Cochrane for Clinicians

Putting Evidence Into Practice

Pharmacotherapy for Posttraumatic Stress Disorder

Sajeewane Seales, MD, MPH, Uniformed Services University of the Health Sciences, Bethesda, Maryland

Paul Seales, MD, Wounded Warrior Regiment – Reserve Medical Entitlements Determination, Quantico, Virginia

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Clinical Question

Is pharmacotherapy effective for reducing symptoms of posttraumatic stress disorder (PTSD) in adults?

Evidence-Based Answer

Selective serotonin reuptake inhibitors (SSRIs) improve symptoms of PTSD and are considered first-line pharmacologic agents. (Strength of Recommendation [SOR]: A, consistent, good-quality patient-oriented evidence.) Mirtazapine and amitriptyline also improve PTSD symptoms. (SOR: B, inconsistent or limited-quality patient-oriented evidence.) SSRI use is associated with an increased risk of treatment withdrawal because of adverse effects compared with placebo.[1]

Practice Pointers

PTSD is characterized by complex behavioral, somatic, and cognitive effects caused by a traumatic event. Psychotherapy and medications are used for treatment of PTSD. The lifetime prevalence of PTSD in North America is more than 9% for the general adult population and may be as high as 17% in U.S. veterans.[2,3] The authors of the review sought to identify medications that are effective for reducing symptoms of PTSD in adults.

The Cochrane review included 66 randomized controlled trials and 7,442 participants ranging from 18 to 85 years of age with a primary diagnosis of PTSD.[1] Doses of medications varied. Patients on concomitant medications were included, but those receiving psychotherapy were excluded. Pharmacotherapies were assessed for the patient-oriented outcomes of treatment efficacy and tolerability. Treatment efficacy was defined as improvement of PTSD symptoms compared with placebo and measured by the Clinical Global Impressions Scale–Improvement score. This scale ranges from a score of 1 (very much improved) to 7 (very much worse), and treatment was considered effective if participants scored 1 or 2.[1] The studies lasted from 13 days to 28 weeks, and treatment tolerability was assessed using the surrogate measure of dropout secondary to adverse events.

SSRIs, including fluoxetine, paroxetine, and sertraline, improved PTSD symptoms compared with placebo (risk ratio [RR] = 0.66; 95% CI, 0.59 to 0.74) based on moderate-certainty evidence. These SSRIs improved symptoms across several PTSD symptom clusters (i.e., reexperiencing/intrusion, avoidance/numbing, and hyperarousal) determined by subscales. Treatment withdrawal due to adverse events increased among patients using SSRIs (RR = 1.41; 95% CI, 1.07 to 1.87; absolute risk of withdrawal overall was 9%).

Low-certainty evidence showed that mirtazapine (RR = 0.45; 95% CI, 0.22 to 0.94) and amitriptyline (RR = 0.60; 95% CI, 0.38 to 0.96) improved PTSD symptoms compared with placebo. There was no statistically significant increase in treatment withdrawal due to adverse events in those taking mirtazapine or amitriptyline compared with placebo. No evidence of benefit was found with the use of other medications such as anticonvulsants and antipsychotics; no studies reported the treatment efficacy of other potential therapies including alpha blockers, benzodiazepines, hypnotics, monoamine oxidase inhibitors, or serotonin-norepinephrine reuptake inhibitors. There were no adequate comparisons of medication types, such as an SSRI vs. amitriptyline.

The results are widely generalizable because the studies included adults with diverse trauma types, duration, severity, and comorbidities. The most common bias introduced in the reviewed studies was attrition bias. However, the lack of blinding for outcome assessors, selective reporting bias, and lack of clarity of randomization were also present.

These are summaries of reviews from the Cochrane Library.

This series is coordinated by Corey D. Fogleman, MD, assistant medical editor.

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CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 618.

Current clinical practice guidelines recommend offering fluoxetine, paroxetine, sertraline, and venlafaxine as first-line medications for PTSD.[4,5] Family physicians should practice shared decision-making and discuss the potential value of SSRIs, amitriptyline, and mirtazapine for the treatment of PTSD. There is no evidence to support the use of other medications to treat PTSD.

The practice recommendations in this activity are available at https://www.cochrane.org/CD002795.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Navy, the U.S. Marine Corps, or the U.S. Department of Defense.

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Antiplatelet Therapy in Chronic Kidney Disease

Madhavi Singh, MD, and Kristen Grine, DO, Penn State College of Medicine, Hershey, Pennsylvania

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Clinical Question

Does antiplatelet therapy prevent myocardial infarction in patients with chronic kidney disease (CKD)?

Evidence-Based Answer

Antiplatelet therapy reduces the risk of myocardial infarction by 0.8% compared with placebo (95% CI, 0.1% to 1.5%; number needed to treat [NNT] = 125) in patients with CKD but is associated with an increased risk of major bleeding (number needed to harm [NNH] = 100).[1] (Strength of Recommendation: C, disease-oriented evidence.)

Practice Pointers

Conditions that increase the risk of CKD, including hypertension, obesity, and diabetes mellitus, are increasing worldwide with a commensurate increase in the global health care expense related to these conditions. Myocardial infarction is three times more likely in patients with CKD compared with those who have normal kidney function. In general, cardiovascular disease is the leading cause of morbidity and mortality in patients with CKD.[2,3] Excessive platelet activation in CKD is postulated to create a prothrombotic state and antiplatelet agents have been extensively used in these patients.[4] The authors of this analysis sought to discern the effectiveness of antiplatelet agents in preventing myocardial infarction.

The 2021 Cochrane review is an update of the 2013 review and included 118 studies (randomized and quasi-randomized), enrolling 51,959 participants. The population included patients 18 years and older with CKD, defined as a glomerular filtration rate of less than 60 mL per minute per 1.73 m^2; those receiving kidney replacement therapy; those with a functioning kidney transplant; or patients with proteinuria (Kidney Disease Outcomes Quality Initiative stages 1 to 5) or elevated creatinine levels (i.e., serum creatinine level higher than 120 µmol per L [1.36 mg per dL]). There were 90 studies (40,597 participants) that compared an antiplatelet agent with placebo or no treatment, and 29 studies (11,805 CKD participants) that compared one antiplatelet agent with another. The studies were conducted across North and South America, Europe, Asia, Australia, and New Zealand; they were single or multicentric trials and were performed in one or multiple countries.

The antiplatelet agents that were studied included, but were not limited to, acetylsalicylic acid (i.e., aspirin); adenosine diphosphate receptor inhibitors (e.g., ticlopidine, clopidogrel); adenosine reuptake inhibitors (e.g., dipyridamole); glycoprotein IIb/IIIa inhibitors (e.g., abciximab, eptifibatide, tirofiban [Aggrastat], defibrotide [Defitelio]); phosphodiesterase 3 inhibitors (e.g., cilostazol); $P2Y_{12}$ antagonists (e.g., prasugrel [Effient], ticagrelor [Brilinta], cangrelor [Kengreal]); and sulfinpyrazone (Anturane). Agents were administered at different doses and via different routes.

Use of an antiplatelet agent compared with placebo probably reduced the risk of fatal or nonfatal myocardial infarction in people with CKD during

a median follow-up of 12 months (moderate-certainty evidence; absolute risk reduction = 0.8% [95% CI, 0.1% to 1.5%]; NNT = 125 [95% CI, 66 to 1,000]; n = 15,289). There was no statistically significant effect on all-cause mortality.

Major bleeding as a risk of antiplatelet therapy was defined as retroperitoneal; intra-articular; intraocular, intracranial, or intracerebral hemorrhage; or gastrointestinal bleeding. It also included bleeding that was fatal, life-threatening, disabling, required transfusion, or needed corrective surgery or hospitalization, with or without a fall in hemoglobin or melena. Antiplatelet use compared with placebo probably increased major bleeding in people with CKD over a median follow-up of six months (moderate certainty of evidence; NNH = 100; 95% CI, 53 to 333; n = 16,194).

A meta-analysis of 50 studies of patients with CKD (27,773 participants) showed a reduction in the risk of myocardial infarction (NNT = 62; 95% CI, 25 to 166; n = 18,382) and an increased risk of major bleeding (NNH = 111; 95% CI, 62 to 333).[5] The Kidney Disease Improving Global Outcomes guideline supports aspirin use for adults with CKD and balancing the increased bleeding risk.[6] The decision to use antiplatelet therapy should be individualized according to the treatment goals of each patient.

The practice recommendations in this activity are available at https://www.cochrane.org/CD008834.

Editor's Note: The absolute risk reduction, CIs, NNHs, and NNTs reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

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