply data on the statistical significance of the difference. Significance was observed in the West study[27] in which, in addition, the patients who did not respond to the simulated treatment improved when the real one was administered.

Along the same line, it was found that this better efficacy of real ECT is independent of the unilateral or bilateral position of the electrodes. However, it should be stated that the unilateral position requires a greater number of sessions to produce a response and its response rate is lower[28]. Unfortunately, valid data are not offered in regards to the response duration, since, during the follow-up, the patients could receive both ECT as well as antidepressants.

On the other hand, it has been demonstrated that the real ECT was more effective than the simulated one and, furthermore, symptomatic improvement was reached without the need to give the eight sessions initially scheduled[29]. However, in a previous study performed on patients with depressive psychosis, other authors[30], who did not obtain differences between real unilateral and simulated ECT, attributed the efficacy of unilateral ECT to the placebo effect caused by increased attention and care and to the fact that an unusual treatment was carried out.

While some studies[19,27,28] point towards a greater efficacy of the real versus simulated ECT, most of those found in the reviewed literature have added certain explanations. The main one refers to the fact that it would be more adequate to speak of superiority of ECT in regards to response rapidness, since the differences in efficacy only occur in the short run, the advantage disappearing in a short time. In this sense, one study is very illustrative[10,31]. It assigns the patients to one of the following treatments: real ECT, or the two first sessions of simulated treatment and the rest with real ECT. It could be observed that, although the first was more effective, the evaluation made after four sessions (which, in the case of the second group, only two would be real ECT), the differences between groups begin to disappear, although the real ECT continues to be superior. These differences are null at the end of the trial, when the improvement is extended to 90% of the patients, the nonrespondents belonging to the real ECT group. However, it can be stated that the proportion of patients who had an antidepressive treatment prescribed before the study was greater in the simulated ECT group.

The short term advantage of ECT was also clear in another study[32] in which the efficacy demonstrated by this treatment did not continue beyond one month of its end. In addition, clinically, improvement was reduced, there being a mean of 38 points (SD=3) in the Hamilton Rating Scale of Depression) (HRSD) in the real group compared to 28 (SD=2.7) in the simulated one.

In regards to the endogenous depression, two aspects stand out. In the first place, the real ECT is more effective than its simulation[11,32], although clinically this advantage is not very significant. In addition, this advantage disappears in the follow-up. Type of treatment is found to be a predictor of result. In the second place, a single session of ECT per week is as effective as three, producing improvement in both cases at two weeks[33]. In this study, the patients were assigned to a real or single session of ECT and the others to a simulated one, a similar therapeutic effect being found. As, in addition, those patients labeled as having good prognosis were those who obtained lower scores in depression after the two weeks of treatment, the authors suggest that it is more likely that the improvement could be attributed to ECT than to placebo effect.

Unilateral ECT versus bilateral ECT

The studies that compare different positions of electrodes offer very different data. On the one hand, the right unilateral ECT at high doses is as effective as the bilateral one in depressed patients, with the additional benefit that it produces less cognitive deterioration[34-36]. However, in a previous study[37], the same authors found that right unilateral ECT at low doses was less effective than at high doses, or with the bilateral position at loss or high doses. In fact, the response rate with right unilateral ECT at low doses only reached 17%, versus about 50% obtained in the other groups. In another previous study[38], the same group concluded that causing generalized seizures was not enough to obtain therapeutic effect. They observed that the bilateral one was shown to be superior to the right unilateral one in the short term, with rates of 70.4% and 28%, respectively. The information supplied by the mentioned study of the year 2000[34] points towards the influence of the electrical dose, so that it would be necessary to noticeably exceed the convulsive threshold to maximize the response with the unilateral electrode position. In regards to the parameter of the electrical dose, it has also been observed that the clinical response varies both based on this dose as well as the site of the electrodes[39].

In patients with endogenous depression, bilateral ECT showed greater effectiveness than the right unilateral one. Furthermore, the high doses meant a better response than the low ones. In this same sense, other authors show that bilateral ECT requires greater intensity of convulsive stimulus than the unilateral one[40]. In the same way, others do not find differences between different positions of the unilateral versus bilateral one[41-43]. However, the dominant unilateral site seems to be more unfavorable than the non-dominant one, as it causes a more extensive state of confusion after treatment, with a more persistent memory deficit[41]. In addition, there is a

statistically significant learning deficit, which is verbal in the case of the left unilateral position and non-verbal in that of the right. On the other hand, in a sample in which most of the patients corresponded to melancholic subtype, no differences were found between non-dominant unilateral and bilateral one in regards to clinical efficacy or in the number of sessions necessary to reach improvement. However, greater deterioration in memory of patients with bilateral site should be stressed[44].

In the case of acute depression that requires hospitalization, improvement is produced both with unilateral-non-dominant and bilateral ECT[45], no differences being found in either the clinical response or cognitive deterioration. The latter occurred in both groups, but with reversible character. In spite of the absence of differences, it stands out that some of the patients assigned to the non-dominant unilateral one had to change to bilateral due to lack of response (they are excluded from the analysis).

In the specific case of elderly population, treatment of depression with ECT provides satisfactory results in up to 96.6 %, without differences in regards to the electrode position or in regards to therapeutic result or in the number of treatments necessary to reach it[46]. Furthermore, a series of predictors having good results were obtained: pathological rage, work deterioration, agitation, subjective depressed mood, anxiety and high baseline HDRS score. On the contrary, a longer duration of the disease has a poor prognosis.

In contrast to this series of studies that were unsuccessful in regards to finding differences between different positions of electrodes, other authors prove that unilateral and bilateral ECT are not equivalent in regards to therapeutic efficacy, which is better in the bilateral case[28]. Specifically, the unilateral one requires greater number of treatments to produce a response which, in turn, is slower than the bilateral one, which produces improvement in only two sessions. In regards to the response duration, there are no data, since the patients could receive both ECT as well as antidepressants during the follow-up. A greater efficacy of bilateral ECT has also been observed, reaching a response rate of 70 % versus 28 % obtained with the unilateral one[40].

Along this same line, when the different electrode positions were compared, it was verified that the efficacy order was the following: bifrontal, bitemporal and right unilateral[13,47]. Furthermore, if the parameter number of days as well as the that of treatments necessary to reach the response are considered, the response is later with the right unilateral ECT than with the bilateral one, while no differences are found between the bifrontal and bitemporal positions. Specifically, the mean days that the subject takes to respond are 49.5 (SD = 29.8) with right unilateral, 33.8 (SD = 15) with bitemporal and 27.2 (SD = 24.4) with bifrontal. These data contrast with the absence of differences obtained previously[48] when comparing these electrode positions, the greater deterioration of memory associated to left unilateral ECT standing out in this case.

Within the framework of melancholic endogenous depression, although both electrode positions, that is unilateral and bilateral, mean improvement, it is greater in the latter[49]. It may also be stressed that, although there are no differences in regards to cognitive deterioration, this is increased with clinical improvement. Using the endogeneity criterion, these same authors[50] also observed that bilateral ECT produced a greater improvement than the unilateral one with simultaneously dominant and non-dominant electrode position. In fact, after the six treatments foreseen, 90.9 % of the patients assigned to unilateral ECT required additional sessions versus one third of those assigned to the bilateral one. On the contrary, Stromgren[42] did not find any differences between bilateral and non-dominant unilateral, there being about 25 % of patients without response to treatment in both cases. In melancholy, the results are contradictory when bilateral is compared with right unilateral. Thus, in one study, it was shown that bilateral ECT was more effective, causing lower scores in depression and a greater improvement percentage besides requiring a lower number of sessions[51]. However, in a later study, such differences were not found, the response rates being superior to 65 % with both electrode positions[52].

ECT versus other treatments

In another one of the first studies performed to assess the efficacy of ECT[53], it could be observed that fluorothyl inhalation, a seizure induction gas, would produce results similar to ECT, with the advantage of producing a lower incidence of memory and learning problems.

During the 1960's, several studies were also performed on an essential amino acid, L-tryptophan. They were based on hypothesis that because there is a deficit of 5-hydroxytryptamine in the brain found in the depressive phases of the bipolar disease, the natural precursor could correct it. When it was compared with ECT[54], it was found that this is more effective in patients whose present episode seriousness includes need for hospitalization, reaching improvement rates of 100 %. In addition, the maintenance of the response at 6 months was high, 60 %. This last datum must be considered with restrictions, since the psychiatrist is free to prescribe other treatments in this period.

Along the same line, L-tryptophan was subjected to the capacity test as a potentiater of the antidepressive effect produced by ECT, obtaining unsuccessful results once again[55]. The same authors suggest three possible explanations for the absence of the role of this amino acid in the ECT action mechanism. First, it is possible that these patients were not responders to L-tryptophan, a very questionable supposition if the results on the biochemical analysis are taken into account. These results show that the baseline serum concentrations and those posterior to the ECT did not shape subgroups with favorable conditions. Second, ECT alone is effective in depression. Third and finally, L-tryptophan would only mean a marginal supplement to the ECT anti-delay effect.

Another substance studied in relationship with ECT in the depression framework is Ergoloid Mesylates. When it was added to treatment with bilateral ECT, in order to decrease its adverse effects, there was an accidental finding[56]. Compared to ECT plus placebo, its use meant a greater antidepressive response. However, once again, these results are biased, as they come from an excessively reduced sample (N = 11) and the treatment can be changed to unilateral ECT in the presence of moderate mental confusion.

In addition, narcotherapy isoflurane (ISONAR), a technique the allows deep anesthesia by inhalation of this anesthetic, has shown better results than ECT in drug resistant patients[57]. Although both treatments include improvement, ISONAR evokes the fastest response after a single session. In addition, the subjects of this group continue to improve during the follow-up, while those in the ECT one tend to relapse.

More recently, transcranial magnetic stimulation (TMS) emerged with the object of being able to substitute ECT in the treatment of depression. When it was compared with non-dominant unilateral ECT in the treatment of drug-resistant depressed patients[58], no differences were found in regards to mood state, functional state or adverse effects, the improvement being 55 % in both cases. Again, the reduced sample size does not offer sufficient statistical power to detect as significant some difference which may exist. When the ECT was compared with this emerging technique, a better response rate was obtained in the patients subjected to the former[59]. It stands out that while this difference is maintained when the analysis is performed on the psychotic group, the same does not occur with that integrated by non-psychotics. Given the study's methodological limitations, such as the absence of blinding or the fact that the ECT group continues with the usual psychodrug treatment while it was interrupted in the TMS one, it is not possible to establish recommendations, even though the data point towards a similar efficacy of both procedures in non-psychotic depressed patients. After performing the follow-up of the patients at six months, the clinical effects of the TMS remain the same as those of the ECT[15].

However, in a recent later study[60], in which psychotic patients were excluded from the sample, blinding was used and the psychotropic drugs permitted to the patient were limited; such differences between ECT and TMS were not found. The authors themselves conclude that, given the non-use of a placebo group, the effects of the TMS could be biased by the interaction between the psychiatric treatment and the patient and could even be secondary to the placebo effect. Another equally recent study also did not show differences between both types of treatment and adds that the TMS is associated to less cognitive deterioration[61].

Another new treatment proposed is Sudarshan Kriya Yoga (SKI), a procedure based on respiration techniques. Its application in patients with melancholy shows no differences with that of ECT18. However, it is seen clinically that the effect size is greater in ECT, with which 93 % remissions is reached compared to 67 % achieved with SKI. The stability of the response reached, maintained until the end of the study, is also outstanding.

Schizophrenia

ECT versus neuroleptics

The use of ECT as an alternative to the neuroleptic based treatment does not have any advantage in regards to efficacy, response rapidness[62], or the rate of hospital readmissions or hospital stay[63]. On the other hand, except for one study[64], the rest show that the use of ECT as adjuvancy to the neuroleptic based treatment also does not contribute any additional therapeutic benefit in either efficacy or response rapidness[65-67]. The real ECT as adjuvancy to trifluoperizine means a greater and more rapid improvement than when it is associated to simulated ECT[64]. However, in the second case, improvement was also obtained after the second week of treatment. Furthermore, this is greater in the psychotic than depressive symptoms, since it deals with patients who have scored low in the baseline of depressed mood, slow-down and hopelessness.

These results differ from those obtained when comparing the association of chlorpromazine to real ECT with its association to simulated ECT, in a group of schizophrenics with poor response to treatment with this drug. In this case, on isolating variables, they found that the improvement was greater in the patients with greater depression score if ECT was added to the neuroleptic than when it was added to simulated ECT, a fact that only reaches statistical significance during the follow-up[66]. On the other hand, in a study with schizophrenic type patients who are in the first episode, the only differences are observed during the first three weeks in the item that measures depression on the Brief Psychiatric Rating Scale (BPRS). In addition, these lack clinical relevance[65]. Finally, the Janakiramaiah et al. study[67], in which it was found that 500 mg of chlorpromazine is as effective as ECT added to such dose or to a lower dose of 300 mg, points to the adequacy of adding ECT in those cases that require a reduction of neuroleptic dose due to their adverse effects.

In reference to the chronicity criterion, one of the first studies performed with ECT[68] compared this with resperine in chronic schizophrenics, finding that although the adjuvancy of ECT to the latter has better results in the first weeks of treatment, the effect does not last in the later ones. However, in spite of being a randomized study, methodologically it is very limited, and furthermore, no statistical analyses are performed of the between-group comparison.

In regards to the use of ECT as a maintenance treatment, a study in which this treatment was initiated after having achieved improvement with ECT plus flupenthixol, due to acute psychotic exacerbation in patients who fulfilled strict drug-resistance criteria, stands out. It was

found that maintenance therapy based on ECT plus neuroleptics (flupenthixol) was more effective than the isolated use of one of the two treatments. After six months of maintenance with this combination, 60 % of the patients remained without relapse versus 7 % of those in the ECT group or group group[14,69].

Unilateral ECT versus bilateral ECT

Bilateral and unilateral ECT have the same effectiveness in schizophrenia when used together with thioridazine[70]. In this study, the sessions were administered daily, a periodicity that differs from most of the other studies. In the same way, no differences were found between both electrode positions in a sample of psychiatric patients that included the diagnoses of schizophrenia and affective psychosis, among others[71].

Real ECT versus simulated ECT

Although the real ECT is superior to the simulated one, it stands out that improvement is also produced in the latter case[72]. However, although this is already clear after six sessions, at the end of the foreseen twelve, 90 % of the patients are in the pathological range compared to 90 % improvement presented by the real ECT group. While other authors also found that the real ECT was more effective than the simulated one[73], a more recent study shows improvement with both, no significant differences being obtained between groups[74].

ECT compared to other treatments

In one of the first studies performed to assess the efficacy of ECT[53], it could be observed that inhalation of flurothyl, a seizure inductor gas, could produce similar results to that of ECT, with the advantage of producing a lower incidence of memory and learning problems.

Manía

ECT versus lithium

Although in a first study, no statistically significant differences were observed between the patients with maintenance lithium who had previously had ECT and those who only took lithium[75], a later study of the same group made it possible to recommend ECT as an alternative to lithium in bipolar patients in manic or mixed phase since, although the improvement occurred with both treatments, ECT showed greater efficacy[12]. In addition, it is mentioned as the treatment of choice in prophylaxis of depression that follows manic episodes, since in this study, deterioration of the depressive manifestations can be observed only in the low lithium treatment group. Furthermore, the severity of baseline depression was shaped as the best predictor of response to ECT. However, these results could be biased by the fact that most of the patients of both treatment groups required neuroleptics during the study phase, it being possible to attribute the results obtained to these narcoleptics.

Real ECT versus simulated ECT

In the manic states, association of ECT to chlorpromazine has shown greater and faster improvement than when a simulated one is associated. However, with the latter, the patients also improve in regards to the baseline measure[76]. The importance of this result is found in the possibility of achieving symptom remission of an acute mania episode without having to resort to high neuroleptic doses, thus minimizing the risk of associated side effects, such as extrapyramidal ones, that limit the intensive neuroleptic therapy. Compared to the heterogeneity of the Small et al.[12] sample, the differential effect of ECT in a homogeneous group of patients, of which none had depressive signs and symptoms, was studied in this other recently commented study.

Parkinson disease

There is a clinical trial[77] in which the antiparkinsonian effect of ECT in patients with drug-resistant Parkinson's and with serious extrapyramidal symptoms is proven. In this study, it was observed that the real ECT versus the simulated one increased the on times. However, the other differences found lack statistical significance, possibly due to lack of statistical power, given the reduced size of the sample. The authors mention changes in the response of the dopamine receptors as a possible explanation of this anti-Parkinsonian effect of ECT.

DISCUSSION AND CONCLUSIONS

The excesses historically committed with the indiscriminate use of ECT only based on empirical foundations have harmed the development and credibility of this therapeutic technology. We have just seen that its efficacy and effectiveness have been confirmed at present, but there are still many questions due to the relative scarceness of good studies that supply greater scientific evidence. In this sense, especially two recent metanalyses[78,79] that verify the efficacy of ECT beyond any reasonable scientific doubt and the results of the systematic review of the Cochrane Library on the use of ECT in elderly depressed patients[80] must be added to the results of the study of our primary sources in depression. Finally, in schizophrenia, the conclusions of the two corresponding reviews of the Cochrane Library must be added[81-83]. However, we still need to perform randomized trials with large samples and well-defined results to gua-

rantee more exact recommendations on the practice of ECT in certain mental disorders.

With the scientific information provided by the best evidence available at present, it can be concluded that: *1)* ECT is an effective short term treatment for depression and it is likely that it is more effective than psychopharmacological treatment; *2)* a faster improvement has been verified in «endogenous» depression with ECT than with imipramine; *3)* ECT is more effective than simulated ECT and pharmacological placebo in depression; *4)* the association of chlorpromazine to ECT does not contribute benefits in psychotic depression; *5)* there are no conclusive data on its efficacy in drug-resistant depression; *6)* the controversy persists on whether the continuity of antidepressive treatment during ECT would be better than its interruption; *7)* bilateral ECT is moderately more effective in depression than the unilateral one and high doses of electrical stimulus are more effective than low ones; *8)* in depression of the elderly, satisfactory results have been observed with ECT, but sufficient scientific evidence based on clinical trials having adequate quality does not exist; *9)* comparison of ECT with other therapeutic procedures in depression, such as the recent TMS, has not achieved conclusive results; *10)* there is limited evidence that supports the use of ECT combined with antipsychotics in some patients with schizophrenia resistant to a single drug; *11)* the association of ECT with antipsychotics, as maintenance treatment after psychotic decompensation means a lower relapse rate than the isolated use of both treatments; *12)* the different position of the electrodes does not seem to vary the efficacy of ECT in schizophrenia; *13)* real ECT is superior to simulated ECT in schizophrenia, especially after a prolonged time period; *14)* ECT is an alternative to lithium in manic or mixed phase bipolar patients, as it has shown greater efficacy; *15)* in the acute phase of mania, chlorpromazine associated to real ECT provides better results than associated to simulated ECT, and *16)* ECT may be useful in Parkinson's disease that is drug-resistant and has serious extrapyramidal symptoms, but the quality information available is not sufficient.

ACKNOWLEDGEMENTS

This present study forms a part of the research project 00/10120 financed by the Health Care Tecnology Assessment Agency of the Institute of Salud Carlos III of the Ministry of Health and Consumer Affairs.

REFERENCES

1. Bernal Delgado E. La revisión sistemática de la evidencia científica. Quaderns de Salut Pública i Administració de Serveis de Salut, 16. Valencia: Escola Valenciana d'Estudis per a la Salut, 2001.
2. Bertolín Guillén JM, Peiró Moreno S, Hernández de Pablo ME, Sáez Abad C. Variabilidad en actitudes y condiciones de utilización de la terapia electroconvulsiva. Resultados de un estudio preliminar. Actas Esp Psiquiatr 2001;29:390-5.
3. Ceballos C, García-Campayo J, Artal A, Valdizan JR. Impacto del metaanálisis en la práctica clínica: el ejemplo de la psiquiatría. Actas Esp Psiquiatr 2001;29:287-92.
4. Cerletti U, Bini L. Un nuovo metodo di shockterapie. L'elettro-shock. Boll Accad Med Roma 1938;64:136-8.
5. Gastó C. Psiquiatría basada en la evidencia. Psiquiatr Biol 1998;5:97-8.
6. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds JM, Gavaghan DJ, et al. Assessing the quality of reports on randomized clinical trials: is blinding necessary? Controlled Clin Trials 1996;17:1-12
7. Peiró S. La medicina basada en la evidencia y la calidad asistencial. En: Aranaz Andrés JM, Vitaller Burillo J, editores. La calidad: un objetivo de la asistencia, una necesidad de la gestión sanitaria. Valencia: Conselleria de Sanitat. Subsecretaría per a l'Agència Valenciana de la Salut, 2002; p. 79-85.
8. Rodríguez Artalejo F. Políticas de salud basadas en la evidencia. Ges Clin Sanit 2001;10:111-3.
9. Soler Insa PA. ¿Guías y protocolos? Por qué y para qué. Psiquiatr Biol 1998;5:225-31.
10.* Freeman CP. The therapeutic efficacy of electroconvulsive therapy (ECT). A double blind controlled trial of ECT and simulated ECT. Scott Med J 1978;23:71-5.
11.* Clinical Research Centre, Division of Psychiatry. The Northwick Park ECT trial. Predictors of response to real and simulated ECT. Br J Psychiatry 1983;144:227-37.
12.* Small JG, Klapper MH, Kellams JJ, Miller MJ, Milstein V, Sharpley PH, et al. Electroconvulsive treatment compared with lithium in the management of manic states. Arch Gen Psychiatry 1988; 45:727-32.
13.* Delva NJ, Brunet DG, Hawken ER, Kesteven RM, Lawson JS, Lywood DW, et al. Characteristics of responders and nonresponders to brief-pulse right unilateral ECT in a controlled clinical trial. J Ect 2001;17:118-23.
14.* Chanpattana W, Kirdcharoen N, Techakasem P, Chakrabhand ML, Tuntirungsee Y, Prasertsuk MS. The use of the stabilization period in electroconvulsive therapy research in schizophrenia. II. Implementation. J Med Assoc Thai 1999;82:558-68.
15.* Dannon PN, Dolberg OT, Schreiber S, Grunhaus L. Three and six-month outcome following courses of either ECT or rTMS in a population of severely depressed individuals. Preliminary report. Biol Psychiatry 2002;51:687-90.
16.* McDonald IM, Perkins M, Marjerrison G, Podilsky M. A controlled comparison of amitriptyline and electroconvulsive therapy in the treatment of depression. Am J Psychiatry 1966;122:1427-31.
17.* Wittenborn JR, Plante M, Burgess F, Maurer H. A comparison of imipramine, electroconvulsive therapy and placebo in the treatment of depressions. J Nerv Mental Dis 1962; 135:131-7.
18.* Janakiramaiah N, Gangadhar BN, Naga Venkatesha Murthy PJ, Harish MG, Subbakrishna DK, Vedamurthachar A. Antidepressant efficacy of Sudarshan Kriya Yoga (SKY) in melancholia: a randomized comparison with electroconvulsive therapy (ECT) and imipramine. J Affect Disord 2000; 57:255-9.
19.* Clinical Psychiatry Committee of British Medical Research Council. Clinical trial of the treatment of depressive illness. Br Med J 1965;1:881-6.
20.* Gangadhar BN, Kapur RL, Kalyanasundaram S. Comparison of electroconvulsive therapy with imipramine in endogenous depression: a double blind study. Br J Psychiatry 1982;141:367-71.

21.* Steiner M, Radwan M, Elizur A, Blum I, Atsmon A, Davidson S. Failure of L-triodothyronine (T-sub-3) to potentate tricyclic antidepressant response. Curr Ther Res 1978; 23(5, Pt 2): 655-9.
22.* Arfwidsson L, Arn L, Beskow J, D'Elia G, Laurell B, Ottosson JO, et al. Chlorpromazine and the anti-depressive efficacy of electroconvulsive therapy. Acta Psychiatr Scand 1973;49:580-7.
23.* Folkerts HW, Michael N, Tölle R, Schonauer K, Mücke S, Schulze-Mönking H. Electroconvulsive therapy vs paroxetine in treatment-resistant depression-a randomized study. Acta Psychiatr Scand 1997;96:334-42.
24.* Dinan TG, Barry S. A comparison of electroconvulsive therapy with a combined lithium and tricyclic combination among depressed tricyclic nonresponders. Acta Psychiatr Scand 1989;80:97-100.
25.* Davidson J, McLeod M, Law-Yone B, Linnoila M. A comparison of electroconvulsive therapy and combined phenelzine-amitriptyline in refractory depression. Arch Gen Psychiatry 1978;35:639-42.
26.* Mayur PM, Gangadhar BN, Subbakrishna DK, Janakiramaiah N. Discontinuation of antidepressant drugs during electroconvulsive therapy: a controlled study. J Affect Disord 2000;58:37-41.
27.* West ED. Electric convulsion therapy in depression: a double-blind controlled trial. Br Med J (Clin Res Ed) 1981; 282:355-7.
28.* Gregory S, Shawcross CR, Gill D. The Nottingham ECT Study. A double-blind comparison of bilateral, unilateral and simulated ECT in depressive illness. Br J Psychiatry 1985;146:520-4.
29.* Brandon S, Cowley P, McDonald C, Neville P, Palmer R, Wellstood-Eason S. Electroconvulsive therapy: results in depressive illness from the Leicestershire trial. Br Med J (Clin Res Ed) 1984;288:22-5.
30.* Lambourn J, Gill D. A controlled comparison of simulated and real ECT. Br J Psychiatry 1978;133:514-9.
31.* Freeman CP, Basson JV, Crighton A. Double-blind controlled trail of electroconvulsive therapy (ECT) and simulated ECT in depressive illness. Lancet 1978;1:738-40.
32.* Johnstone EC, Deakin JF, Lawler P, Frith CD, Stevens M, McPherson K, et al. The Northwick Park electroconvulsive therapy trial. Lancet 1980;2:1317-20.
33.* Jagadeesh HN, Gangadhar BN, Janakiramaiah N, Subbakrishna DK, Jain S. Time dependent therapeutic effects of single electroconvulsive therapy (ECT) in endogenous depression. J Affect Disord 1992;24:291-5.
34.* Sackeim HA, Prudic J, Devanand DP, Nobler MS, Lisanby SH, Peyser S, et al. A prospective, randomized, double-blind comparison of bilateral and right unilateral electroconvulsive therapy at different stimulus intensities. Arch Gen Psychiatry 2000;57:425-34.
35.* McCall WV, Dunn A, Rosenquist PB, Hughes D. Markedly suprathreshold right unilateral ECT versus minimally suprathreshold bilateral ECT: antidepressant and memory effects. J Ect 2002;18:126-9.
36.* Heikman P, Kalska H, Katila H, Sarna S, Tuunainen A, Kuoppasalmi K. Right unilateral and bifrontal electroconvulsive therapy in the treatment of depression: a preliminary study. J Ect 2002;18:26-30.
37.* Sackeim HA, Prudic J, Devanand DP, Kiersky JE, Fitzsimons L, Moody BJ, et al. Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. N Engl J Med 1993; 328: 839-46.
38.* Sackeim HA, Decina P, Kanzler M, Kerr B, Malitz S. Effects of electrode placement on the efficacy of titrated, low-dose ECT. Am J Psychiatry 1987;144:1449-55.
39.* Lisanby, SH, Devanand DP, Prudic J, Pierson D, Nobler MS, Fitzsimons L, et al. Prolactin response to electroconvulsive therapy: effects of electrode placement and stimulus dosage. Biol Psychiatry 1998;43:146-55.
40.* Malitz S, Sackeim HA, Decina P, Kanzler M, Kerr B. The efficacy of electroconvulsive therapy. Dose-response interactions with modality. Ann N Y Acad Sci 1986;462:56-64.
41.* Halliday AM, Davison K, Browne MW, Kreeger LC. A comparison of the effects on depression and memory of bilateral ECT and unilateral ECT to the dominant and non-dominant hemispheres. Br J Psychiatry 1968;114:997-1012.
42.* Stromgren LS. Unilateral versus bilateral electroconvulsive therapy: investigations into the therapeutic effect in endogenous depression. Acta Psychiatr Scand 1973;240 (Suppl):8-65.
43.* Lamy S, Bergsholm P, D'Elia G. The antidepressant efficacy of high-dose nondominant long-distance parietotemporal and bitemporal electroconvulsive therapy. Convuls Ther 1994;10:43-52.
44.* Horne RL, Pettinati HM, Sugerman AA, Varga E. Comparing bilateral to unilateral electroconvulsive therapy in a randomized study with EEG monitoring. Arch Gen Psychiatry 1985;42:1087-92.
45.* Janicak PG, Sharma RP, Israni TH, Dowd SM, Altman E, Davis JM. Effects of unilateral-nondominant vs bilateral ECT on memory and depression: a preliminary report. Psychoph Bull 1991;27:353-7.
46.* Fraser RM, Glass IB. Unilateral and bilateral ECT in elderly patients. A comparative study. Acta Psychiatr Scand 1980; 62:13-31.
47.* Letemendia FJ, Delva NJ, Rodenburg M, Lawson JS, Inglis J, Waldron JJ, et al. Therapeutic advantage of bifrontal electrode placement in ECT. Psychol Med 1993;23:349-60.
48.* Fleminger JJ, de Horne DJ, Nair NP, Nott PN. Differential effect of unilateral and bilateral ECT. Am J Psychiatry 1970; 127:430-6.
49.* Taylor MA, Abrams R. Short-term cognitive effects of unilateral and bilateral ECT. Br J Psychiatry 1985;146:308-11.
50.* Abrams R, Taylor MA. Diencephalic stimulation and the effects of ECT in endogenous depression. Br J Psychiatry 1976;129:482-5.
51.* Abrams R, Taylor MA, Faber R, Ts'o TO, Williams RA, Almy G. Bilateral versus unilateral electroconvulsive therapy: efficacy in melancholia. Am J Psychiatry 1983;140:463-5.
52.* Abrams R, Swartz CM, Vedak C. Antidepressant effects of high-dose right unilateral electroconvulsive therapy. Arch Gen Psychiatry 1991;48:746-8.
53.* Small JG, Small IF, Sharpley P, Moore DF. A double-blind comparative evaluation of flurothyl and ECT. Arch Gen Psychiatry 1968;19:79-86.
54.* Herrington RN, Bruce A, Johnstone EC. Comparative trial of L-tryptophan and ECT in severe depressive illness. Lancet 1974;2:731-4.
55.* D'Elia G, Lehmann J, Raotma H. Evaluation of the combination of tryptophan and ECT in the treatment of depression. I. Clinical analysis. Acta Psychiatr Scand 1977;56: 303-18.
56.* Sachs GS, Gelenberg AJ, Bellinghausen B, Wojcik J, Falk WE, Farhadi AM, Jenike M. Ergoloid mesylates and ECT. J Clin Psychiatry 1989;50:87-90.
57.* Langer G, Karazman R, Neumark J, Saletu B, Schönbeck G, Grünberger J, et al. Isoflurane narcotherapy in depressive

patients refractory to conventional antidepressant drug treatment. A double-blind comparison with electroconvulsive treatment. Neuropsychobiology 1995;31:182-94.
58.* Pridmore S. Substitution of rapid transcranial magnetic stimulation treatments for electroconvulsive therapy treatments in a course of electroconvulsive therapy. Depress Anxiety 2000;12:118-23.
59.* Grunhaus L, Dannon PN, Schreiber S, Dolberg OH, Amiaz R, Ziv R, et al. Repetitive transcranial magnetic stimulation is as effective as electroconvulsive therapy in the treatment of nondelusional major depressive disorder: an open study. Biol Psychiatry 2000;47:314-24.
60.* Grunhaus L, Schreiber S, Dolberg OT, Polak D, Dannon PN. A randomized controlled comparison of electroconvulsive therapy and repetitive transcranial magnetic stimulation in severe and resistant nonpsychotic major depression. Biol Psychiatry 2003;53:324-31.
61.* Janicak PG, Dowd SM, Martis B, Alam D, Beedle D, Krasuski J, et al. Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for mayor depression: preliminary results of a randomized trial. Biol Psychiatry 2002;51:659-67.
62.* Bagadia VN, Abhyankar RR, Doshi J, Pradhan PV, Shah LP. A double blind controlled study of ECT vs chlorpromazine in schizophrenia. J Assoc Physicians India 1983;31:637-40.
63.* May PR, Tuma AH. Treatment of schizophrenia. An experimental study of five treatment methods. Br J Psychiatry 1965;111:503-10.
64.* Abraham KR, Kulhara P. The efficacy of electroconvulsive therapy in the treatment of schizophrenia. A comparative study. Br J Psychiatry 1987;151:152-5.
65.* Sarkar P, Andrade C, Kapur B, Das P, Sivaramakrishna Y, Harihar C, et al. An exploratory evaluation of ECT in haloperidol-treated DSM-IIIR schizophreniform disorder. Convuls Ther 1994;10:271-8.
66.* Agarwal AK, Winny GC. Role of ECT phenothiazine combination in schizophrenia. Indian J Psychiatry 1985;27: 233-6.
67.* Janakiramaiah N, Channabasavanna SM, Narasimha Murthy NS. ECT/chlorpromazine combination versus chlorpromazine alone in acutely ill schizophrenic patients. Acta Psychiatr Scand 1982;66:464-70.
68.* Naidoo, D. The effects of reserpine (serpasil) on the chronic disturbed schizophrenic: a comparative study of rauwolfia alkaloids and electroconvulsive therapy. J Nerv Mental Dis 1956;123:1-13.
69.* Chanpattana W, Chakrabhand ML, Sackeim HA, Kitaroonchai W, Kongsakon R, Techakasem P, et al. Continuation ECT in treatment-resistant schizophrenia: a controlled study. J Ect 1999;15:178-92.
70.* Wessels WH. A comparative study of the efficacy of bilateral and unilateral electroconvulsive therapy with thioridazine in acute schizophrenia. S Afr Med J 1972;46: 890-2.
71.* Reichert H, Benjamin J, Keegan D, Marjerrison G. Bilateral and non-dominant unilateral ECT: I. Therapeutic efficacy. Can Psychiat Assoc J 1976;21:69-78.
72.* Taylor P, Fleminger JJ. ECT for schizophrenia. Lancet 1980; 1:1380-2.
73.* Brandon S, Cowley P, McDonald C, Neville P, Palmer R, Wellstood-Eason S. Leicester ECT Trial: results in schizophernia. Br J Psychiatry 1985;146:177-83.
74.* Ukpong DI, Makanjuola ROA, Morakinyo O. A controlled trial of modified electroconvulsive therapy in schizophrenia in a Nigerian teaching hospital. West Afr J Med 2002; 21:237-40.
75.* Small JG, Milstein V, Klapper MH, Kellams JJ, Miller MJ, Small IF. Electroconvulsive therapy in the treatment of manic episodes. Ann N Y Acad Sci 1986;462:37-49.
76.* Sikdar S, Kulhara P, Avasthi A, Singh H. Combined chlorpromazine and electroconvulsive therapy in mania. Br J Psychiatry 1994;164:806-10.
77.* Andersen K, Balldin J, Gottfries CG, Granerus AK, Modigh K, Svennerholm L, et al. A double-blind evaluation of electroconvulsive therapy in Parkinson's disease with «on-off» phenomena. Acta Neurol Scand 1987;76:191-9.
78. The UK ECT Review Group. Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. Lancet 2003;361:799-808.
79. Kho KH, van VreeswijK MF, Simpson S, Zwinderman AH. A meta-analysis of electroconvulsive therapy efficacy in depression. J Ect 2003;19:139-47.
80. Van der Wurff FB, Stek ML, Hoogendik WL, Beekman ATF. Electroconvulsive therapy for the depressed elderly (Cochrane Review). En: The Cochrane Library, Issue 3, 2003. Oxford: Update Software.
81. Tharyan P. Electroconvulsive therapy for schizophrenia (Cochrane Review). En: The Cochrane Library, Issue 1, 2001. Oxford: Update Software.
82. Tharyan P, Adams CE. Electroconvulsive therapy for schizophrenia (Cochrane Review). En: The Cochrane Library, Issue 3, 2003. Oxford: Update Software.
83. Bertolín Guillén JM, Henández de Pablo ME, Sáez Abad C. Terapia electroconvulsiva: una estrategia terapéutica de segunda línea para la esquizofrenia [fe de erratas publicada en Ges Clin Sanit 2003;5:7]. Ges Clin Sanit 2001;3:120.