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The Utility of Allopregnanolone as an Objective Screening Tool for Postpartum Depression: A Systematic Review

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ADMINISTRATIVE INFORMATION

Support - N/A.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 December 2023 and was last updated on 22 December 2023.

INTRODUCTION

Review question / Objective To identify the feasibility and accuracy of using serum ALLO levels as a screening tool during pregnancy to predict postpartum depression and anxiety risk.

Rationale 3α,5α-3-hydroxypregnan-20-one, or allopregnanolone (ALLO), is an endogenous metabolite of progesterone, and low levels of ALLO are currently being proposed in the etiology of PPD as well as other reproductive and non-reproductive mood disorders in both sexes. The allopregnanolone depression hypothesis is currently being illustrated by the recent Food and Drug Administration (FDA) approval of synthetic versions of allopregnanolone for the treatment of severe PPD. These new drugs are Brexanolone, which is a costly 60-hour inpatient infusion, and even more recently approved and Zuranolone, a once-a-day pill for 14 days. Both of these medications supplement allopregnanolone, thus is makes sense to ask if there is a correlation between laboratory levels and clinical status. Currently, there is no systematic review of the literature on the use of serum ALLO levels as a predictive and reliable measure of PPD risk in pregnant patients.

Condition being studied Postpartum depression (PPD) is estimated to affect one in ten mothers in the United States.1 Worldwide, the estimated prevalence rate of PPD is 17%.2 PPD is a common mood disorder that affects women at a pivotal time as they transition into their new role as mothers. The diagnosis of PPD is hard to make due to our limited understanding of its pathophysiology as well as the multitude of risk factors associated with this disorder. The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) does not explicitly classify PPD as a standalone diagnosis, instead,

PPD is defined as a major depressive episode that coincides with peripartum onset, meaning symptom occurrence during pregnancy or within four weeks of delivery.

METHODS

Search strategy A systematic literature review was done using PubMed and EBSCO. EBSCO services were used to search MEDLINE, Academic Search Premier, CINAHL Ultimate, and Cochrane Central Register of Controlled Trials. Grey literature was also searched using Medrxiv and Google Scholar. The following boolean/phrase search strategy was used with the following terms, ("postpartum depression" or "postnatal depression" or "ppd" or "pnd" or "post-partum depression" or "post-natal depression") AND ("allopregnanolone" OR "allo"). Databases were searched from inception through September 6th, 2023. This search strategy was developed with the assistance of the Sacred Heart University Health Sciences Librarian on August 31, 2023.

Participant or population Persons over the age of 18 who are pregnant or within one year of pregnancyPregnant persons.

Intervention Measurement of ALLO serum levels during pregnancy.

Comparator N/A.

Study designs to be included All study designs measuring serum ALLO in currently pregnant or postpartum patients.

Eligibility criteria Participants over the age of 18 who are pregnant or within one year of pregnancy, studies available in the English language, studies measuring serum ALLO in currently pregnant or postpartum patients, mood disorder outcomes measured with validated depression and anxiety inventory scales.

Information sources Pubmed, MEDLINE, Academic Search Premier, CINAHL Ultimate, and Cochrane Central Register of Controlled Trials. Grey literature was also searched using Medrxiv and Google Scholar.

Main outcome(s) Diagnoses of Postpartum Depression.

Quality assessment / Risk of bias analysis The quality of included studies were evaluated by two independent reviewers using the Newcastle-Ottawa Scale.

Strategy of data synthesis Authors plan to conduct qualitative synthesis for this systematic review.

Subgroup analysis Outcomes will be considered overall, but also will be assessed in two subgroups: Early Pregnancy (Trimester 1 and 2) and Late Pregnancy (Trimester 3).

Sensitivity analysis Meta-analysis not planned.

Language restriction English.

Country(ies) involved United States.

Keywords Allopregnanolone; Postpartum Depression; Screening.

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