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Review Article

A COMPREHENSIVE REVIEW OF NOVEL MODULATOR THE GABAA RECEPTOR, BREXANOLONE FOR THE TREATMENT OF POST-PARTUM DEPRESSION

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ABSTRACT

Postpartum Depression (PPD), a significant depressive disorder that starts during pregnancy and also can occur postpartum. Similar to other types of depression, it is characterised by sadness and/or loss of interest in previously enjoyed activities as well as a decreased capacity for pleasure. It can also be accompanied by symptoms like cognitive impairment, feelings of guilt or worthlessness, or suicidal thoughts. PPD has a detrimental effects on the mother itself as well as child and whole family. Up to 20% of women may experience postpartum depression after giving birth. It has been linked to decreased mother-infant bonding and negative impacts on the child's cognitive, behavioural, and emotional growth. There were no approved drugs to treat postpartum depression up until recently. Psychotherapy and drugs were used as treatments, although not all women experience a positive response or remission, and sometimes the response is delayed. A naturally occurring neuroactive steroid called allopregnanolone, its serum levels sharply decrease after giving birth. It has been hypothesised that this hormone fluctuation contributes to the pathophysiology of postpartum depression. It is given as a 60-hour continuous infusion while being monitored and is expected to affect neuronal excitability by acting as an allosteric modulator of γ-aminobutyric acid-A receptors. In this review, we have summarized brexanolone, first dug approved by US Food and Drug Administration (US FDA) for the treatment of postpartum depression. Evidences from *in silico*, *in vitro*, *in vivo* and clinical studies have demonstrated that it provides rapid and effective alleviation from depressive symptoms.

Keywords: Postpartum depression, Brexanolone, γ-aminobutyric acid-A receptors (GABA)

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INTRODUCTION

Postpartum depression is a serious and debilitating condition characterised by a substantial depressive episode that is chronologically and pathophysiologically linked to pregnancy. It exhibits indicators including cognitive loss, feelings of shame or worthlessness, or suicidal thoughts, and, like other kinds of depression, is marked by melancholy and/or anhedonia [1, 2]. When the episode begins during gestation or within four weeks after childbirth, PPD is defined as unipolar major depression with the modifier "with peripartum onset" in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) of the American Psychiatric Association (APA) [3]. Despite the brief period, the first year after delivery is regarded by many specialists as the postpartum phase [4, 5]. Extreme anxiety and feelings of helplessness toward their unborn kid are common among PPD-afflicted women. 30% of women who have given birth during the previous year report having PPD [6]. Around 10–20% of mothers experience post-partum depression (PPD), with an 8–20% prevalence in the USA [1, 7-10]. These numbers are undoubtedly underreported because of the stigma associated with mental illness and the minimising that occurs from both mothers and medical providers. Evidence suggests that the amount of PPD that is self-reported can also depend on factors including education, race, and ethnicity. During the postpartum period, about 50% of mothers report feeling depressed (often referred to as "baby blues"). However, these feelings are typically mild and fleeting, do not meet the criteria for a major depressive episode, and are not formal psychiatric diagnoses; postpartum depression extends in symptom severity beyond this. Even when it is justified, it is likely that the stigma attached to diagnosing PPD will lead to underreporting of the condition and its acceptance as "baby blues." [11] For moms with PPD, there is a higher risk of morbidity and mortality, with suicide accounting for one in seven postpartum fatalities [12-14]. However, PPD has wide-ranging repercussions that go beyond the woman who is afflicted. The infants' needs are often given less attention by affected mothers, which might affect the infants' height, weight, emotional development, and behavioural maturity. A broken or absent mother-child bond may hinder a child's social and interpersonal development. These effects could last until adolescence and be long-lasting [11, 15, 16].

Predisposing factors

Risk factors for PPD include low socioeconomic status, a lack of social support, and a personal or family history of depression. It is suspected that a complicated interaction between genetic and environmental factors, with a heritability as high as 40%, affects the development of PPD. PPD is connected to hormonal changes, sleep loss, and this genetic-environmental paradigm during the peripartum period. The hormonal imbalance, which includes variations in oestrogen, progesterone, cortisol, oxytocin, and allopregnanolone-a, a progesterone derivative contribute to this disorder. Early PPD symptoms include anhedonia, anergia, low mood, suicidality, and problems with sleep, food, and attention [3, 17-20]. In a thorough analysis in more than 50 countries, it was shown that the frequency of PPD was higher in countries with high rates of income inequality, maternal and infant mortality, and the number of women of reproductive age who worked more than forty hours per week. There may also be distinctions between countries with comparable economic standing. These findings suggest that there may be environmental variables that predispose individuals to PPD [21].

Pathophysiology

On the precise mechanism of PPD, there is no consensus worldwide. But it is evident that the aetiology of the illness is influenced by both psycho-social and biological factors. The aetiology of PPD has been linked to the GABAergic theory of depression, neurobiological differences and lastly neurosteroids [22].

GAB aergic theory of depression

According to the studies, depression changes the GABA receptors' $GABA_A$ subunit composition, blocking GABA neurotransmission. GABAergic transmission is hypothesised to influence the control of

hippocampal neurogenesis and neuronal development, which have a role in the cognitive and memory problems that can be seen in depression. Examples of GABAergic drugs that have been shown in animal research to correct the behavioural impairments displayed in depressed animal models are progabide and fengabine. The calming of stress, which is heightened in depression and may contribute to PPD, is thought to be facilitated by GABA. Stress has a stronger influence on cognition when GABA isn't present to mediate it [23, 24].

Neurobiological changes

Functional magnetic resonance imaging (fMRI) studies in human and animal models are being used to investigate the role that neurobiological changes play in the development of PPD. Depressed mothers showed considerably less activation in brain networks linked to normative parenting in response to their new-born's emotional facial expressions and the sound of their infant crying than did non-depressed mothers [25, 26]. PPD has been associated with altered connectivity in the corticocortical and corticolimbic systems, particularly in the amygdala, anterior cingulate cortex, dorsal lateral prefrontal cortex, and the hippocampus, according to studies using fMRI in the resting state [27, 28]. Previous evaluations of MRI studies have shown that the neurobiological presentation of PPD differs significantly from that of major depression, despite the fact that there are various interpretations of the relative relevance of these changes [29, 30].

Neurosteroidal regulation

In addition to modifying the brain reward system and regulating biological processes that have previously been connected to the formation of severe depression, reproductive hormones also play a role in managing emotion processing and cognition [19, 31]. Dysregulation of the endocrine system was also identified as a potential contributing factor in research by Ahokas *et al.* [32], Gregoire *et al.* [33], and Gregoire *et al.* [33]. Allopregnanolone, a neurosteroid produced from progesterone, is essential for controlling $GABA_A$ receptors. The central nervous system produces the endogenous progesterone metabolite allopregnanolone, a neuroactive steroid that alters neuronal excitability by acting as a positive allosteric modulator on the $GABA_A$ receptor [30]. Due to their ability to control the $GABA_A$ receptor, neuroactive steroids have been discovered as potential PPD therapies in rodent and human models. Allopregnanolone levels rise throughout pregnancy and reach their peak in the third trimester. After giving birth, allopregnanolone levels rapidly fall. It has been suggested that the inability of $GABA_A$ receptors to adapt to changing allopregnanolone levels plays a role in the emergence of PPD [11, 22]. High levels of allopregnanolone are associated with a lower incidence of PPD, but low levels are associated with an increase in depressive symptoms in expecting moms. However, allopregnanolone-mediated signalling has also been recognised as a key therapeutic target. In tests for the treatment of PPD, the allopregnanolone analogue brexanolone has shown to reduce depression scores [34-36].

Diagnosis of postpartum depression

As per the DSM-V major depressive episode (MDE) diagnostic criteria, which include at least four of the following symptoms, like increased or decreased appetite, sleep disturbance, psychomotor agitation or retardation, low energy, feelings of worthlessness, low concentration, and suicidal ideation [3]. In the first four weeks after birth, depressive symptoms may be regarded to have a postpartum beginning in the case of an MDE. But according to study, women have depressive episodes far more frequently in the first three months after giving birth, and this heightened sensitivity to mental illness may linger for a year or more [37]. PPD has a wide range in the severity of the symptoms and when they first appear. The symptoms that women with PPD display range from severe functional impairment, agony, and suicidality to subjective mood changes including irritation, anxiety, and sadness. Fluctuations in eating and sleep patterns are among the symptoms that can result in weight changes. Another typical sign is excessive concern for the welfare of the youngster. While some women may experience symptoms before giving birth, others may experience them after. These symptoms must last longer than two weeks in order to be distinguished from "baby blues," which are common in new mothers and typically go away within this time frame. PPD has historically been dignosed using signs of Major Depressive Disorder (MDD) due to similarities in presentation. Unfortunately, this has resulted in therapy and symptom management that are ineffectual [3, 6].

Screening for postpartum depression

In an effort to mitigate these severe negative impacts of PPD, more attention has been placed on the importance of early and accurate detection and treatment of depression during or during pregnancy [38, 39]. It might be more challenging to recognise depression during the postpartum time due to the typical physical and emotional demands of being a new mother, such as changes in energy and appetite, lack of sleep, and increased concern for the infant. Experts have suggested screening for PPD at these specific settings because family practise [40], paediatric settings [41], and the first postnatal obstetrical visit (typically 4-6 w after delivery) are the ones where new mothers interact with the healthcare system most frequently in the first three months after delivery. The most popular PPD screening tool is the Edinburgh Postnatal Depression Scale (EPDS), a 10-item self-report that prioritises emotional and functional factors above somatic symptoms [42]. However, languages and cultures differ in terms of sensitivity and specificity [38, 43]. Two more regularly used screening tools with evidence of validity during pregnancy are the Postpartum Depression Screening Scale (PDSS) and the 9-item Physician's Health Questionnaire (PHQ-9) [44]. These screening technologies may occasionally give false-positive results. Therefore, a clinical interview is required to definitively diagnose PPD.

Current treatment

There are numerous therapy alternatives available for women who have postpartum depression. Untreated postpartum depression may have consequences such as infant developmental delays, increased maternal morbidity, and a higher probability of recurring postpartum depression [48]. The recommended course of treatment for mild-to-moderate depression is psychotherapy. Combining antidepressant medication and psychotherapy is one strategy for treating moderate-to-severe postpartum depression [45]. When choosing which medication to utilise for the treatment of moderate-to-severe postpartum depression, it is crucial to consider if the patient responded to an antidepressant before experiencing postpartum depression [22, 46]. The first-line effective treatment for depression is an SSRI, such as citalopram or sertraline, if the patient has never used an antidepressant before or if a medication history is unavailable. They respond well to patients and have manageable side effect profiles [37, 46]. When choosing a medication for PPD, it is important to consider the mother's intentions to breastfeed the kid. According to the National Institute of Mental Health, "while there is not convincing evidence that the amount of antidepressant medicine in the breastmilk is sufficient to cause harm for the newborn, many women want to avoid even this minor potential risk" [47]. When selecting the course of treatment, the speed of the reaction must also be taken into account. When opposed to other anti-depressants, which take three to four weeks to start working, brexanolone has the benefit of not delaying the beginning of response.

Pharmacokinetics

Brexanolone is administered intravenously due to its limited oral bioavailability and quick metabolism. Following absorption, it goes through a substantial uptake by the tissues, having a distribution volume that is roughly 3L/kg. [54] Regardless of the plasma drug concentrations, the plasma protein binding is also considerable, with more than 99% of it being protein-bound. It follows a linear pharmacokinetics in the dose range of 30 mcg/kg/h to 270 mcg/kg/h, which is three times the maximum advised dose. The mean steady state plasma concentration (Cmax) was found to be around 52 ng/ml and 79 ng/ml, respectively, for the typical prescribed doses of 60 mcg/kg/h and 90 mcg/kg/h [55]. Brexanolone inhibits CYP2C9, yet *in vitro* research indicates that therapy with brexanolone had no impact on the pharmacokinetics of drugs that are CYP2C9 substrates, removing the need for dosage adjustment. Brexanolone's pharmacokinetics (PK) did not

significantly change in patients with severe renal or hepatic impairment [22]. With a plasma clearance rate of around 1l/h/kg and a terminal half-life of 9 h, it is eliminated from the body. Less than 1% of the metabolites are excreted unchanged after the administration of a radiolabelled medication, while 47% and 42% of the metabolites are eliminated in the faeces and urine, respectively. Although the drug`s PK is unaffected in patients with hepatic or renal impairment, use in patients with end-stage renal disease is not advised due to the solubilizing agent's accumulative tendency in the intravenous drug formulation [56].

Pharmacodynamics

In mammalian cells expressing the 122, 43, and 63 receptor subunits from recombinant human $GABA_A$ receptors, brexanolone potentiated GABA-mediated currents. However, no conclusive human pharmacodynamic investigations have been carried out to determine the precise reaction on the GABA receptor activity [22]. No equivalent response was seen at therapeutic doses, despite the dose-response curve showing an association of increased sedation at sub-therapeutic doses. However, the incidence of sedation increased when antidepressants and benzodiazepines were administered concurrently, which is likely due to its interaction with $GABA_A$ receptor. In a study involving 30 healthy persons, it was discovered that there was no QT interval prolongation up to 90 mcg/kg/h, which is 1.9 times the highest infusion rate advised. To learn more about the drug's pharmacodynamics, more human research are required [22, 56].

Mechanism of action

Brexanolone works by positively regulating the GABA a receptors found extra-synaptically and at the level of synapses. [48] The drug's chemical composition is similar to that of allopregnanolone. Allopregnanolone, a progesterone derivative, is a neurosteroid that, upon production in neurons and glial cells, has an autocrine activity [49]. This reduced metabolite of progesterone possesses the properties of being an anxiolytic, anti-stress, sedative-hypnotic as well as an anticonvulsant by agonistically modulating the GABA a receptor. Although the binding sites are distinctive from that of barbiturates and benzodiazepines, they are capable of modulating all isoforms of GABA A receptors even the benzodiazepine sensitive α4 and α6 subunits. Although allopregnanolone has sensitivity to all isoforms of GABAA receptor, it binds with high affinity to α/β/δ type extra synaptic GABAA receptor, which is the type of receptor mostly expressed when the body is in a stressed state. α/β/γ type synaptic GABAA receptor, despite being expressed both during the normal and stressed times, the difference in the α subtype expression makes it more sensitive to the receptor which has α 4 and α 5 subunits expressed. Thus the order of sensitivity is as follows: α/β/δ type extra synaptic GABAA receptor>α(α 4,α 5)/β/γ type synaptic GABAA receptor>α(α 1,α 2)/β/γ type synaptic GABAA receptor. By binding to the receptor, it exerts a positive allosteric modulating action that augments the influx of chloride ions seven to ten-fold, enhancing the inhibitory GABAergic transmission [50, 51]. The levels of allopregnanolone alter significantly during pregnancy. Pregnancy-related levels rise, especially in the third trimester, and then naturally fall following delivery. This sudden drop in neuro-steroid levels has an effect on neurogenic circuits, generating an imbalance between inhibitory and excitatory signalling, which may help explain why postpartum depression develops [35, 52]. Brexanolone, an allopregnanolone aqueous formulation based on β-cyclodextrin, aids in preventing the rapid decrease of the neurosteroid's blood level and restores the GABAergic neurotransmission [51]. This helps symptoms resolve quickly, in contrast to SSRIs, which take three to six weeks for their therapeutic benefits to manifest. Brexanolone may contribute to an increase in BDNF, which explains the drug's potential long-term advantages [53].

Neuroactive steroid administration in animal models

Neuroactive steroid $GABA_A$ Receptor positive allosteric modulators (PAMs) have the potential to represent a unique strategy for the treatment of depression and PPD therapy. The SGE-516, a synthetic neuroactive steroid $GABA_A$ receptor PAM, has been studied using the $GABA_A$ subunit and corticotropin-releasing hormone-potassium-chloride co-transporter-2 (CRH-KCC-2) deficient mouse models of PPD. Mice with genetic deletions of the $GABA_A$ receptor subunit (Gabard/) or the KCC2 potassium/chloride co-transporter (KCC/CRH) in the paraventricular nucleus of the brain have PPD-like behaviours and are unable to inhibit the activation of the HPA axis by stress [57, 58]. Gabard/or KCC/CRH mice who received late-pregnancy SGE-516 treatment displayed improvements in mother care and depressive-like behaviours [59]. Treatment with SGE-516 also decreased the HPA axis dysregulation brought on by stress in this mouse model, decreasing the stress-related surge in corticosteroids [59]. Importantly, giving these mice a benzodiazepine had no influence on the depressive symptoms they displayed. This finding suggests that the neuroactive steroid pharmacology that underpins the antidepressant effects of SGE-516 involves positive allosteric regulation and/or trafficking of both synaptic and extrasynaptic $GABA_A$ receptors [59-61]. The outcomes of these genetic mouse studies give critical mechanistic insight that is congruent with clinical studies utilising benzodiazepines or brexanolone injection in patients with depressive symptoms and support the neuroactive steroid and GABA theory in PPD.

Clinical studies

Allopregnanolone was originally evaluated in a clinical setting to treat PPD. It was assessed as a treatment for severe PPD in a proof-of-concept, open-label research by Kanes SJ *et al.* Four women received the medication because they had severe PPD, as indicated by a baseline Hamilton Rating Scale for Depression (HAMD) score of 20 on the 17 items. The dosage was adjusted to reflect the third-trimester levels of allopregnanolone. The mean HAMD total scores decreased to values that are compatible with symptom remission. There were 14 documented adverse effects, and none of them were severe. Brexanolone showed activity in severe PPD and was reported to be well tolerated [59]. A Phase 2 trial confirmed the considerable improvement in postpartum depression HAM-D scores following brexanolone therapy [36]. In this investigation, 21 women participated in a double-blind, randomised, placebo-controlled experiment at four hospitals in the United States. Patients were randomised to receive intravenously administered placebo (n = 11) or brexanolone (n = 10) continuously for 60 h. Patients were then monitored for 30 d. The mean decrease in HAM-D total score from baseline in the brexanolone group was 21 points (SE 2.9), while it was 8.8 points (SE 2.8) in the placebo group (difference-12 2, 95% CI-20.77 to-3.67; p=0 0075; effect size 1). There were no fatalities, serious adverse events, or discontinuations as a result of adverse events in either group [36]. Two phase 3 double-blind, randomised, placebo-controlled trials were conducted in the USA at 30 clinical research facilities and specialised psychiatric units by Meltzer-Brody S *et al.* Patients in trials 1 and 2 were randomly assigned (1:1:1) to receive a single intravenous injection of either brexanolone 90 g/kg per hour (BRX90), brexanolone 60 g/kg per hour (BRX60), or a matching placebo for a duration of 60 h. In study 1, the least-squares (LS) mean reduction in HAM-D total score from baseline was 19 points (SE 1) in the BRX60 group and 17 points (SE 1) in the BRX90 group compared with 14 points (SE 1) in the placebo group (difference-5 points [95% CI-8.8 to-2]; p=0.0013 for the BRX60 group;-3 points [95% CI-6.9 to-05. At 60 h in Study 2, the LS mean reduction in HAM-D total score from baseline in the BRX90 group was 14.6 points (SE 0.8), compared to 12.1 points (SE 0.8) for the placebo group (difference-2.5 [95% CI-4.5 to-0.5, p=0.0160). Thus, it was determined that the administration of brexanolone injection for post-partum depression resulted in significant and clinically significant decreases in HAM-D total score at 60 h compared to placebo, with a quick onset of action and a long-lasting treatment response throughout the research period. [62]Cooper MC *et al.* compared the effectiveness of brexanolone injection with selective serotonin reuptake medications for treating postpartum depression using matching adjusted indirect comparisons (MAICs) and network meta-analyses. In comparison to SSRIs, MAICs displayed greater variations from the brexanolone baseline values across all time points. Brexanolone and SSRI differences (95% CIs) on the HAM-D were 12.79 (8.04-17.53) [day 3], 5.87 (-1.62 to 13.37) [week 4], and 0.97 (-6.35 to 8.30] [last observation]. The variations in CFB for the EPDS were 7.98 (5.32-10.64) on day 3, 6.35 (3.13-9.57) in week 4, and 4.05 (0.79-7.31) on the last observation. The MAICs show that BRX90 considerably enhances the HAM-D and EPDS results at day 3 in comparison to SSRIs. The absolute difference between SSRIs and

BRX90 for the EPDS and HAM-D outcomes decreased over time, but the MAICs still show that BRX90 generally provides equivalent or better results over time compared to SSRIs. [63] Brexanolone infusion's efficacy, tolerability, and safety in the treatment of postpartum depression were the subjects of a meta-analysis by Zheng W *et al.* (PPD). Brexanolone recipients who had PPD showed a significantly better response than those who got a placebo. Risk ratio (RR) = 1.34, 95% CI 1.03–1.73, indicating that the reaction started after 24 h, peaked at 36 h (RR = 1.51, 95% CI 1.06-2.13, P = 0.02), and persisted until day 7 (RR = 1.32, 95% CI 1.01–1.73). Similar results were observed in PPD patients treated with brexanolone, who experienced significantly longer remissions that peaked at 60 h (RR = 2.20, 95%CI 1.31-3.70) and persisted for 72 h (RR = 1.96, 95%CI 1.41-2.72). After receiving brexanolone infusions, the rate of discontinuation for any cause was significantly higher (RR = 2.68, 95%CI 1.35-5.32). Because of intolerance and adverse drug reactions, the discontinuation rates for the active medication and the placebo were comparable. The researchers came to the conclusion that a single brexanolone infusion for PPD seemed to have an ultra-rapid, up to one-week-long antidepressant effect. Brexanolone's therapeutic effects must be further investigated in long- and short-term RCTs [64]. The important clinical trials are summarized in table 1.

Table 1: Summary of important clinical trials on brexanolone

S. No.	Author/year	Status	Study participants/groups	Outcome parameters	Results
1	Kanes S *et al.*/2017 [55]	Phase II	(N= 4)	HAM-D score at start of study, at 60 h and at 84 h	Brexanolone was well tolerated and demonstrated activity in severe PPD
2	Kanes S *et al.*/2017 [36]	Phase II	(N=21) Brexanolone (n=10) and placebo (n=11)	Mean reduction of HAM-D score of Brexanolonevs placebo	When compared to placebo, Brexanolone infusion led to a significant and clinically significant decrease in total HAM-D total score
3	Meltzer-Brody S *et al.*/2018 [62]	Phase III	(N=138) Three groups to receive a single intravenous injection of either brexanolone 90 µg/kg per h, brexanolone 60 µg/kg per h, or matching placebo for 60 h	Mean reduction of HAM-D score of Brexanolonevs placebo	Compared to placebo, brexanolone injection for postpartum depression significantly and clinically meaningfully reduced the HAM-D total score at 60 h.
4	Cooper MC *et al.*/2019 [63]	Meta-analysis	26 studies were included	Indirect treatment comparisons (ITCs) of HAM-D and Edinburgh Postnatal Depression Scale (EPDS) outcomes between brexanolone and SSRIs	When compared with SSRIs, brexanolone showed larger differences in change from baseline for both patient and clinician-reported PPD outcomes and at all investigated time points between placebos
5	Zheng W *et al.*/2019 [64]	Meta-analysis	N = 267; 3 RCTs were included Brexanolone vs placebo	Antidepressant response and short-term (up to 72 h) remission, risk ratio	For PPD, a single brexanolone infusion appears to produce an ultra-rapid, up to one-week-long antidepressant effect.

Adverse effect profile

The most frequent side effects of the medication include somnolence, headaches, and dizziness. Continuous monitoring is required during the infusion period, with oxygen saturation levels being checked every two hours. If there is a sudden loss of consciousness or severe sedation, the infusion should be stopped [56]. After a dose stoppage, the patient often regains consciousness within 15 to 60 min, at which point the infusion can be resumed at the same dose or a lower one. Although *in vitro* studies have revealed that the CYP2C9 enzyme inhibits the action of drugs, this has not been proven in a clinical study setting. Other CNS depressants such as alcohol, opioids, benzodiazepines, and antidepressants should not be used concurrently and require special supervision. With the medicine, no evidence of tolerance or dependence has been found. It is preferable to alter the dosing schedule or stop taking the medication entirely if depression or suicidal thoughts deepen [65]. While breastfeeding mothers were required to stop during the majority of the brexanolone studies, a study of these mothers revealed a low relative infant dose (RID) of 1.3%, which is below the advised threshold of 10% RID. The guideline concludes by stating that the mother and doctor should discuss the decision to breastfeed [66]. Patients with mild to moderate renal impairment and moderate to severe hepatic impairment don't require any dosage adjustments. Sulfobutylether cyclodextrin (SBECD), a solubilizing chemical used in intravenous formulations, is contraindicated in patients with significant renal impairment because it tends to accumulate while being eliminated by the kidneys in normal individuals [56, 67].

Cost

The drawback of the medication is its price, which can limit its use. While generic SSRIs cost about $62.50 for 30 tablets, one continuous infusion is projected to cost roughly $34,000 [68]. Brexanolone, however, was found to be 58% more likely to be cost-effective at the $150,000 per QALY level when compared to SSRIs after consideration of the treatment, administration costs, and other medical costs. Brexanolone had an average quality-adjusted life year of 6.23 as opposed to SSRI's 5.979 QALYs [68].

CONCLUSION

In PPD, brexanolone provides rapid and effective alleviation from depressive symptoms. Due to logistical and practical issues that prevent its broad usage, brexanolone is only used in individuals with severe PPD. This medication is constrained by the need for hospitalisation, intravenous administration, danger of sleepiness, and loss of consciousness risks. Brexanolone has an intriguing potential to enhance maternal health throughout the postpartum period and has a favourable risk-benefit ratio when used to treat moderate-to-severe PPD. Family connections, child development, and public health in general may all benefit from effective PPD therapy. Research is currently being done to develop oral formulations in an effort to make effective PPD treatment more widely available.

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All authors have contributed equally

CONFLICT OF INTERESTS

Declared none

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