

# Is There a Role for Second Generation Antipsychotics in the Treatment of PTSD?

Gerardo Villarreal\*

Department of Psychiatry and Neuroscience, University of New Mexico, R.G. Murphy VA Medical Center, San Pedro Dr SE, Albuquerque NM, USA

\*Corresponding author: Gerardo Villarreal, Department of Psychiatry and Neuroscience, University of New Mexico, R.G. Murphy VA Medical Center, 1501 San Pedro Dr SE, Albuquerque NM 87108, USA, Tel: + 505-265-1711; E-mail: gvillarr@salud.unm.edu

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## Description

Posttraumatic Stress Disorder (PTSD) is common in civilians and veterans and is often chronic and disabling [1&2]. The Selective Serotonin Reuptake Inhibitors (SSRIs) and venlafaxine are considered first line treatment for PTSD although only sertraline and paroxetine have FDA approval [3]. These medications have been shown to improve most PTSD symptoms and in particular, irritability [4&5]. However, they have little effect on insomnia [4&5] which is serious problem in PTSD patients [6]. Military veterans tend to have little or no response to antidepressant medications [7-10]. Second Generation Antipsychotics (SGAs) are often used in the treatment of PTSD, particularly for insomnia [11]. A review of SGAs randomized trials in the treatment of PTSD found the most evidence of benefit from quetiapine and risperidone, particularly for re-experiencing and hyperarousal symptoms [12].

However, a large Veterans Administration (VA) funded trial of risperidone as an adjunct medication in military veterans unresponsive to SSRI's found it was no better than placebo for global PTSD severity, although a post-hoc analysis did show improvement in re-experiencing and hyperarousal symptoms, this was not considering clinically significant [13]. A randomized, placebo-controlled trial of quetiapine as single agent in PTSD, found significant improvement on global PTSD symptom severity and also for experiencing and hyperarousal clusters [14].

Significant improvement was seen in measures of anxiety and depression [14]. A post hoc analysis of data from that trial found the strongest effect was on insomnia (unpublished data). These findings are consistent with anecdotal evidence, a survey of 2613 Veterans Administration providers found that quetiapine was the most frequently prescribed atypical antipsychotic to veterans with PTSD (47%). The reasons for prescribing quetiapine was its perceived efficacy, particularly for sleep and sedation [11].

Therefore, there is a rationale to use SGAs, in particular quetiapine, in the treatment of PTSD, since its benefit on insomnia may complement the effect if antidepressants on irritability. The main limitation of SGA are their metabolic side effects, including changes in insulin sensitivity and lipid metabolism, which increase the risk metabolic syndrome, type 2 diabetes and cardiovascular disease [15]. The new VA/DoD practice guidelines emphasize the use of exposure-based therapies and recommend against using SGAs in PTSD [3].

Clinicians treating patients with PTSD, in particular those with chronic and severe symptoms face a predicament. These patients are often unable or unwilling to engage in exposure-based therapies and there is evidence of high dropout rates and low engagement in these therapies in real-world settings [16]. Only 2 medications are FDA-

approved for the treatment of PTSD and in general few pharmacological interventions are recommended [3]. Prescribers often utilize off-label medications [17].

The SGAs, in particular quetiapine, may have a role in the treatment of selected PTSD cases with severe insomnia and other hyperarousal and re-experiencing symptoms; the benefit of SGAs may complement the effect of SSRIs on irritability. Close monitoring of metabolic parameters, weight and BMI is advised. In cases with early weight gain behavioral interventions targeting nutrition and exercise counseling should be considered, since they have been effective in lowering weight and BMI in patients with schizophrenia taking SGAs [18,19]. Metformin has been useful in this regard [20] and thus should be considered when these medications are used, and weigh gain is evident. The SGAs and quetiapine may have a role in treating PTSD but should be reserved for treatment-resistant and severe PTSD cases.

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