

## Brexanolone Therapy for Postpartum Depression

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*Madam*, Postpartum depression (PPD) is a common psychiatric disorder affecting 28-63% of Pakistani women- the highest prevalence among all Asian countries.<sup>1</sup> It is defined as depressive symptoms such as constant low mood, sadness and low energy experienced by mothers in the initial days or weeks after childbirth.<sup>2</sup> Other signs and symptoms include anxiety, altered sleep and eating patterns.<sup>2</sup> These symptoms may be attributed to peripartum fluctuations in reproductive hormones.

Its adverse effects also extend to the newborn resulting in impaired cognitive development and behavioural problems.<sup>3</sup> If left untreated, PPD may lead to poor mother-infant attachment and contribute to long-term maternal morbidity.<sup>2</sup> The stigma related to psychiatric diseases along with lack of financial resources and the burden of infant care often averts the mother from seeking treatment.<sup>2,3</sup>

The American College of Obstetricians and Gynecologists (2015) recommends screening of all women during the perinatal period with a standardized tool.<sup>3</sup> The Edinburgh Postnatal Depression Scale (EPDS) is the preferred method used in most cases.<sup>3</sup> The use of standard antidepressants such as Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin-Noradrenaline Reuptake Inhibitors (SNRIs), and tricyclic antidepressants have failed to achieve complete remission of signs and symptoms.<sup>4</sup> Till date, no pharmacological treatment options have been employed specifically for PPD.<sup>2</sup> Therefore a new treatment modality with prompt onset of action and better effectiveness than the standard antidepressants is required.

A double-blind placebo-controlled trial published in The Lancet in 2017 investigated Brexanolone, an intravenous formulation of allopregnanolone, a positive allosteric modulator of  $\gamma$ -aminobutyric acid (GABA) receptors for the treatment of PPD.<sup>4</sup> Administration of this drug for PPD resulted in a huge improvement in HAM-D (Hamilton

score Scale for despair) total score at 60 h compared to placebo.<sup>2</sup> The mean reduction in HAM-D total score at 60h was 21.0 points in the brexanolone group compared to placebo (8.8 points). The mean difference between the placebo group and brexanolone injection group was statistically significant.

A similar phase 3 randomized control trial in 2018, tested the effectiveness of brexanolone injection buffered with citrate and diluted with sterile water.<sup>2</sup> This trial confirmed the findings of the previous study and concluded that brexanolone injection significantly reduces postpartum depressive symptoms.<sup>2</sup>

Hitherto, no major side effects have been attributed to this new drug.<sup>5</sup> Although some patients experienced headache, dizziness and somnolence.<sup>2</sup> Thus, brexanolone is the first drug approved by the US Food and Drug Administration for the treatment of PPD. However, currently it is only administered to short term inpatients at specifically approved sites in order to carefully monitor its risks and adverse outcomes before it is used widely. Although it has not been used in Pakistan yet, the high disease burden in the country suggests the need for introducing latest treatment strategies to counter the morbidity associated with PPD. Despite their limited effectiveness, conventional therapies such as SSRIs and Cognitive Behavioral Therapy are currently employed. There is hope that the high efficacy of brexanolone along with its minimal side effect profile will make it a state-of-the-art drug which may help control the increasing prevalence of PPD in Pakistan and improve maternal and child health in the future.

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