Selective Serotonin Reuptake Inhibitors for Posttraumatic Stress Disorder

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Q. What are selective serotonin reuptake inhibitors?

A. Selective serotonin reuptake inhibitors (SSRIs) are a class of medications used to treat depression, anxiety, and PTSD. Two SSRIs are approved by the U.S. Food and Drug Administration (FDA) for the treatment of PTSD: paroxetine (Paxil) and sertraline (Zoloft). SSRIs increase the serotonin level in the brain by preventing its reuptake by the presynaptic neurons. As a consequence, serotonin remains available to bind to postsynaptic neurons and exert its mood enhancing effects.

Q. What are the potential mechanisms of action underlying SSRIs for the treatment of PTSD?

A. Negative cognitions and mood are a symptom cluster of PTSD that can parallel indicators of depression. SSRIs may be effective in treating PTSD, and this cluster specifically, by remediating emotion regulation difficulties, and by supporting the downregulation of negative affect via a boost in the neurotransmitter serotonin (MacNamara et al., 2016). An increase in serotonin can enhance activity in the prefrontal regions of the brain that are known to be involved in the initiation and maintenance of emotion regulation (Kohn et al., 2014). The increase in serotonin in the brain may decrease anxiety and sleep difficulties which, in turn, allows for greater regulation of mood that is impaired in PTSD (MacNamara et al., 2016).

Q. Are SSRIs recommended as a treatment for PTSD in the Military Health System (MHS)?

A. Yes. The *2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder* recommends sertraline, paroxetine, and fluoxetine as monotherapy for PTSD for patients diagnosed with PTSD who choose not to engage in or are unable to access trauma-focused psychotherapy, with a "strong for" strength of recommendation. These three specific SSRIs have stronger evidence to support their use in the treatment of PTSD compared to other SSRIs.

The MHS relies on the VA/DoD clinical practice guidelines (CPGs) to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.

Q. Do other authoritative reviews recommend SSRIs as a treatment for PTSD?

A. Yes. Other authoritative reviews have substantiated the use of SSRIs for the treatment of PTSD.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency for Healthcare Research and Quality (AHRQ) and Cochrane.

- AHRQ: A 2018 systematic review update of psychological and pharmacological treatments for adults with PTSD found that fluoxetine and paroxetine reduced PTSD symptoms, with a moderate strength of evidence, and found that sertraline reduced PTSD symptoms, with a low strength of evidence (Forman-Hoffman et al., 2018).
- Cochrane: A 2006 systematic review of pharmacotherapy for PTSD including 17 trials compared an SSRI with a placebo, and found evidence for the efficacy of paroxetine and sertraline, but not for citalopram or fluoxetine (Stein, Ipser, Seedat, Sager, & Amos, 2006).

Q. What conclusions can be drawn about the use of SSRIs as a treatment for PTSD in the MHS?

A. The *2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder* recommends sertraline, paroxetine, and fluoxetine as monotherapy for PTSD for patients diagnosed with PTSD who choose not to engage in or are unable to access trauma-focused psychotherapy. The CPG recommends individual, manualized trauma-focused psychotherapy over pharmacologic interventions for the primary treatment of PTSD. Notably, a recent trial evaluated sertraline, prolonged exposure, and a combination of the two, and found no differences between the three treatments (Rauch et al., 2019). This new research will be taken into account in the next update of the PTSD CPG. Clinicians should consider several factors when choosing a treatment with their patient. Treatment decisions should take into account practical considerations such as availability and patient preference that might influence treatment engagement and retention.

References

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