respiratory effort against an obstructed airway. His oxygen saturation dropped to 60% on room air. Supplemental oxygen was applied, improving his oxygen saturation to 80% on room air. He could answer simple questions and follow commands. He denied respiratory discomfort. He had a new productive cough and bilateral rales. Empirically, he was given 10 mg of intravenous furosemide along with a single albuterol nebulizer treatment. A portable chest x-ray showed a normal cardiac silhouette with bilateral perihilar and upper lobe ground-glass opacity, consistent with noncardiogenic edema. His oxygen saturation improved for the next several hours with application of oxygen. Thirty minutes after stopping supplemental oxygen, saturation declined, and oxygen was restarted. His cough returned, now with blood-tinged sputum. He was admitted to the medicine unit, and for the next several hours, his cough resolved, and oxygen saturation improved. He was discharged home the next day.

Because of persistent depressive symptoms, he consented to proceed with ECT, which was performed 5 days later. The same anesthesia and paralytic doses were used. He was also given 0.1 mg of glycopyrrolate intravenously several minutes before anesthesia, and 10 mg hydralazine after seizure termination. His airway was closely monitored to avoid and promptly treat soft tissue obstruction or laryngospasm. He went on to receive a total of 11 more treatments using this protocol without incident. His depression remitted.

Negative pressure pulmonary edema develops when a patient takes a deep breath against a closed airway, creating a large negative intrathoracic pressure. Patients develop respiratory distress, particularly if the upper airway obstruction is not relieved. Signs include cough with pink frothy sputum, rales on lung auscultation, and diffuse interstitial and alveolar infiltrates on chest x-ray; cardiac size is typically normal because these patients are euvolemic. Treatment is aimed at maintaining airway patency, while providing supplemental oxygen and positive-pressure ventilation if necessary.

Clinically, our patient presented with classic signs and symptoms of NPPE. Oxygen desaturation occurred immediately after his attempt at taking a deep breath before full resolution of muscle paralysis. He recovered with rapid intervention and supportive care. Although he did receive furosemide, the benefit is uncertain when pulmonary edema is not due to fluid overload. He also received nebulized albuterol at the onset of symptoms; bronchospasm is not thought to be involved in the pathogenesis of NPPE, but beta agonists may help increase the rate of alveolar clearance of fluid.

Negative pressure pulmonary edema can occur in any patient receiving anesthesia, with an incidence rate of up to 0.1%.[1] Laryngospasm is the most probable cause of upper airway obstruction in patients receiving ECT, and may occur as a result of oral secretions, use of a laryngeal mask airway, or retropulsion of the bite block causing direct laryngeal stimulation. Several factors may predispose patients to laryngospasm, including recent upper respiratory tract infection, history of reactive airway disease, and dry cough. Young male athletes are known to be at highest risk for NPPE because of their ability to generate a large negative intrapleural pressure.

The differential diagnosis for pulmonary edema after ECT includes NPPE, neurogenic pulmonary edema, cardiogenic pulmonary edema, and aspiration pneumonitis. Neurogenic pulmonary edema is thought to result from centrally mediated adrenergic excitation-induced pulmonary vasoconstriction and increased permeability of pulmonary capillaries; it is known to occur in epileptic patients after a seizure.[2] Vital signs are markedly elevated, and pulmonary symptom onset may be delayed. Chest x-ray findings are usually in the bilateral lung apices. Management of this condition and NPPE is the same. Cardiogenic pulmonary edema presents similarly, though findings on chest x-ray may reveal perihilar prominence, pulmonary venous congestion, and enhanced interstitial markings. Treatment goes beyond supportive care, aimed at improving hemodynamic stability. Clinical clues of aspiration pneumonitis include visualization of gastric contents in the oropharynx, witnessed aspiration, and unconfirmed nil per os status. In addition, distribution of alveolar disease on chest radiograph is usually focal. These patients are typically placed in Trendelenburg position to drain gastric content out of the mouth, the oropharynx is suctioned, and antibiotic treatment may be needed. If aspiration of solid food is suspected, flexible bronchoscopy may be indicated to remove particulate matter from the bronchi. Intubation and mechanical ventilation may also be necessary.

In our patient, several prophylactic measures were taken to reduce the risk of recurrence of pulmonary edema. Glycopyrrolate was administered to reduce production of oral secretions in an attempt to minimize laryngeal irritation. Hydralazine was administered to reduce the increased effect of catecholamines on vascular permeability. Lastly, attention was given to airway management to avoid laryngeal spasm. With these interventions, the patient completed his course of ECT.

There are 10 published case reports of pulmonary edema after ECT. Our case adds to the 3 published NPPE cases, of which only 1 went on to receive additional ECT treatment.[3]

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Effect of Transcranial Direct Current Stimulation Protocol for Treating Depression Among Hemodialysis Patients

A Proof-of-Concept Trial

To the Editor:

Depressive symptoms are commonly presented among patients undergoing hemodialysis, with an overall prevalence of about 40%.[1] The treatment of depression in patients undergoing hemodialysis is challenged by the lack of properly controlled trials of pharmacological strategies.[2] In

response, noninvasive neuromodulation approaches such as transcranial direct current stimulation (tDCS) may be an option for these patients because tDCS clinical effects have an antidepressant effect for different populations.[3] The effects of tDCS for patients undergoing hemodialysis have not been assessed hitherto.

We conducted an open-label trial on the efficacy of a 10-day tDCS protocol for patients undergoing hemodialysis diagnosed as having depression. Patients undergoing hemodialysis in an academic service underwent screening by a trained psychiatrist. All participants were diagnosed as having major depressive episodes according to *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, criteria. Patients underwent a 10-session tDCS protocol consisting of tDCS sessions every other day during a 3-week period. The sessions took place during the hemodialysis sessions. The anode was located over the left dorsolateral prefrontal cortex, and the cathode was positioned contralaterally. We used a direct current of 2.0 mA for 20 minutes. Participants were not receiving any other modality of treatment for depression and provided informed consent. The study was approved by the local institutional review board.

A total of 8 patients fulfilled eligibility criteria (75% females, mean age of 54 ± 14.9 years). Baseline assessment showed a Hamilton Rating Scale for Depression (HRSD) mean score of 17.5 (±5.39), whereas the Beck Anxiety Inventory mean baseline score was 13.5 (±7.27). After the end of treatment, HRSD = −17 scores dropped 9.87 (±5.6) points ($t_7 = 4.90$; $P = 0.0017$), and HRSD-17 scores remained stable during 1 month of follow-up ($t_7 = 1.16$; $P = 0.288$). Exploratory analysis also showed a significant reduction of anxiety symptoms (mean change of 5.12 ± 1.94; $t_7 = 2.64$; $P = 0.03$) as assessed by the Beck Anxiety Inventory. The improvement was also sustained during follow-up ($t_7 = 1.67$; $P = 0.137$). Regarding possible cofounders, we performed multiple regressions as to verify the influence of clinical (clinical diagnosis, time under hemodialysis protocol, number of comorbidities, psychiatric history) and demographical (sex, income, education) variables. We found no cofounder related to primary outcome. There were no severe adverse effects. Every patient referred a mild transient paresthesia under the electrode site during stimulation. We had no dropouts.

Our results indicate a possible clinical benefit of tDCS protocol in ameliorating depressive symptoms in patients undergoing hemodialysis. The study's limitations include the small sample size, its unblinded nature, lack of a control group, and short length. Moreover, our results may be overestimated because of intrinsic characteristics such as the placebo effect and Hawthorne effect.

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M.B. has equity in Soterix Medical Inc, and the City University of New York has patents on brain stimulation with M.B. as inventor. The other authors have no conflicts of interest or financial disclosures to report.

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Butyrylcholinesterase Atypical Mutation in a Patient Undergoing Electroconvulsive Therapy

Dear Editor:

We report the first case of a patient with a butyrylcholinesterase (BChE) atypical mutation that was detected during an electroconvulsive therapy (ECT) course.

The patient was a 22-year-old man with a 5-year history of schizophrenia, worsened by polysubstance abuse.

Having been treated with antipsychotic medicines for several months without any therapeutic response, the decision was made to commence a course of ECT. Medications at that stage were a combination of 800 mg of clozapine and 500 mg of loxapine daily.

At the first ECT session, anesthesia was induced with propofol (80 mg), and suxamethonium (30 mg) was used to provide muscle relaxation.

At the conclusion of treatment, the patient remained apneic, and this continued for 20 minutes, necessitating noninvasive ventilation support followed by orotracheal intubation and propofol infusion.

The assumption was made that the patient may have a BChE deficiency. However, laboratory testing revealed a level of 7228 IU (Normal > 4500IU).

During the second session, 130 mg of propofol was given together with a lower (20 mg) dose of suxamethonium. Again, a prolonged period of hypoventilation was observed and lasted 15 minutes.

Further treatments were carried out using rocuronium and sugammadex without any complications.

In an effort to ascertain the reason for the prolonged apnea, a biological analysis showed a mutated BChE gene (BCHE) (polymerase chain reaction and Mbo I digestion enzyme restriction).

This mutation pattern explained the prolonged action of suxamethonium in the first 2 treatments.[1]

Succinylcholine is metabolized by BChE, a hepatically derived enzyme responsible for the hydrolysis of ester linkages in some drugs such as suxamethonium and mivacurium. There are several forms of mutations that can affect these genes: heterozygous mutations (affecting between 1 of 25 and 1 of 480 patients) and homozygous mutations (affecting between 1 of 3200 and 1 of 5000 patients).

Moreover, the frequency of mutated allele presence in the European population ranges from 1.62% and 1.92%. The BChE atypical mutation occurs in 1 out of 3000 patients in the white population.

This kind of mutation reduces the enzyme affinity for its substrates. The main consequence of this enzyme function disorder is a longer period of muscular paralysis that also exposes the patient to prolonged apnea. Usually, prolonged apnea after suxamethonium comes about as a result of either pseudocholinesterase deficiency or mutation or acquired conditions leading to a decrease in the plasma cholinesterase activity, such as hepatic dysfunction; pregnancy; medications including acetylcholinesterase inhibitors, steroids, antidepressants, and oral contraceptives; or organophosphate poisoning.[2,3] In ECT, apnea after suxamethonium