2021

Comparative Research of Effective Treatment Measures for Postpartum Depression

Aunica Novacek
University of North Dakota

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Department of Physician Assistant Studies, University of North Dakota School of Medicine & Health Sciences
Grand Forks, ND 58202-9037

Abstract

Postpartum depression is a mood disorder that includes depressive symptoms during the time period following childbirth. There are various possibilities for what may cause this disorder, but the drastic change in hormones after delivery can play a role. With the chance this disorder may be fatal to both the mother and child, an appropriate, effective, and safe treatment is necessary to control depressive symptoms. The standard, first-line pharmacotherapeutic option is a selective serotonin reuptake inhibitor (SSRI) antidepressant. SSRI antidepressants are well understood, but these medications may take time to become effective. Knowing this, medical professionals can find a more rapid option that would be appropriate; thus, hormone replacement therapy is an alternative. In this review, numerous scientific databases were evaluated, including PubMed, Cochrane, and DynaMed. Keywords and mesh terms were searched to obtain a total of 384 studies. After various exclusion criteria were evaluated, a final total of 19 research articles were included. The results of this literature review showed that both treatment options of SSRI antidepressants and hormone replacement therapy are effective, and various side effects, risks, and contraindications are present with both therapy options. Currently, Brexanolone, an endogenous hormone, is the only FDA-approved indicated medication for postpartum depression. Clinically, psychotherapy and SSRIs are used as first-line options. Further research is necessary to evaluate the effectiveness and possible adverse effects with all options of antidepressants, hormone replacement therapy, and the possibility of a bridge therapy to decrease depressive symptoms.

- Keywords: Postpartum depression, drug therapy, physiopathology, hormone replacement therapy, SSRIs, Brexanolone, safety, contraindications, and adverse events.

Introduction

- Postpartum depression affects about 6.5%-20% of all postpartum women and can be quite dangerous if unnoticed or untreated (Warren, Fedorowicz, & Ehrlich, 2018).
- The typical treatment for postpartum depression includes psychotherapy or counseling and first-line, pharmacotherapy of a selective serotonin reuptake inhibitor (SSRI) antidepressant.
- It is thought that hormone changes may impact this disorder; these changes include a decline in estrogen and progesterone following childbirth (Warren et al., 2018).
- With these hormone changes, it may be appropriate to use reproductive hormone replacement therapy as an alternative treatment.
- The purpose of this study is to compare the use of typical SSRI antidepressant medication and hormone replacement therapy safety, efficiency, and efficacy on postpartum depression symptoms to promote a healthier and happier experience for the mother, child, and family.

Statement of the Problem

- For new-onset, moderate-to-severe postpartum depression, SSRIs are the typical first-line therapy.
- According to Cooper, Kilvert, Hodgkins, Roskell, and Eldar-Lissai (2019), "current pharmacological treatments, including SSRIs, are associated with a slow rate of improvement (6-12 weeks), and there is a lack of reliable evidence to support the onset of efficacy occurring within the first week" (p. 2).
- Hormone replacement therapy is "well suited for postpartum depression because it occurs after 100-fold decreases in estradiol between late pregnancy and 48 hours postpartum" (Moses-Kolko, Berga, Kalro, Sit, & Wisner, 2009, p. 3).
- Further usage of hormone replacement therapy could include estrogen, progesterone, and even a new medication, Brexanolone, an FDA-approved endogenous hormone treatment for postpartum depression.
- Researching the different treatment options can help medical professionals understand what causes postpartum depression, leading to a more effective therapy regimen.

Research Questions

- In postpartum females, does the use of hormone replacement therapy compared to medication therapy using SSRI antidepressants decrease postpartum depression symptoms more effectively?
- In postpartum females, does the use of hormone replacement therapy compared to the use of SSRI antidepressants decrease or increase morbidity and mortality in the short and long-term therapy for postpartum depression?
- In postpartum females, does bridge treatment using hormone replacement until SSRI becomes clinically efficacious compared to a standardized treatment with either hormone replacement therapy or SSRIs improve safety and recovery speed of postpartum depression?

Postpartum depression: major depressive episodes with a perinatal onset as those beginning in either pregnancy or within the first four weeks postpartum (DSM-5)
(Schiller et al. 2014)

Literature Review

Hormone Changes in Postpartum Depression

•Schiller et al. (2014) found that the reproductive hormones control many aspects in the body including, "thyroid function, lactogenic function, hypothalamic-pituitary-adrenal (HPA) axis, and the immune system" (p. 5).

• Warren et al. (2018) found and understood that "reproductive hormones are involved in emotion processing, arousal, cognition, motivation, regulation of biological systems implicated by significant depression, and modulation of neurocircuitry in normal and abnormal affective states" (para. 13).

SSRI Treatment Effectiveness for Postpartum Depression

•Warren et al. (2018) evaluated numerous SSRIs. Results of one study showed when comparing SSRIs (sertraline, paroxetine) to placebo, SSRIs are associated with increased treatment response (risk ratio 1.43, 95% Cl (1.01-2.03), number needed to treat [NNT] 3-278 with treatment response in 36% of the placebo group) in which were persistent findings at 12 weeks postpartum.

Hormone Replacement Therapy Effectiveness for Postpartum Depression

•Dennis et al. (2008) found that at six weeks, progesterone treatment showed women who received a single dose of the synthetic progestogen were significantly more likely to report depressive symptoms using either self-reported (EPDS >11, relative risk (RR) 1.75, 95% confidence interval (CI), 1.12 to 2.72) or clinician-rated measures (MADRS >9, RR 1.74, [CI] (1.08 to 2.81)).

•For estrogen, at four weeks, the results showed a significant decrease in EPDS scores among women in the estrogen group compared to those who received a placebo (WMD -3.20, 95% CI (-5.97 to -0.43)). This was consistent at 18 weeks (Dennis et al., 2008)

•In evaluation of the new treatment Brexanolone, English et al. (2019) results showed all three studies included demonstrated statistically significantly mean reductions in baseline HAM-D total score at hour 60 for the BRX90 treatment arm compared to the placebo. Specifically, results showed mean reduction differences between BRX90 and the placebo treatment to be -12.2 (p=0.008), -3.7 (p=0.02) and -2.5 (p=0.02).

Safety of SSRIs and Hormone Replacement Therapy

•SSRI safety evaluation showed various contraindications and adverse effects of increased risk of suicide, neurological changes, arrythmias, gastrointestinal effects, or even serotonin syndrome (Heimberg & Ehrlich 2018).

•English et al. (2019) found that Brexanolone has a black box warning significant for suicidality, syncope, and loss of consciousness. Sedation related effects showed sedation (15%), dizziness (13.6%), fatigue (3.6%), loss of consciousness (4.3%), and amnesia (0.7%).

•Moses-Kolko et al. (2009) explained estrogen can cause numerous effects including hypertension, changes in vaginal secretions, and breast tenderness. There is also an increased risk for cancer, and clotting disorders, and decreased breastmilk production.

Comparative Research of Both Treatments in Postpartum Depression

•Kim et al. (2014) showed sertraline (an SSRI) is an efficacious option, finding between 50% to 67% of women respond to treatment at around six to eight weeks.

•The final understanding of Ng et al. (2010) showed that estrogen supplementation through transdermal patches or sublingual preparations produced rapid and significant decreases in depression severity, with an occasional adverse reaction.

•For SSRIs, the response and remission rates were quite variable and not shown to be as effective.

•Cooper et al. (2019) had strong statistical analyses showing greater effect with Brexanolone therapy compared to SSRIs at numerous time points. At all time points, SSRIs had smaller reductions in EPDS, and HAM-D compared with BRX90 (HAM-D: 0.97, [CI] (-6.35 to 8.30) [Bucher ITC] and 2.02, [CI] (-3.18 to 7.22) [NMA]; EPDS: 4.05, [CI] (0.79–7.31) [Bucher ITC] and 3.76, [CI] (0.62–6.90) [NMA]).

Bridge Therapy in Postpartum Depression

•Joffe and Cohen (1998) included analysis of an antidepressant with cotreatment with estrogen. This therapy showed improvement with antidepressant therapy but no additional effect with estrogen. Similar findings were found in Newport et al. (2002).

Discussion

In postpartum females, does the use of hormone replacement therapy compared to medication therapy using SSRI antidepressants decrease postpartum depression symptoms more effectively?.

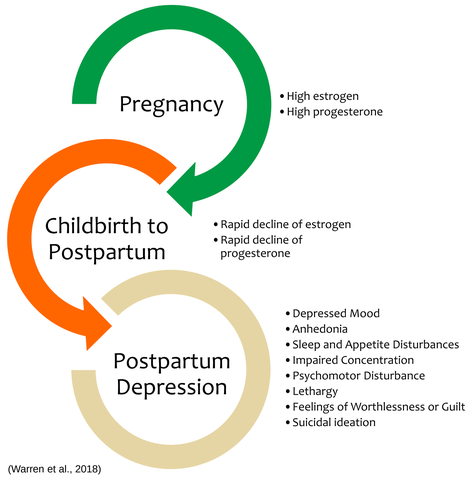
- The initial treatments for postpartum depression typically begins with psychotherapy or counseling for some women and antidepressant treatment for others (Clinical Key, 2020).
- Warren et al. (2018) compared typical antidepressants to placebo and cognitive behavioral therapy, showing effectiveness of treatment and increasing the evidence behind the effectiveness of SSRIs.
- Explained by English et al. (2019) and Warren et al. (2018), Brexanolone is a new and FDA approved medication for postpartum depression that significantly reduces depressive symptoms from a 60 hour, continuous IV infusion.
- Further research showed estrogen treatment, including transdermal and sublingual routes, significantly reduced postpartum depression symptoms (Moses-Kolko et al., 2009; Schiller et al., 2014; Dennis et al., 2008; Studd & Panay, 2009).
- However, Dennis et al. (2008) found that progesterone monotherapy increased depressive symptoms.
- Cohen et al. (2010) and Kim et al. (2014) explained that SSRI antidepressants are the superior therapy in the treatment of postpartum depression.
- Cooper et al. (2019) includes direct statistical analyses showing that Brexanolone hormone replacement is quicker, safer, and more effective compared to SSRIs.
- The remaining articles included agree that both medication options are effective therapies for postpartum depression.

In postpartum females, does the use of hormone replacement therapy compared to the use of SSRI antidepressants decrease or increase morbidity and mortality in the short and long-term therapy for postpartum depression?

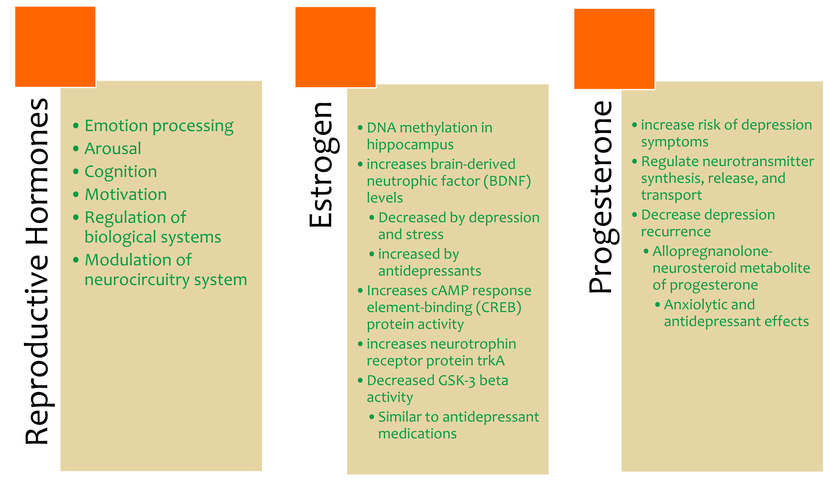
- Adverse effects of SSRIs range from minor symptoms of nausea and vomiting to significant adverse reactions such as loss of consciousness (Heimberg & Ehrlich, 2018; English et al., 2019).
- With SSRIs, there may be passing of these medications to infants with breastfeeding (Kramer et al., 2018).
- There is a known black box warning for all antidepressant medications for an increased risk of suicidal thoughts (Heimberg & Ehrlich, 2018).
- Hormone replacement therapy has increased risk of clotting disorder, thromboembolic events, and increased difficulty with breastfeeding due to decreased milk production (Moses-Kolko et al., 2009).

In postpartum females, does bridge treatment using hormone replacement until SSRI becomes clinically efficacious compared to a standardized treatment with either hormone replacement therapy or SSRIs improve safety and recovery speed of postpartum depression?

- With SSRIs taking time to become therapeutic, initial treatment with hormone replacement therapy and coadministration of antidepressant may be an effective option in the future.
- Joffe and Cohen (1998) found no additional improvement with the addition of estrogen to antidepressant therapy.
- Further research found there was limited safety and benefit of a co-treatment option (Newport et al., 2002).



(Warren et al., 2018)



(Schiller et al., 2014)

Applicability to Clinical Practice

- With the information included, medical providers can prescribe the most effective, efficient, and safe medication option to decrease postpartum depression symptoms based on medical research evidence and statistical analyses.
- This allows physician assistants and other medical professionals to understand postpartum depression, the possible etiology following childbirth, and adequate treatment options.
- For now, Brexanolone is the only FDA approved medication indicated for postpartum depression, but psychotherapy and antidepressants are often used clinically.
- Until further research is conducted, these options should be utilized, understood, and explained to the patients to make the best possible clinical decision for both mother and child.

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Acknowledgements

- I would like to thank my advisor, Russell Kauffman, PA-C, and my instructor, Daryl Sieg, PA-C, for their patience and guidance to mold my scholarly project into what it has become.
- Further gratitude is extended to my primary care preceptor, Dr. Jessica Simmons, for her insight into clinical applicability of my scholarly project research.
- I want to thank Tara Kern for her assistance in understanding statistical analyses present throughout the included research.
- Stacy Dahl and the University of North Dakota writing center helped edit and provide feedback with citations, sentence structure, and all aspects of my scholarly project.
- I would like to thank my classmates for continuous support and reassurance throughout this process.
- Finally, I would like to thank my family for the additional support, confidence, and always providing a bright side whenever necessary throughout my physician assistant journey.