The role of ECT in depression

Ellen Hartland[1], Vimal Sivasanker[2,*]

[1] FY1 trainee in psychiatry

[2] Consultant psychiatrist, Hertfordshire Partnership University NHS Foundation Trust, Hatfield, UK

***Corresponding author email: v.sivasanker@nhs.net**

Abstract

Electroconvulsive therapy (ECT) remains an important, potentially life-saving, tool in the treatment of depression. Its efficacy in depression is second to none, yet it remains underused by psychiatrists. It is a very safe treatment, safer than antidepressants in some patients. Adverse effects, particularly memory impairment, are increasingly better managed with improved treatment parameters, such as the use of high-dose unilateral ECT. National guidelines support the use of ECT, although not as robustly as the Royal College of Psychiatrists, which recommends earlier consideration and use of ECT than is currently the case. ECT was the first neuromodulation treatment for depression. Several others have since been developed, supported by a variable degree and quality of evidence.

Introduction

ECT is a highly effective treatment in psychiatry. Indeed, it is one of the most effective treatments in the whole of medicine. It can be regarded as the most effective treatment for major depressive disorder (1-2). A sustained response (defined as a 50% or greater reduction in baseline HAM-D-24 score) to a course of ECT has been reported in 79% of people (3), with remission rates of 60-80% (3-4). However, despite both its efficacy and safety (1), it remains a much stigmatised, often feared therapy, and is consequently often under-utilised (5-6). This is of significance, not just to psychiatrists, but also to society, because of the worldwide prevalence of depression. The 2010 Global Burden of Disease Study found depression to be the 11th greatest cause of disability and mortality in the world (7-8).

Effectiveness

ECT has been found to be significantly more effective than simulation or "sham" ECT (1,9). Several meta-analyses have indicated that ECT is the most effective treatment available for depression (1, 10, 11).

Antidepressant therapy is far more widely used but comparison of the evidence suggests that ECT is far more effective at treating severe depression (1). The UK ECT Review Group analysis of the results drawn from 18 randomised controlled trials (RCTs), involving a total of 1114 participants, found that ECT improved the symptoms of depressive illness significantly more than a range of different pharmacological therapies (including tricyclic antidepressants, monoamine oxidase inhibitors, tryptophan and paroxetine) (1). This translated to a difference of 5.2 points on the Hamilton Depression Rating Scale (HDRS) in favour of ECT (1).

When RCTs from this meta-analysis are individually considered, the results from the individual trials show that ECT is more effective than antidepressant medication. When compared with imipramine (1), the remission rate was 93% in the ECT group compared to 73% in the imipramine group (12). A trial which compared ECT and paroxetine showed a reduction in baseline symptoms with ECT treatment of 71%, compared to 28% with paroxetine (13).

Real versus sham ECT produced a mean positive improvement of 9.7 points on the HDRS (1), whereas antidepressant therapy typically results in a 2 - 4 point improvement on the HDRS over placebo (14, 15). In another study, remission rates were estimated to be between 70 - 90% for ECT and 28% for citalopram (16).

The rapid improvement with ECT can be an important advantage, making it a potentially life-saving therapy for severe depression (3, 9). The ECT CORE report found that 54% of participants had an initial response to ECT after just three sessions, 79% achieved a sustained response, and 75% went into remission, compared to remission in less than half of those initially treated with antidepressant medication (3).

A recent meta-analysis found that the presence of psychotic features and older age predicted response, and remission, with ECT (17), so this group of patients should be referred swiftly for ECT when clinically indicated.

Another recent meta-analysis examining the efficacy of continuation and maintenance ECT found significantly fewer relapses and recurrences for ECT combined with pharmacotherapy than for pharmacotherapy alone at 6 months and 1 year (18). It is hardly surprising that, when an effective treatment is stopped, symptoms of the illness being treated will re-emerge. The evidence suggests that there should be a move away from the mindset of setting a pre-determined endpoint for ECT and not necessarily stop it if it is keeping patients well.

Safety

ECT is a low-risk procedure, which entails a mortality rate similar to that of anaesthesia use for minor surgical procedures (19), despite frequently being administered to elderly people and those with major medical problems (9). The mortality rate for ECT is estimated to be less than 1 in 73440 treatments (20). For certain patients, ECT will provide a safer option than antidepressant therapy, (19, 21, 22). In the elderly population, ECT may prove to be safer than pharmacology, especially as this group are more vulnerable to adverse effects of medication (23). One retrospective study of 192 elderly patients with depression found that mortality was lower in the ECT treatment group compared to those treated pharmacologically (20).

ECT also has a role in pregnancy, as many commonly used psychotropic medications may either have a teratogenic effect on the foetus, or else the effect is simply not known (24-26). ECT appears to be relatively safe in pregnancy (27). A recent meta-analysis found that the most common specific risk in pregnancy is premature contractions and preterm labour, but these effects are uncommon and not clearly linked to ECT. Miscarriage rate is not significantly different from that in the general population. No association between ECT and congenital anomalies in infants was found (28).

The main adverse effect of ECT is some degree of cognitive impairment in a number of domains, in particular memory; short-term memory worsening seems to affect women more than men, and the under 40s more than the over 65s (29); this is most prominent in the first few days following treatment and will normally subside within 2 - 3 weeks of ending a course of ECT (9). After this time, patients tend to function as well, and in some cases better, in cognitive tests than they did before ECT was started (9). One study found evidence of transient impairment of memory and executive function following ECT, but, in general, cognitive function was largely unaffected after ECT, with some functions improving and others remaining stable up to 6 months after treatment (29). Nonetheless, cognitive impairment can be a distressing adverse effect of ECT treatment and for some, memory loss in particular, can persist (30).

There is ongoing work to refine and evaluate modes of administration to minimise adverse effects (31), as one of the main barriers to patients agreeing to ECT is the fear of memory loss (32). A recent study showing high-dose unilateral ECT does not appear inferior in efficacy to bitemporal ECT, and may result in fewer cognitive adverse effects (33), should re-ignite interest in unilateral treatment as well as re-opening the debate about what the default mode of administration should be.

The adverse effects of ECT can be particularly distressing to patients as they seem instantaneous and directly caused by the doctor, as opposed to adverse effects from medications, where the association with the physician is diluted. However, antidepressants can produce many different adverse side effects that can also be distressing and cause associated medical problems (34). Selective serotonin reuptake inhibitors (SSRIs), for example, can cause gastrointestinal disturbance, insomnia or agitation, decreased libido and hyponatraemia (35); the last of these, in the elderly population, can precipitate falls and lead to serious or potentially fatal sequelae (36). Despite this, guidance to monitor electrolytes with SSRI use is not directly referenced in either the NICE (National Institute of Health and Care Excellence) guidance or the BNF (British National Formulary) (35, 37) (as opposed to the guidance for antipsychotics, which state that blood monitoring should be initiated before starting antipsychotic therapy (35)). The NICE guidance on ECT for depression urges that patients must be "fully informed of the risks associated with ECT, and with the risks and benefits specific to them" (37). This perhaps indicates an underlying assumption that SSRIs are safe and therapies such as ECT and antipsychotics are less so.

ECT in UK clinical guidance for depression

ECT clearly has a place in the treatment of depression in the UK (9, 37). NICE guidance recommends that ECT should be actively considered for "severe depression that is life threatening and when a rapid response is required, or where other treatments have failed" (37). The guidance further qualifies that ECT should not be used as a routine therapy for persons with moderate depression, but can be considered if their condition has failed to respond to multiple pharmacological treatments and psychological therapy (37).

There remain some differences between NICE guidance and the Royal College of Psychiatrists position on ECT (9), which is that ECT should not be relegated to a "last-ditch response" only to be used when all else has failed. For example, the NICE guidance advocates using ECT with caution in several instances, such as "for pregnant women, the young and the elderly" (37) This differs from the Royal College ECT handbook, which indicates that, if there is concern about teratogenicity of medications, ECT can be considered first line for pregnant women with severe depression (9). The NICE caution over use in the elderly (37) is over-emphasised; certainly age alone should not be used as a barrier to a highly effective treatment (38, 39). Historically, most ECT patients have been elderly and most practitioners will seek to work with their anaesthesia and referring colleagues to optimise any medical comorbidities to allow ECT to be given.

Alternative neuromodulation techniques

ECT continues to have a key role in the treatment of depression. It should be noted that other neuromodulation therapies which might offer alternatives to medication are now becoming available. The best developed of these is repetitive transcranial magnetic stimulation (rTMS), which involves stimulation of the superficial layers of the cerebral cortex with a series of magnetic pulses. It has been shown to be safe and was approved by NICE for the treatment of depression in December 2015 (40). rTMS has the advantage of not requiring anaesthesia and, via the use of neuroimaging, being able to target specific areas of the brain relevant to depression (40). The available research clearly indicates that rTMS seems to be effective and safe but is not as effective as, and therefore not a replacement for, ECT (41). However, in some patients for whom medication has not worked, rTMS may be a more acceptable (and better tolerated) treatment. It certainly benefits from the lack of historical stigma that remains attached to ECT.

Other neuromodulatory treatments for depression currently available via research studies or tertiary referral centres include transcranial direct current stimulation (42), magnetic seizure therapy (43), vagus nerve stimulation, deep brain stimulation, and ablative neurosurgery (9).

Conclusion

Depression is a prevalent and serious condition and currently ECT is the most effective treatment available. It is a fast acting and potentially life-saving therapy. The remission and response rates are unrivalled. The current tragedy is that patients are suffering needlessly with ongoing symptoms of depression, in both psychiatric wards and the community, often because of the reluctance of psychiatrists even to consider referring for ECT in a timely manner because of their own, their patients', or their patients' carers' misgivings about the treatment. Earlier discussion with patients about ECT as a therapeutic option is warranted in this era of patient choice and patient-centred care.

ECT was the first effective treatment of any kind in psychiatry as well as the first neuromodulation therapy in psychiatry. It is highly likely that new neuromodulation treatments will play an increasing role in the treatment of depression in the future. The NICE approval of the use of rTMS indicates this progress on the part of regulatory bodies and professionals in the field. Given that these treatments are being further developed and refined, the body of evidence is still growing. At present, however, after over 75 years of experience, ECT remains the original and still the most effective treatment for depression.

References

1. Carney S, Cowen P, Dearness K, Eastaugh J. Efficacy and safety of electroconvulsive therapy in depressive disorders: A systematic review and meta-analysis. The Lancet. 2003 Mar 8;361(9360):799.

2. Greenhalgh J, Knight C, Hind D, Beverley C, Walters S. Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: systematic reviews and economic modelling studies. Health Technology Assessment (Winchester, England). 2005 Mar;9(9):1.

3. Husain MM, Rush AJ, Fink M, Knapp R, Petrides G, Rummans T, Biggs MM, O'Connor K, Rasmussen K, Litle M, Zhao W. Speed of response and remission in major depressive disorder with acute electroconvulsive therapy (ECT): a Consortium for Research in ECT (CORE) report. The Journal of Clinical Psychiatry. 2004 Apr.

4. Eranti S, Mogg A, Pluck G, Landau S, Purvis R, Brown RG, Howard R, Knapp M, Philpot M, Rabe-Hesketh S, Romeo R. A randomized, controlled trial with 6-month follow-up of repetitive transcranial magnetic stimulation and electroconvulsive therapy for severe depression. American Journal of Psychiatry. 2007 Jan;164(1):73-81.

5. McFarquhar TF, Thompson J. Knowledge and attitudes regarding electroconvulsive therapy among medical students and the general public. The Journal of ECT. 2008 Dec 1;24(4):244-53.

6. Payne NA, Prudic J. Electroconvulsive therapy part II: A biopsychosocial perspective. Journal of Psychiatric Practice. 2009 Sep;15(5):369.

7. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet. 2012 Dec 15;380(9859):2197-223.

8. The Stationery Office. Psychiatric morbidity among adults living in private households, 2000. London, UK: The Stationery Office; 2001.

9. Waite J, Easton A (editors). The ECT handbook. 3rd ed. London, UK: RCPsych Publications; 2013.

10. Kho KH, van Vreeswijk MF, Simpson S, Zwinderman AH. A meta-analysis of electroconvulsive therapy efficacy in depression. The Journal of ECT. 2003 Sep 1;19(3):139-47.

11. Pagnin D, de Queiroz V, Pini S, Cassano GB. Efficacy of ECT in depression: a meta-analytic review. The Journal of ECT. 2004 Mar 1;20(1):13-20.

12. Janakiramaiah N, Gangadhar BN, Murthy PN, Harish MG, Subbakrishna DK, Vedamurthachar A. Antidepressant efficacy of Sudarshan Kriya Yoga (SKY) in melancholia: a randomized comparison with electroconvulsive therapy (ECT) and imipramine. Journal of Affective Disorders. 2000 Jan 1;57(1-3):255-9.

13. 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 Psychiatrica Scandinavica. 1997 Nov;96(5):334-42.

14. Thase ME. The small specific effects of antidepressants in clinical trials: what do they mean to psychiatrists? Current Psychiatry Reports. 2011 Dec 1;13(6):476-82.

15. Gibbons RD, Hur K, Brown CH, Davis JM, Mann JJ. Benefits from antidepressants: synthesis of 6-week patient-level outcomes from double-blind placebo-controlled randomized trials of fluoxetine and venlafaxine. Archives of General Psychiatry. 2012 Jun 1;69(6):572-9.

16. Trivedi MH, Rush AJ, Wisniewski SR, Nierenberg AA, Warden D, Ritz L, Norquist G, Howland RH, Lebowitz B, McGrath PJ, Shores-Wilson K. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR* D: Implications for clinical practice. American Journal of Psychiatry. 2006 Jan 1;163(1):28-40.

17. Van Dierman L, Van Den Ameele S, Kamperman AM, Sabbe BC, Vermeulen T, Schrijvers D, Birkenhäger TK. Prediction of electroconvulsive therapy response and remission in major depression: meta-analysis. The British Journal of Psychiatry. 2018 Feb;212(2):71-80

18. Elias A, Phutane VH, Clarke S, Prudic J. Electroconvulsive therapy in the continuation and maintenance treatment of depression: systematic review and meta-analyses. Australian & New Zealand Journal of Psychiatry. 2018 May; 52(5):415-24

19. Flint AJ, Gagnon N. Effective use of electroconvulsive therapy in late-life depression. The Canadian Journal of Psychiatry. 2002 Oct;47(8):734-41.

20. Watts BV, Groft A, Bagian JP, Mills PD. An examination of mortality and other adverse events related to electroconvulsive therapy using a national adverse event report system. The Journal of ECT. 2011 Jun 1;27(2):105-8.

21. Kerner N, Prudic J. Current electroconvulsive therapy practice and research in the geriatric population. Neuropsychiatry. 2014 Feb;4(1):33.

22. Philibert RA, Richards L, Lynch CF, Winokur G. Effect of ECT on mortality and clinical outcome in geriatric unipolar depression. The Journal of Clinical Psychiatry. 1995 Sep;56(9):390.

23. Gálvez V, Ho KA, Alonzo A, Martin D, George D, Loo CK. Neuromodulation therapies for geriatric depression. Current Psychiatry Reports. 2015 Jul 1;17(7):59.

24. Spodniakova B, Halmo M, Nosáľová P. Electroconvulsive therapy in pregnancy-A review. Journal of Obstetrics and Gynaecology. 2015 Oct 3;35(7):659-62.

25. Pompili M, Dominici G, Giordano G, Longo L, Serafini G, Lester D, Amore M, Girardi P. Electroconvulsive treatment during pregnancy: a systematic review. Expert Review of Neurotherapeutics. 2014 Dec 1;14(12):1377-90.

26. Yonkers KA, Wisner KL, Stowe Z, Leibenluft E, Cohen L, Miller L, Manber R, Viguera A, Suppes T, Altshuler L. Management of bipolar disorder during pregnancy and the postpartum period. American Journal of Psychiatry. 2004 Apr 1;161(4):608-20.

27. Miller LJ. Use of electroconvulsive therapy during pregnancy. Hospital & Community Psychiatry. 1994;45(5):444-50.

28. Burrell-Ward H, Fromson JA, Cooper JJ, De Oliveira G, Almeida M. Recommendations for the use of ECT in pregnancy: literature review and proposed clinical protocol. Archives of Women's Mental Health. 2018 May 23:1-8

29. Vasavada MM, Leaver AM, Njau S, Joshi SH, Ercoli L, Hellermann G, Narr KL, Espinosa R. Short-and-long-term cognitive outcomes in patients with major depression treated with electroconvulsive therapy. The Journal of ECT. 2017 Dec 1;33(4):278-85

30. Philpot M, Collins C, Trivedi P, Treloar A, Gallacher S, Rose D. Eliciting users' views of ECT in two mental health trusts with a user-designed questionnaire. Journal of Mental Health. 2004 Aug 1;13(4):403-13.

31. Loo CK, Schweitzer I, Pratt C. Recent advances in optimizing electroconvulsive therapy. Australian & New Zealand Journal of Psychiatry. 2006 Aug;40(8):632-8.

32. Robertson H, Pryor R. Memory and cognitive effects of ECT: informing and assessing patients. Advances in Psychiatric Treatment. 2006;12:228-38.

33. Semkovska M, Landau S, Dunne R, Kolshus E, Kavanagh A, Jelovac A, Noone M, Carton M, Lambe S, McHugh C, McLoughlin DM. Bitemporal versus high-dose unilateral twice-weekly electroconvulsive therapy for depression (EFFECT-Dep): a pragmatic, randomized, non-inferiority trial. American Journal of Psychiatry. 2016 Feb 19;173(4):408-17.

34. Gartlehner G, Hansen RA, Morgan LC, Thaler K, Lux L, Van Noord M, Mager U, Thieda P, Gaynes BN, Wilkins T, Strobelberger M. Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: an updated meta-analysis. Annals of Internal Medicine. 2011 Dec 6;155(11):772-85.

35. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press http://www.medicinescomplete.com [accessed 4/3/16].

36. Ganguli A, Mascarenhas RC, Jamshed N, Tefera E, Veis JH. Hyponatremia: incidence, risk factors, and consequences in the elderly in a home-based primary care program. Clinical Nephrology. 2015 Aug;84(2):75-85.

37. National Institute for Health and Care Excellence (NICE). Depression in adults: recognition and management: Clinical guideline [CG90]. National Institute for Health and Care Excellence (NICE); 2018.

38. Fink M. Is the practice of ECT ethical? The World Journal of Biological Psychiatry. 2005 Jan 1;6(sup2):38-43.

39. Geduldig ET, Kellner CH. Electroconvulsive therapy in the elderly: new findings in geriatric depression. Current Psychiatry Reports. 2016 Apr 1;18(4):40.

40. National Institute for Health and Care Excellence (NICE). Repetitive transcranial magnetic stimulation for depression: Interventional procedures guidance [IPG542]. NICE; 2015.

41. Müller HH, Moeller S, Lücke C, Lam AP, Braun N, Philipsen A. Vagus nerve stimulation (VNS) and other augmentation strategies for therapy-resistant depression (TRD): review of the evidence and clinical advice for use. Frontiers in Neuroscience. 2018 Apr 10;12:239

42. Palm U, Hasan A, Strube W, Padberg F. tDCS for the treatment of depression: a comprehensive review. European Archives of Psychiatry and Clinical Neuroscience. 2016 Dec 1;266(8):681-94.

43. Daskalakis ZJ, Sun Y. Novel stimulation approaches with ECT: why everything old may be new again. Neuropsychopharmacology. 2017 Jul;42(8):1561