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Experts Call for Immediate Suspension of ECT, Others Push Back

Michael Vlessides

July 24, 2020

Experts are calling for the immediate suspension of electroconvulsive therapy (ECT) for major depression.

A new review by investigators led by John Read, PhD, University of East London, United Kingdom, concludes there is no evidence to show that ECT is effective in either its target demographic or its target diagnostic group. They say its use should be suspended until more robust research proves it is safe and effective.

However, the review's conclusions have been met with passionate opposition from expert psychiatrists who say ECT can be a lifesaving treatment for patients, many of whom have exhausted all other treatment options. Other clinicians maintain that the review itself is fraught with methodologic shortcomings that invalidate its conclusions.

"We've concluded there is no adequate research on which to base an answer to the question, 'Does ECT work?,' " Read told *Medscape Medical News*. "We're not actually saying ECT doesn't work. We're saying there's no way to know whether it works or not on the basis of the current research, which, after 80 years of the treatment being used, is pretty amazing."

On the other hand, Read said there is substantial evidence to suggest ECT causes significant adverse events. "Depending who you ask, the psychiatrists or the patients, somewhere between 12% and 55% of patients get permanent or persistent memory loss," he said.

"So there is a very serious cost to its use, and if there's a serious cost, you...have to know that there's a very strong efficacy benefit, and we just don't know that. That's why we're calling for suspension until there is adequate research," Read added.

The study was published in a recent issue of *Ethical Human Psychology and Psychiatry.*

Widespread Use

ECT remains a popular treatment modality for resistant depression. Global data show that it is used to treat almost a million patients every year. Although ECT continues to be the subject of comparative research, the investigators say that most of these studies do not adhere to the same standards that govern clinical trials of other psychiatric medications and medical interventions.

The investigators also note that to date, only 11 placebo-controlled studies of the efficacy of ECT have been conducted. They write that the last study to compare ECT with sham or simulated ECT (SECT) — in which a general anesthetic was administered but the electricity was not — was performed in 1985. Nevertheless, this relatively small body of evidence has been the basis of many meta-analyses.

In the current review, the authors evaluated the impartiality and robustness of these previous meta-analyses and the quality of the studies that were included.

"The primary goal is not to assess whether or not ECT is effective," they write. "The intent, instead, is to determine whether the available evidence is robust enough to answer that question."

For Read, the decision to analyze the current state of ECT research was both personal and professional.

"As a young nursing attendant in a Bronx hospital, I had the job of sitting with people as they came around from ECT. It was my job to try to explain why they didn't know who they were, where they were, why their head was throbbing, and why people would do something like that to them," he said.

"On the research side, this is my sixth review, and in each one we've reached the same conclusion," Read added.

Other research stands in direct opposition to the current review's findings. Many studies have concluded that ECT is safe and effective for patients with depression.

Ongoing Debate

A 2018 registry analysis showed no additional risk for cognitive impairment in patients who underwent ECT up to 40 years after therapy. A 2018 study also showed that ECT was efficacious and cost-effective for patients with treatment-resistant depression.

However, the ECT debate continues. As reported early last year, there seems to be little common ground between clinicians who believe in the utility of ECT for depression and those who vehemently do not.

For the current review, Read and colleagues performed a Medline search for meta-analyses of the efficacy of ECT for depression. Meta-analyses were only included if they comprised placebo-controlled trials that compared ECT with SECT.

Once the meta-analyses were identified, investigators assessed their component studies. This assessment was conducted by two independent reviewers who used a 24-point quality scale developed by the authors. This scale, the authors note, combines the "risk of bias" domains of the Cochrane Handbook Risk of Bias Tool with criteria related to quality of study design and reporting, as well as several criteria specific to ECT research.

The two reviewers were blinded to each other's ratings. Interrater differences were resolved collectively.

The literature search yielded 83 potential articles; after exclusion criteria were applied, 14 remained. Three of these articles were literature reviews, one discussed different types of statistical analyses used in ECT research, one was a meta-analysis in Hungarian, one was a meta-analysis that compared ECT with SECT in a selected population of elderly people, and three focused on transcranial magnetic stimulation.

This left five meta-analyses for the review. These included from one to seven of the 11 studies in question:

- Janicak et al, 1985
- Kho, van Vreewijk, Simpson, & Zwinderman, 2003
- Mutz et al, 2019
- Pagnin, de Queiroz, Pini, & Cassano, 2004
- UK ECT Review Group, 2003

The review revealed shortcomings with both the meta-analyses and the studies they included. The investigators found that the mean quality scores of the 11 studies (10.27 ± 2.45 and 11.91 ± 2.91) were not statistically different between the two raters (P = .17), whose scores were significantly correlated (P = .001).

Among the 264 total ratings, the investigators found 55 inconsistencies, which were all resolved by discussion. The mean final quality score for the 11 studies included in the review was 12.27 ± 3.20/24; eight scored 13 or less.

The results of these studies do little to support the benefits of ECT relative to SECT, the reviewers note. Indeed, only four concluded that ECT is significantly superior to SECT. Five found no significant difference, and the remaining two had mixed results.

What's more, only two of what the investigators describe as "higher quality" studies reported follow-up data. Of these, one produced an effect size of 0.065 favoring ECT, the other showed a small benefit in favor of SECT (effect size, 0.299).

The investigators describe the five meta-analyses included in the review as "flawed," stating that the meta-analyses "pay little or no attention to the multiple limitations of the studies they include."

These limitations include the number of patients included in the studies (which average 37 patients); lack of a description of randomization and blinding processes; lack of patient ratings; selective reporting of findings; and the absence of assessment of patient quality of life. Furthermore, the authors note that none of the 11 studies "convincingly" demonstrate double-blinding.

Given these shortcomings, the investigators say the meta-analyses of ECT fail to prove the following:

- The short- and long-term efficacy benefits of ECT over SECT;
- Whether ECT is effective among patients who have failed other treatments for depression;
- Whether ECT prevents suicide;
- Whether ECT improves patients' quality of life;
- Whether ECT is more effective in women than men;
- Whether ECT is effective in children or adolescents.

"Shoddy" Research

The authors conclude that the review's findings demonstrate the weakness of evidence that currently supports the use of ECT for depression.

"I would never have guessed how shoddy some of this research was," said review coauthor Irving Kirsch, PhD, a lecturer on medicine at Beth Israel Deaconess Medical Center, Boston, Massachusetts. Many of these shortcomings, Kirsch said, involve blinding and placebo effects.

"It's not clear how you could ever run a truly blinded trial of ECT, given how pronounced the immediate side effects are," he told *Medscape Medical News*. "And one of the things that's underappreciated is the pronounced responses to placebo treatment with depression and severe depression. These can last for a very long time."

Kirsch noted that more invasive placebo treatments, such as SECT, tend to have more pronounced effects.

"Not all placebos are created equal. We know, for example, that placebo injections are more effective than placebo pills and that placebo surgery can be extremely powerful," he said.

The authors call for an immediate suspension of ECT until new studies address these research shortcomings.

"The doctors who perform ECT aren't evil or stupid, they're just ignorant of the research. What they see is very temporary benefit in some of the patients. The research suggests that about a third — half at most — get a very temporary lift in mood, which seems to be the sort of euphoria you get from mild brain injury," Read explained.

"I have seen people who haven't spoken or eaten for several weeks start speaking and eating, but we know that 4 weeks later, they're going to be just as depressed as they were, or worse. And now they're going to have brain damage as well," said Read.

He added that physicians often don't see long-term patient outcomes, just the immediate effect of ECT.

A "Lifesaver"

No recent randomized controlled trials regarding ECT have been conducted because "no IRB [institutional review board] on planet earth will allow such a trial because of the overwhelming evidence of efficacy and the risk of anesthesia with no ECT," noted Mark S. George, MD, the Layton McCurdy Endowed Chair in Psychiatry at the Medical University of South Carolina, Charleston.

It is a "logical fallacy" to conclude that ECT does not work because the trials were flawed, said George, who was not involved with the current review

"This is not supported by anything they have looked at," he told *Medscape Medical News*. "It's not really a scientific study when you make conclusions that aren't based on your data, or not what you set out to do. That's what I find egregious here."

The way he sees it, the utility of ECT is unquestionable. "It is our most effective acute treatment for depression, and it's our most effective treatment for suicide," he said.

"The authors of this review don't see the patients that I see every day, who are catatonic, who can't eat, who are suicidal. For those people, ECT is a lifesaver," George added.

FDA's Position

Sameer Jauhar, MBChB, PhD, a consultant psychiatrist at the South London and Maudsley NHS Foundation Trust, London, United Kingdom was equally unimpressed with the quality of the review.

"I try to approach everything with an open mind," he said. "But as a doctor, if I'm reading about evidence, I expect a well-conducted meta-analysis and/or very clear systematic review with an adequate level of peer review."

The current review, said Jauhar, doesn't meet these criteria. He said the article reads more like a narrative review, one in which the authors dictated their own arbitrary criteria of study quality.

Most important, he said, is the fact that ECT has been the focus of a great deal of research. "The best quality synthesis of the evidence I've come across is the UK ECT Review Group's 2003 meta-analysis, published in *The Lancet*, which asked this very question. None of the studies has changed since then."

Jauhar also noted that in 2018, the US Food and Drug Administration (FDA) reclassified ECT from class III (higher risk) to class II (moderate risk). Use of ECT was also limited to treatment of "catatonia or a severe major depressive episode associated with major depressive disorder or bipolar disorder in patients age 13 years and older who are treatment-resistant or who require a rapid response treatment due to the severity of their psychiatric or medical condition."

The FDA also noted that "[t]he safe use of ECT for treatment of these conditions has been well studied and is better understood than other uses. Therefore, sufficient information exists to establish special controls that mitigate known risks and provide a reasonable assurance of safety and effectiveness for these two uses of ECT devices."

As part of the FDA's 2018 reclassification, ECT manufacturers were required to file a premarket approval application for all uses that were not reclassified. The full text of the order is available in the Federal Register.

"So the FDA has been through it, *The Lancet* has been through it, and the findings were clear," said Jauhar. "It's very easy to poke holes in studies that were conducted 30 or more years ago. But the fact is, the field has moved on."

Jauhar acknowledged there are patients who have had bad experiences with ECT, and he accepts that such events occasionally occur. Nevertheless, he said, "as a piece of scientific work, I don't know how anyone can give any credibility to this review at all."

Jauhar also noted that the journal in which the review was published has a 2019 CiteScore of 0.3 and ranks in the 15th percentile of the Scopus Clinical Psychology category. He further noted that Kirsch is a member of the journal's editorial board.

"I would say that the level of peer review here was negligible at best," Jauhar said. "In addition, the 'findings' are driven more by ideology than evidence."

Asked to respond to Jauhar's comments, Kirsch noted that although he is on the journal's advisory board, he has not been actively involved. Kirsch added that he serves on about a dozen academic advisory boards and serves as a reviewer for many top scientific and medical journals, including *The Journal of the American Medical Association* and *The New England Journal of Medicine*.

"Our article was peer reviewed," Kirsch said, "and we revised it following the first round of reviews." The review process did not differ from those he has gone through with more than 250 published peer-reviewed articles on which he was an author or coauthor, he noted.

A Growing Movement

Despite such expert opposition, the movement to suspend ECT continues. Recently, Sarah Price Hancock, MS, CRC, CPMC, who is herself a recipient of more than 100 ECT treatments, authored an international petition to standardize, regulate, and audit the modality. Hancock hopes to present the document, which currently has more than 6600 signatures, to the American Psychiatric Association and similar international societies.

A version of the petition was presented to the UK's National Health Service on July 2, the 59th anniversary of the death by suicide of Ernest Hemingway, who had received some 20 ECT treatments himself.

"Hopefully by his 60th anniversary, America and the world will be taking his death and the thousands living with adverse reactions more seriously by auditing, regulating, and tracking patients with a history of ECT to provide much needed comprehensive brain injury rehabilitation as necessary," Hancock told *Medscape Medical News*.

Among the signatories of the petition is Sue Cunliffe, MbChB, who underwent ECT for depression in 2004, with devastating effects. "I was left really badly brain damaged, and so I've never been allowed to work again," she told *Medscape Medical News.*

Cunliffe said the immediate effects of the treatment were profound. She said her hands shook, her balance and coordination were impaired, and her memories evaporated. However, she found a neuropsychologist who she says was able to help her recover control of her life. "Now at least I'm able to plan my life so that I can live with the brain damage."

Kirsch acknowledged that sorting through the ECT literature can be daunting. "If you're a physician, you try to keep up with the literature, but the problem is, the literature is so old and done in ways which would not pass muster right now. The data are really poor, and I guess it's just that people aren't aware of it."

George agreed that the therapy is not without its shortcomings.

"Does ECT have cognitive side effects? Unfortunately, it does. But so do lots of lifesaving therapies in medicine, like cancer chemotherapy," he said.

"Nobody really gets well with a single ECT session. It's usually eight to 12 over 3 or 4 weeks. So it's not particularly durable. That's why we often combine ECT with other forms of brain stimulation," George added.

He noted that the recent advent of alternative forms of ECT — including right unilateral ultrabrief pulse ECT and focal electrically administered seizure therapy — are beginning to address some of these shortcomings.

"The holy grail of brain stimulation is to be able to do things less invasively, and we're moving slowly in that direction," he said. "But right now, we don't have anything that is as acutely as effective as ECT. It is our lifesaver at the moment."

The review authors as well as George, Jauhar, Cunliffe, and Hancock report no relevant financial relationships.

Ethical Hum Psychol Psychiatry. doi:10.1891/EHPP-D-19-00014. Abstract

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Cite this: Experts Call for Immediate Suspension of ECT, Others Push Back - *Medscape* - Jul 24, 2020.