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Review Article

Perinatal SSRI Antidepressant Use: The Ongoing Ethical Dilemma and Continued Need for Practice Recommendations

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Abstract

There is conflicting information regarding the risks and consequences of fetal exposure to antidepressant medications, specifically SSRIs. Providing pregnant women with accurate information regarding the risks and benefits associated with antidepressants is a critical public health issue. Unfortunately, clinical practice guidelines vary and sometimes offer contradictory recommendations regarding pharmacological treatment during pregnancy, because not enough is known about the effects of antidepressant medication on the fetus. Not surprisingly, both pregnant women and healthcare providers such as psychiatrists, psychiatric mental health nurses, and physicians express feelings of conflict when considering prescribing/taking SSRI's. Current guidelines also do not provide guidance on presenting adequate informed consent for this potential conflict. This paper explores the literature on fetal harms and maternal-fetal conflict that are associated with antidepressant medication used in pregnancy and discuss the need for enhanced collaborative care. It also offers specific recommendations for addressing the ethical challenges that arise when pregnant women are considering antidepressant treatment.

Keywords: Pharmacological treatment; Depression during pregnancy; Ethical dilemmas

Introduction

The perinatal period can be an emotionally challenging time for many women [1-3] and, recently, the global COVID pandemic has certainly added greatly to the overall emotional distress [4-6]. Mental health disorders during the perinatal period are common. Studies have indicated that the prevalence of depression during pregnancy ranges from 7% to 25% [7] with an overall rate of 15%.

The last two decades have brought the use of selective serotonin uptake inhibitors (SSRIs) to the forefront of conventional treatment. This has become the frequent choice of practitioners to prescribe to their patients upon a depression diagnosis, regardless of the severity of the illness [8,9]. Yet, concurrent research has also demonstrated that SSRI's cross the placenta and can cause damage to the fetus' developing nervous and cardiac systems [10,11]. To this end, more and more national and international authorities have coalesced Clinical Practice Guidelines (CPGs) to address this possible conflict.

An international review on current CPGs regarding the treatment of perinatal depressive symptoms and perinatal use of antidepressants recommend psychotherapy as an initial treatment for mild to moderate depression and for antidepressants to be prescribed in cases of severe depression, with a preference for the SSRI sertraline [12]. More complicated is the management of continued antidepressant use for a woman who was prescribed an SSRI and is now debating its continuation during pregnancy. Four CPGs advise continuing antidepressants (the Danish Psychiatric Society; the German Society for Psychiatry and Psychotherapy, Psychosomatics and Neurology (DGPPN); the Nordic Federation of Societies of Obstetrics and Gynaecology (NFOG); and the Scottish Intercollegiate Guidelines Network (SIGN), even though there is a lack of evidence supporting this recommendation. Another five CPGs do not specifically advise or discourage continuation (the American Psychiatric Association (APA), the British Columbia (BC); the National Institute for Health and Care Excellence (NICE); the Dutch Society of Obstetrics and Gynaecology (NVOG); and the Ministry of Health, Singapore (MOH)) [12]. These CPGs are in place because the current consensus states that not enough is known about the effects of antidepressant medication on the fetus and sufficient research has determined some level of deleterious effect on the fetus, therefore recommending an individualized approach [10,11-15] and cautioning against prescribing on the outset [16].

Despite being codified in CPGs and the limitations of evidence on the risks and benefits of Antidepressant Medication (ADM) during pregnancy, some medical specialists are not using this stepped approach. Research has also found that many physicians, especially family practitioners and gynecologists, may prescribe antidepressants as a first-line course of treatment for even mild depression and that, frequently, medication is prescribed instead of investigating possible more suitable psychosocial interventions [8,9,17-19]. Significant portion of women are being prescribed and are taking SSRIs during pregnancy. One large study in the United showed that the proportion of pregnancies with antidepressant use increased from 5.7% in 1999 to 13.4% in 2003 [20]. Another study in the United Kingdom found that 10% of women treated before pregnancy continued their use of

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antidepressants at the start of the third trimester [21].

Women and providers expressed frustration that sometimes medication is offered/prescribed without much discussion and without delving into detail about the patient experience [22]. Not surprisingly, both healthcare providers (e.g., psychiatrists, psychiatric mental health nurses, and physicians) and pregnant women express feelings of conflict when considering prescribing/taking SSRIs [22-24]. This paper explores the complex maternal-fetal conflict that arises when considering pharmacological treatment for depression during pregnancy and discusses the need for enhanced collaborative care. It offers specific recommendations for addressing the ethical challenges that arise during the perinatal period when women are considering antidepressant treatment.

Potential impact of SSRIs during pregnancy *vs*. untreated depression

There has been extensive research on the possible physical effects of maternal SSRI usage on fetal development [10,11,13,14,25]. SSRI use has been associated with an increased risk of congenital malformations [16,26]. possibly causing pulmonary hypertension, poor neonatal adaptation syndrome, and delayed neurological development). [11,13,15]. Fear of possible adverse effects on the developing baby is one of the contributing factors for a woman's decision to discontinue her medication when planning to become or being pregnant [21,23,27,28]. Additional concerns that women expressed included strong maternal feelings of shame, guilt, and confusion about prenatal use of ADMs and general discontent with using and potentially becoming dependent on ADMs [22-24].

There are also significant risks to the fetus posed by not treating maternal depression adequately during pregnancy, including miscarriage, preeclampsia, preterm birth, and low birth weight [29-32]. Depression during pregnancy is also linked with an increased risk for emotional, behavioral, and cognitive difficulties, and psychopathology in the child [33,34]. Additionally, untreated depression can lead to long term disability and has been associated with an increased risk of maternal suicide [16,35].

There is a need to consider the potential impact of antidepressant medication on fetal development against the severity of illness for the mother and the risk of untreated depression [36]. In general, it does seem that many pregnant women express a desire to seek out nonpharmacological resources before using medication to treat their depression [5,37-40]. When the intervention needs to be 'stepped up',women and their providers are faced with the decision to start or continue on an antidepressant medication, seemingly without guidance on how to make the decision [9,41,42].

Ethical dilemmas and maternal-fetal conflict

Pregnancy creates a unique circumstance in medical ethics because the fetus can be accessed only through intervention to the pregnant woman and, at times, conflict may arise between fetal and maternal interests [43]. Ethical dilemmas such as maternal-fetal conflict arise when providers face a situation in which respecting women's autonomy might conflict with providers' beliefs about what is best for the fetus. In these cases, providers should ask themselves 'who is the patient: the woman, the unborn fetus, or both?' [44]. Ethical decision-making in the field of perinatal health must include the process of informed consent, respect for the autonomy of the pregnant woman, fetal safety, and maternal risk. These issues are emotionally laden as they involve concurrently protecting the rights of women as well as the best interests of the fetus [43].

Perinatal care providers may face this conflict when examining the possible maternal risks and benefits versus fetal risks and benefits associated with the use of antidepressant medication during pregnancy [45]. Due to the conflicting nature of the research, it may be almost impossible for a pregnant woman to have a clear understanding of the benefits and harms of antidepressant medication [46] and she will look to her healthcare provider to resolve the issue for her. When a maternal-fetal conflict arises, the attending physician may try to respect the woman's autonomy yet can unintentionally impose a medical decision on the mother [46].

If a pregnant woman refuses treatment, maternal-fetal conflict may arise between her right to make medical decisions that affect her health and fetal health, and the government's position that it has the right to intervene on behalf of the fetus [46]. These challenges increase in complexity when clinicians must consider both the needs of the pregnant woman and her fetus as well as the effects of depression on her decision-making capacity. Providing pregnant women with accurate and balanced information is a critical public health issue [47].

As researchers will never be able to conduct a truly randomized control trial on pregnant women and SSRI usage because of the obvious ethical dilemmas, nor fully control for possible confounders such as etiology or type of depression [48], defining the true benefit of SSRI usage on reducing the risk of unmedicated perinatal depression may never be able to be measured. Therefore, choices about whether or not to utilize these medications will rely solely on the patient-provider decision making dyad.

Informed decision making and shared decision making

Maternal-fetal conflict may be present in the decision-making process when SSRIs are recommended for treatment of moderate to severe depression in pregnancy. Depressed women report significant decisional conflict concerning their treatment [23,24]. Women who express uncertainty about which treatment path is best for them may not receive adequate treatment and have reported higher levels of depression [23]. In a qualitative study, all of the women participants were aware that medication could have adverse effects and were most worried about how unknown risks of the antidepressants could affect the fetus. They all wanted to hear about possible negative side effects and reported relying first and foremost on gynecologists for reliable information and assistance with decision making [49]. One way to cope with the conflict is to use the Shared Decision-Making (SDM) approach.

SDM is a widely promoted ethical approach to clinical practice. This approach may strengthen patient-provider relationships and can be used throughout the evolving treatment process, from the beginning of treatment for psychiatric recovery and rehabilitation [50]. SDM assumes that both the providers and the patient have valuable knowledge to offer; physicians bring professional and medical expertise to the conversation, while clients bring their lived experiences and insights regarding the effectiveness of the care they

have received. In this way, the practitioner and patient exchange knowledge, deliberations, and concerns and strive to reach a common agreement regarding treatment options [51].

For suitable decision-making, the provider should take into consideration the psychiatric history and use of antidepressant medications, current psychiatric symptoms, previous attempts of tapering medication, availability of alternative treatment options such as preventive psychotherapy, and the presence of a social support network [12]. Few studies have examined the actual decision-making process between provider and patient, or provider beliefs and practices regarding SSRI prescription during pregnancy [51-53]. Without this information, clinicians have little guidance on how to enhance collaborative care and the informed consent process.

Increasing clients' knowledge of treatment options, helping clients clarify their values and preferences regarding different treatments, outcomes, and treatment risks, and providing guidance can significantly improve the decision-making process [51-53]. An informed, guided decision process using decision aids reduces anxiety and increases patient confidence and quality of healthcare [54]. It has been shown that SDM interventions also improve patient satisfaction without increasing consultation time [55].

Conclusions and Recommendations for Enhancing SDM

Recommended clinical practice regarding the perinatal use of SSRIs and proper prescription patterns remain unclear, thus complicating decision-making for both mothers and medical providers.

Based on the review, the recommendations are:

1. Incorporating SDM when communicating with pregnant women diagnosed with mild, moderate or severe depression, as well as improved support and guidance for clinicians who provide care for these clients [51-54]. Nurses and providers can support their clients using SDM methods and encourage clients to take an active role in choosing their treatment [56]. Transparent sharing of information and clear communication are essential to establish treatment decisions that support clients in their personal goals. Psychiatric nurses play a vital role. As they engage with clients during assessments, one-on-one counseling, and coping skills education within the supportive structure of the milieu; nurses continuously assess treatment effectiveness and medication side effects. Because nurses are the most trusted health care professionals, skill and proficiency at soliciting patients' values and preferences for their plan of care are essential. Psychiatric nurses are in a pivotal position to educate patients about the use of SDM tools with their prescribing clinician, helping the patient select targeted psychosocial interventions or/and choose a medication that best fits their lifestyle [56]. Based on the current state of the evidence, is to follow the ACOG's guidelines and address each situation individually about if, and when, to prescribe, while also employing SDM techniques.Women should be offered comprehensive mental health services at the time of diagnosis or treatment instead of, or in addition to, medication. Interventions such as psychotherapy [57] and cognitive behavior therapy [58,59] have been found effective in reducing depressive symptoms, yet many women report that they were not offered or were not accessible during care [60,61].

2. The healthcare provider should be encouraged to involve a psychiatrist or other mental health professional in order to ensure accurate information and proper treatment are being offered to the mother. Surprisingly, the majority of physicians who prescribe antidepressants are general practitioners or gynecologists, and this may affect the SDM process [62]. Gynecologists may not have sufficient education in the field to be able to adequately assist pregnant women with these decisions [63]. Integrative perinatal depression care in obstetric settings does exist, but they have yet to be considered as part of regular gynecology clinic protocol [64]. The woman's obstetrician or family doctor should have the option to collaborate with a multidisciplinary team, including a psychiatrist and nurses, to discuss if medication is warranted, what other options are available, and if the woman is simultaneously receiving mental health care [16]. While it is true that large-scale, community-based interventions have demonstrated that collaborative care is desired by both providers and clients, and provides effective treatment [64-66], these multidisciplinary treatment options do not yet exist on a wide enough scale to have a true impact on the treatment of women with depression during pregnancy [67].

3. Qualitative studies of both provider and maternal attitudes toward medication, depression diagnosis, and treatment plans should be conducted to supplement understanding of the women and providers' perspectives regarding pharmacological treatment. More must be learned about physician adherence to current guidelines [68] and risk perception of antidepressant use during pregnancy [69]. Also, quantitative studies involving specialist and general practitioner prescription patterns [69], women's actual compliance with ADM treatment, and physician adherence to current CPGs [68] should be initiated on a larger scale, in order to better understand if there is a true gap between clinical CPGs and practice.

In conclusion, SSRIs have increasingly been prescribed to women to treat depression. Increased usage during pregnancy has led to the understanding that these medications could harm the fetus, which, in turn, led to the creation of CPGs to assist clinicians and women decide what treatment plan to pursue. Despite the research on both the physical effects of SSRIs on the fetus and the universal agreement that pregnant women diagnosed with depression must receive concurrent mental health services in addition to or instead of medication, there is a gap between medical consensus and actual practice [23,68]. Little is known about how perinatal women suffering from depression and their providers consider decisions regarding the use of antidepressants. In order to address the ethical dilemmas that arise because of possible maternal-fetal conflict, additional emphasis should be placed on health care provider education about perinatal SSRI use, increased access to mental health professionals for women during pregnancy, and the incorporation of SDM tools regarding SSRI use into gynecological practice. It is important to improve women's health and health care during pregnancy with a focus on SDM methods [70-82].

Declaration

Author Agreement Statement: I the undersigned declare that

this manuscript is original, has not been published before and is not currently being considered for publication elsewhere.

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