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#### Review

## Clinical management of perinatal anxiety disorders: A systematic review



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#### ABSTRACT

*Background:* In the last few decades, there has been a growing interest in anxiety disorders (AnxD) in the perinatal period. Although AnxD are diagnosed in 4–39% of pregnant women and in up to 16% of women after delivery, evidence on their clinical management is limited.

Methods: A systematic review was conducted on pharmacological and non-pharmacological treatment of AnxD in the perinatal period. Relevant papers published from January 1st 2015 were identified searching the electronic databases MEDLINE, Embase, PsycINFO and the Cochrane Library.

Results: 18 articles met inclusion criteria. Selected studies supported the use of cognitive-behavioural therapy (CBT) for obsessive-compulsive disorder (OCD), panic disorder (PD) and specific phobia both in pregnancy and postpartum. Selective serotonin reuptake inhibitors (SSRIs) led to significant OCD and PD improvement both in pregnancy and postpartum with no side effects for the babies. In the largest clinical sample to date, 65% of postpartum patients who entered the open-label trial of fluvoxamine (up to 300 mg/day) experienced a 30% or greater decrease in the total score of the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS). During pregnancy, SSRIs and tricyclic antidepressants (TCAs) led to remission of panic symptoms and healthy outcomes for the babies.

Limitations: Study design, mostly case reports, and enrolment of subjects mainly from outpatient specialty units might have limited community-wide generalisability.

Conclusions: Keeping in mind the scantiness and heterogeneity of the available literature, the best interpretation of the available evidence appears to be that CBT should be the first treatment offered to pregnant and breastfeeding women with AnxD. However SSRIs can represent a first line treatment strategy, and not exclusively in cases where AnxD is refractory to CBT.

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#### 1. Introduction

Even though pregnancy is a period of emotional well-being for most women, one fourth of pregnant women are affected by a mental disorder, with one-twelfth experiencing one of these disorders for the first time (Vesga-Lopez et al., 2008). Over the last few decades, more attention has been focused on anxiety disorders (AnxD), which were more extensively investigated in antenatal period (Goodman and Chenausky, 2014) than in postpartum.

AnxD are diagnosed in 4–39% of pregnant women (Goodman and Chenausky, 2014) and prevalence rates are even higher if comorbid disorders are also considered (Marchesi et al., 2014).

Although prenatal AnxD increase the risk of post-partum depression (Goodman and Chenausky, 2014), their effects on obstetric outcomes are debated. Regarding neonatal/infant outcomes, a low brain-derived neurotrophic factor (BDNF) level in the blood cord; no heart rate response to the mother anxiety; increase cortisol reactivity to stress (not replicated in other two studies) and early attention dysfunction, were found in infants of mothers with prenatal AnxD (Goodman and Chenausky, 2014).

With regard to the post-partum period, AnxD are diagnosed in 16% of women (Vesga-Lopez et al., 2008; Austin et al., 2010; Wenzel et al., 2005; Reck et al., 2008) and up to 50% if comorbid major depression is also taken into account (Austin et al., 2010; Wenzel et al., 2005).

Untreated AnxD increase the risk of postpartum depression (Prenoveau et al., 2013) and have been associated with maternal low self-confidence (Zietlow et al., 2014); early complications in the offspring (e.g. behavioural inhibition, mother-infant interaction problems, insecure attachment), and later adverse child development (Glasheen et al., 2010).

Recent reviews have mostly focused on prevalence rates and clinical presentation of AnxD in pregnant and postpartum women (Goodman and Chenausky, 2014; Ross and McLean, 2006). This is the first systematic review on pharmacological and non-pharmacological treatment approaches of perinatal AnxD.

#### 1.1. Aim of the study

We systematically reviewed the available literature on the treatment of perinatal AnxD and we provide recommendations for clinical management and future research.

#### 2. Materials and methods

We conducted this review according to the methods recommended by the Cochrane Collaboration and documented the process and results in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Liberati et al., 2009; Higgins and Green, 2011).

#### 2.1. Information sources and search strategy

Studies were identified by searching the electronic databases MEDLINE, Embase, PsycINFO, and the Cochrane Library. We combined the search strategy of free text terms and exploded MESH headings for the topic of pharmacological and non-pharmacological treatment of AnxD in perinatal period combined as following: (((((pregnan\*) OR perinatal) OR breastfeeding[MeSH Terms])) AND ((anxiety[MeSH Terms]) OR anxiety disorder[MeSH Terms])) AND (((treatment) OR therap\*) OR pharmacotherap\*). The strategy was first developed in MEDLINE and then adapted for use in the other databases (Appendix A). Studies published in English through January 1st, 2015 were included. In addition, further studies were retrieved from the reference listings of relevant articles and consultation with experts in the field.

#### 2.2. Inclusion criteria

#### 2.2.1. Study population and study design

We considered studies that included women with AnxD during perinatal period. All anxiety disorders were considered if diagnostic criteria used were specified. Studies enroling women with OCD were also considered, even though OCD was moved out from AnxD in the DSM5. However, we chose to include OCD in the review because the sequential order of the DSM5 chapters on AnxD and OCD and related disorders, reflects "the close relationship" among them (American Psychiatric Association, 2013). Further, the first-choice treatment of OCD is similar to those of AnxD and therefore the clinical management of OCD during the perinatal period is largely overlapping to that of AnxD.

Participants younger than 18 years of age were also considered. Among hospital-based studies, inpatients, day-hospital and outpatient subjects were included while emergency care records were excluded as being considered non-representative. All experimental and observational study designs were included. Narrative and systematic reviews, letters to the editor and book chapters were excluded.

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