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SSRI Saftey During Pregnancy

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SSRI SAFETY DURING PREGNANCY

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Abstract

Depression is one of the most common disorders in our country today. The most frequently used treatment for depression is the antidepressant drug class, selective serotonin reuptake inhibitors (SSRIs). Due to a higher incidence of depression during pregnancy, researchers have been meticulously trying to determine the risks and benefits of SSRI use and risks of depression to the mother and her fetus. The purpose of this project is to provide healthcare providers with current evidence about SSRI use during pregnancy. A brochure was presented to healthcare providers which addressed the risks and benefits of SSRI use and the risks of depression during pregnancy. The knowledge of current data on SSRIs safety during pregnancy will allow providers to be able to make an informed decision and provide education to their patients on the use of antidepressants during pregnancy.

Introduction

Depression is a debilitating disorder that impacts 25% of women to some degree during the course of their life (American Pregnancy Association, 2011). The classification of depression consists of a person exhibiting depressive symptoms for at least two weeks. These symptoms include sadness, mood swings, difficulty concentrating, change in sleep pattern, change in usual energy or motivation, no interest in usual activities, anxiety, crying often, feeling worthless or hopeless, eating too much or too little, and thoughts of suicide or death. There is not one particular cause to depression, although there is some factors that can potentiate symptoms. These factors include genetics, possible change in structure or chemistry of brain, increased stress, and hormone changes (U.S. Department of Health and Human Services, 2009).

At some point during their pregnancy, 23% of women can potentially suffer from depression (American Pregnancy Association, 2011). Depressive symptoms can mimic various hormonal changes during pregnancy, such as a decrease in appetite or energy level. This assumption can potentially be reason for delay in initiating treatment and lack of diagnosis by providers (American Pregnancy Association, 2011).

As with any disorder, there are factors that can potentiate its symptoms. For depression during pregnancy, these factors include relationship troubles, personal or family history of depression, history of infertility or miscarriage, stressful life occurrence, pregnancy complications, and past abuse or trauma. Depression during pregnancy can cause a woman to not take proper care of herself which can lead to inadequate nutrition, prenatal care, and an increase in the use of alcohol, tobacco, and drugs. This can further increase stress and have adverse effects on the fetus. These symptoms can potentially cause low birth weight, premature

birth, and development delays as well as pregnancy and delivery difficulties (American Pregnancy Association, 2011).

One of the most common pharmacological treatment options for depression is the use of selective serotonin reuptake inhibitor (SSRI) medications. In recent years, their use during pregnancy has been controversial due to their unknown teratogenic effects. As with every medication, the benefits and risks should be considered before prescribing or consuming. When an expectant mother exhibits depressive symptoms, there is potential stress on her unborn baby. To prevent or alleviate these symptoms, the use of SSRIs may be warranted. SSRI medications cross the placenta, and therefore have an effect on the fetus. Although exact adverse effects to the fetus are unknown, some research has linked side effects such as cardiac abnormalities, withdrawal symptoms (such as tremor, restlessness, high muscle tone, and abnormal crying), and developmental problems or delays (MGH Center for Women's Mental Health, 2007).

Due to the controversial use of SSRIs during pregnancy, the positive indications should be compared with the adverse effects. The consequences of not treating maternal depression needs to be compared with the SSRIs potential effects on the neonate's health when determining if their use during pregnancy is warranted. A decision between the provider and patient needs to be made with the health of mother and fetus at upmost importance. The risks and benefits of SSRI use during pregnancy as well as current clinical recommendations will be addressed in this paper in order to provide a resource for providers and women of childbearing age. This will ultimately allow expectant mothers to make an informed decision on SSRI use during pregnancy.

Purpose

The purpose of this paper is to provide a resource for providers of women of childbearing age that outlines the benefits and risks of SSRI use during pregnancy. The ultimate goal is to

help provide current, evidence-based care during pregnancy. A number of studies evaluate how depression and SSRI use can affect the mother and fetus. The research will be presented in order to help provide the tools necessary to have a balanced approach to care for depression during pregnancy.

Significance

A number of previous studies have investigated the benefits versus risks of SSRI use during pregnancy. The possible side effects to the fetus versus relapse of the mother's depression are at stake. Potential adverse effects to the fetus and neonate due to SSRI exposure or due to maternal depression needs to be explored to determine the best options. Previous studies have found a connection between relapse of maternal depression and adverse effects to the neonate. Some studies have found potential adverse effects to the neonate due to SSRI exposure to the fetus.

Expectant mothers and all women of childbearing age need to have accurate data regarding the effects SSRI use and untreated depression in order to make an informed decision about their health and the health of their unborn child. Depressive symptoms can put stress on the fetus and SSRI use may have possible risks to the baby's health as well. It is very important to assure there is a balanced approach to depression treatment during pregnancy.

Due to constant changes in our world today as well as new research and developments in the medical field, providers need the most current data available. With the data provided from this project, providers will be able to educate their patients with the most up to date information and better provide treatment options for patients with depression. Patients essentially put their life in the hands of their provider, which is why they deserve to have the most current information about their condition and possible treatments. Since each patient ultimately has the

choice to follow their provider's recommendations, patients need to know risks and benefits so an informed decision can be made.

Due to a number of limitations and gaps in research, the American College of Obstetricians and Gynecologists (ACOG) and the American Psychiatric Association (APA) have formulated current recommendations for providers on treatment options for depression while pregnant. Since there are risks (as described previously) to both having depression and taking antidepressant medication while pregnant, ACOG and APA have put together an evidence based approach to treating depression in pregnant women and women of childbearing age while keeping the benefits and risks in mind (Yonkers et al, 2009). These current recommendations are discussed later in this paper.

Theoretical Framework

Ernestine Wiedenbach's prescriptive theory provides a great framework for this project. Her theory relates to "the helping art of clinical nursing" (Current Nursing, 2012). Wiedenbach felt there were four key components to nursing: philosophy, purpose, practice, and art.

She describes these components as:

1) Philosophy: the nurse's approach and confidence to life and how they used it.

2) Purpose: what nurse wants to get done by keeping the patient as the main focus

3) Practice: the nurse's visible encounters, which are influenced by her confidence and considerations in how she treats her patient with the help they need.

4) Art: be able to recognize the patient's request so that a plan can be made to help the patient. The nurse also needs to know how to avoid problems that may occur in the future. (Current Nursing, 2012)

The philosophy of this review in regards to Wiedenbach's theory is to provide current, evidenced-based research to providers so they are able to treat depression in pregnant patients with confidence. The purpose is that patients who are suffering from depression need proper treatment. With pregnancy, treatment options can become an issue, as they are not only looking out for their best interest, but also the best interest of their unborn child. Practice involves the education and treatment options the provider gives to the patient with the best interest of their well-being and their child's in mind. Art has to do with being able to notice the symptoms the patient is having and knowing when to start talking about treatment options. Complications can occur with untreated depression and patients need to know what treatment is available as well as the benefits and risks.

Process

The target audience of this project is women of childbearing age, pregnant women, and providers who see women of childbearing age. With this in mind, a search was performed using the UND Harley French Library website. The following databases were used: CINAHL, PubMed, National Institute of Mental Health (NIMH), Medscape, Physicians Weekly, American Congress of Obstetrician and Gynecologists (ACOG), and American Psychiatric Association (APA). The key words used in the search were: pregnancy, in utero, SSRI safety, SSRI benefits, SSRI use, birth defects, preterm birth, depression, depression prevalence, depression statistics, antepartum depression, and treatment. The searches were limited in years from 2006 to 2012, although a couple studies used were from earlier years. All searches were limited to full text articles and in the English language. This review includes an analysis of fifteen articles. There were also other studies, literature reviews, and reputable websites used for facts and as supporting agents throughout this paper.

The articles were used to form a literature review that addresses the risks and benefits of SSRI use during pregnancy. From this research, an educational brochure was created to educate healthcare providers who care for women of childbearing age and pregnant women so they are able to make an informed decision regarding the use of SSRIs during pregnancy. The brochure was given to family practice, internal medicine, and OB-GYN providers. Providers were given time to evaluate the brochure and share with appropriate patients. The providers were contacted later to determine the worthiness of the brochure for them in their practice. They were asked how the brochure benefited their practice and patients, how patients reacted to the information, what additional information was needed, and what was learned from the information given to them.

Literature Review

View of Problem

The main purpose of the studies reviewed revolves around SSRI exposure and/or depression during pregnancy. There were a number of different views regarding SSRI use during pregnancy studied. Majority of the studies compared potential adverse fetal or neonatal outcomes due to exposure to SSRIs and depression, depression without SSRI use, and no depression diagnosis without uses of SSRIs. Four studies investigated the risk of preterm birth associated with maternal depression and SSRI exposure. Three studies evaluated pregnancy and obstetric outcomes after SSRI exposure. Two studies examined congenital malformations after SSRI exposure. One study compared the effects of SSRI use versus depression without pharmacological treatment. Other topics studied in relation to SSRI exposure and/or maternal depression without treatment were physical anomalies, infant weight at birth, neonatal

adaptation, temperament, and outcomes, fetal safety, bone mineral density, fetal neurobehavioral development, maternal weight gain, and preeclampsia.

Clinical Guidelines

A number of studies have aimed to determine the benefits versus risks of SSRI use during pregnancy, however there are no clear established guidelines today. The American College of Obstetricians and Gynecologists and the American Psychiatric Association have each concluded that the use of SSRIs during pregnancy should be determined on a case by case basis to prevent major depression symptoms in the mother. Recent data shows the overall risk of SSRI use is minimal and there are potential adverse effects to the fetus and mother when depression is uncontrolled. Due to this research, if depression is not controlled and the risk to the fetus is very low, medication can be used (Yonkers et al., 2009).

Any suicidal or acute psychotic patient should be referred to psychiatry for further evaluation. Whether a patient is pregnant or is planning to become pregnant and she has moderate to severe symptoms, Yonkers et al. (2009) states providers should strongly recommend antidepressant treatment. If a patient has mild to no symptoms for at least six month, they can decrease or taper and discontinue their medication. However, if the patient has severe, recurrent depression, psychosis, bipolar disorder, or a history of suicide attempt; the patient should not discontinue their medication. The use of psychotherapy has also been beneficial in treating depression, alone or with medication.

One SSRI medication, paroxetine (Paxil), has been found to have more adverse effects than other SSRIs. Researchers have found a higher incidence of cardiac defects in newborns when exposed to paroxetine during the first trimester of pregnancy. Even though the data from previous studies is not strong, the US Food and Drug Administration has classified paroxetine as

class D. A class D pregnancy category means there is evidence the medication has fetal risks and should only be used in life threatening emergencies (Yonkers, et al., 2009).

Relevant Characteristics

There were a number of similar characteristics among the studies. The three main points researched were SSRIs, newborns, and pregnant women. To do with SSRIs, there were seven studies that disclosed the type (Colvin, Slack-Smith, Stanley, & Bower, 2011; Kornum, Nielsen, Pedersen, Mortensen, & Norgaard, 2010; Kulin et al., 1998; Mulder, Ververs, Heus, & Visser, 2011; Pedersen, Henriksen, Vestergaard, Olsen, & Bech, 2009; Roca et al., 2011; Suri et al., 2007), six studies that disclosed the dose (Dubnov-Raz, Hemila, Vurembrand, Kuint, & Maayan-Metzger, 2011; Kornum et al., 2010; Kulin et al., 1998; Mulder et al., 2011; Roca et al., 2011; Suri et al., 2007), and three studies the disclosed the duration (Dubnov-Raz et al., 2011; Mulder et al., 2011; Roca et al., 2011).

A number of studies looked at different characteristics of the newborn. The infant's weight at birth (Colvin et al., 2011; Dubnov-Raz et al., 2011; Kornum et al., 2010; Lund, Pedersen, & Henriksen, 2009; Oberlander, Warburton, Misri, Aghajanian, & Hertzman, 2006; Pedersen et al., 2009; Roca et al., 2011; Wisner et al., 2009; Suri et al., 2007) and gestation age (Dubnov-Raz et al., 2011; Huot, Brennan, Stowe, Plotsky, & Walker, 2004; Kornum et al., 2010; Li, Liu, Odouli, 2009; Lund et al., 2009; Oberlander et al., 2006; Pedersen et al., 2009; Roca et al., 2011; Suri et al., 2007) were compared in nine of the fifteen studies. Eight studies indicated if an infant was born with a malformation or birth defects (Colvin et al., 2011; Dubnov-Raz et al., 2011; Kornum et al., 2010; Lund et al., 2009; Mulder et al., 2011; Pedersen et al., 2009; Roca et al., 2011; Wisner et al., 2009). Six studies compared the infant's APGAR score at birth (Colvin et al., 2011; Dubnov-Raz et al., 2011; Lund et al., 2009; Roca et al., 2011; Wisner et al.,

2009; Suri et al., 2007) and four studies looked at the infants length at birth (Colvin et al., 2011; Dubnov-Raz et al., 2011; Lund et al., 2009; Wisner et al., 2009) and if the infant required a hospital stay longer than three days, NICU admission, or special care nursery admission (Lund et al., 2009; Oberlander et al., 2006; Wisner et al., 2009; Suri et al., 2007). Three studies evaluated the newborn's head circumference (Dubnov-Raz et al., 2011; Lund et al., 2009; Wisner et al., 2009), gender (Dubnov-Raz et al., 2011; Huot et al., 2004; Pedersen et al., 2009), and delivery mode (Dubnov-Raz et al., 2011; Roca et al., 2011; Wisner et al., 2009). A few more newborn characteristics included in some of the studies' data were fetal complications, respiratory distress, jaundice, convulsions, and feeding difficulty.

Every study compared at least a few maternal characteristics within their data. All but one study (Huot et al., 2004) assessed maternal smoking, alcohol, and/or drug use during pregnancy. All but one study (Kulin et al., 1998) evaluated maternal age. Pregnancy and delivery course and/or past medical history was included in data of all but three studies (Dubnov-Raz et al., 2011; Kurki, Hiilesmaa, Raitasalo, Mattila, & Ylikorkala, 2000; Latendresse & Ruiz, 2011). Maternal characteristics in a few of the studies included other prescriptions taken during pregnancy, body mass index, weight, marital status, income, educational level, race, environmental toxin exposure, sleep patterns, physical activity, nutrition, and domestic violence.

Study Results

Each study assessed depression and/or SSRI use of pregnant women. There were a number of similar findings between studies however there were some important differences noted such as neonatal malformations, APGAR scores at birth, and head circumference (Colvin et al., 2011; Dubnov-Raz et al., 2011; Kornum et al., 2010; Pedersen et al., 2009; Wisner et al., 2009). The studies' objectives varied some but the main focus was neonatal and maternal

outcomes compared with maternal SSRI use and depression however there were more studies that addressed neonatal outcomes versus maternal outcomes.

One of the most common adverse effects of SSRIs studied was preterm birth. Multiple articles found SSRI exposure to increase the risk of preterm birth (Colvin et al., 2011; Kornum et al., 2010; Latendresse & Ruiz, 2011; Lund et al., 2009; Mulder et al., 2011; Oberlander et al., 2006; Roca et al., 2011; Wisner et al., 2009; Suri et al., 2007), but the sample size of Latendresse and Ruiz (2011), Roca et al. (2011), and Suri et al. (2007) was small which could affect the study's reliability. Latendresse and Ruiz (2011) detected a connection between high corticotropin-releasing hormone (CRH) levels and preterm birth; however, there was no association between CRH levels and maternal SSRI use and the study's sample size was low which potentially affects the data's reliability. A connection between increased preterm birth and depression was found as well (Li et al., 2009; Wisner et al., 2009). Li et al. (2009) revealed an association between preterm births and depression with maternal obesity, increased stress, low education level, and history of infertility as well as social and reproductive risk factors.

Neonatal malformation and birth defects is a common concern with any medication during pregnancy. However, among all of the studies that analyzed neonatal malformations, only one study found an increased risk (Kornum et al., 2010). Kornum et al. (2010), found SSRI exposure to have a 5.1% risk (versus 3.5% risk with no SSRI exposure) of neonatal malformations. Although this study found an increased risk, the risk is still considerably low. Furthermore, an increased risk was also found with escitalopram and sertraline. Even though overall use of SSRIs does not appear to have an increased risk of neonatal malformations, Pedersen et al. (2009) found higher incidence of septal heart defects with sertraline and

citalopram. Both of these studies had a large sample size, but Kornum et al. (2010) had a low number of participants that took escitalopram, which would question its reliability.

The U.S. Food and Drug Administration (FDA) classifies all prescription medications by categories to determine their safety during pregnancy. All SSRIs are classified as pregnancy category C, except for paroxetine, which is classified as category D. The FDA changed paroxetine from category C to D in 2005 due to increased risk for congenital malformations, especially cardiac defects, when a fetus is exposed during the first trimester (U.S. Food and Drug Administration, 2010). Of all the studies used in this review, only one study found an increased risk of neonatal malformations with paroxetine exposure. Pedersen et al. (2009) found that neonates exposed to paroxetine had a 5% chance of major malformations, compared to a 3.15% chance without any SSRI exposure. However, this same study did not find an increased incidence of cardiac defects with paroxetine when compared with unexposed infants.

In 2006, the FDA issued a public health advisory that reported one study found SSRI exposure after 20 weeks gestation to cause a six-fold increase in persistent pulmonary hypertension of the newborn (PPHN) (U.S. Food and Drug Administration, 2012). This statement was followed by a safety announcement in 2011 that stated additional studies have had different results which indicates the risk of PPHN with SSRI exposure to be uncertain. In this review, five studies mentioned PPHN risks, however none of the studies actually assessed its risks (Dubnov-Raz et al., 2011; Kornum et al., 2010; Mulder et al., 2011; Wisner et al., 2009; Suri et al., 2007).

The Center for Disease Control (2009) defines low birth weight as less than 2500 grams or 5.5 pounds. A majority of the articles reviewed found that SSRI exposure increased the risk of low birth weight. However, the average birth weight of all the infants exposed to SSRIs in

these articles was greater than 6.75 pounds, which indicates the infants did not have low birth weight. (Colvin et al., 2011; Dubnov-Raz et al., 2011; Kulin et al., 1998; Lund et al., 2009; Mulder et al., 2011; Oberlander et al., 2006; Roca et al., 2011; Wisner et al., 2009; Suri et al., 2007). Of the studies that evaluated low birth weight with SSRI exposure, five of those studies also assessed the effects of depression (Lund et al., 2009; Mulder et al., 2011; Oberlander et al., 2006; Wisner et al., 2009; Suri et al., 2007). Two of the studies showed no increase in low birth weight (Lund et al., 2009; Suri et al., 2007). The other three studies showed depression caused a slight increase in lower birth weight, however the average birth weight of all the infants exposed to depression was greater than 7.1 pounds (Mulder et al., 2011; Oberlander et al., 2006; Wisner et al., 2009). Even though SSRI exposure and depression may put a neonate at risk for lower birth rate, the chance of the birth weight being classified as low is very minimal.

An Apgar score is a test done on infants at one and five minutes after birth to determine their health status. The test looks at the infant's breathing, heart rate, muscle tone, reflexes, and skin color. A score greater than seven out of ten is considered normal (MedlinePlus, 2012). A number of studies assessed Apgar scores of infants exposed to SSRIs during pregnancy versus non-exposed infants and found minimal differences in score numbers when compared with infants not exposed (Colvin et al., 2011; Dubnov-Raz et al., 2011; Lund et al., 2009; Mulder et al., 2011; Roca et al., 2011; Wisner et al., 2009; Suri et al., 2007). Alder et al. (2007) found that 9% of infants exposed to SSRIs and 8% of infants whose mother had depression but did not use SSRIs had a score of less than seven at five minutes when compared to infants that were not exposed to SSRIs or depression, which was only 1%. Wisner et al. (2009) found similar results with lower Apgar scores, except a higher percentage was found in SSRI exposed infants and a lower percentage was found in infants not exposed to SSRIs or depression without SSRI use.

These studies present conflicting data, but it should be known that SSRI exposure and depression without the use of SSRIs could potentially decrease Apgar scores at birth. Even though Apgar scores do not predict an infant's health for the future, a lower Apgar score does put an infant at increased risks.

Since SSRI medications cross the placenta to the fetus, neonates may be at risk for withdrawal symptoms after birth. These may include: respiratory distress, jaundice, and feeding difficulties. When an infant is born with any of these symptoms, they are at higher risk for a longer hospital stay or possible admission to the neonatal intensive care unit. Oberlander et al. (2006) evaluated withdrawal symptoms and a slight increase was found in infants exposed to SSRIs. There was a 7.5% increase of respiratory distress and a 1.5 increase of jaundice and feeding difficulties in neonates exposed to SSRIs when compared with neonates only exposed to depression and neonates not exposed to SSRIs or depression (Oberlander et al., 2006). Other studies also found an increased length of hospital stay for infants exposed to SSRIs in utero (Lund et al., 2009; Oberlander et al., 2006; Wisner et al., 2009; Suri et al., 2007) though one of these studies (Suri et al., 2007) had a small sample size which could potentially decrease the data's reliability. However, a probable cause for an increase in neonatal intensive care unit admissions or longer hospital stays could be due to providers being more cautious after delivery as they are aware the mother took antidepressants during pregnancy (Suri et al., 2007).

There is minimal research available about the effect of maternal depression to the fetus. Depression that is not treated during pregnancy has been linked to poor nutrition, suicide, and an increased incidence of tobacco and alcohol use as well as neonatal irritability, agitation, decreased activity and attentiveness, and less facial expressions (American Pregnancy Association, 2011). Huot et al. (2004) found infants exposed to maternal depression in utero

had atypical neonatal temperaments and elevated neonatal stress. The cause of these neonatal changes was potentially due to higher cortisol levels, altered maternal hormone levels (which is evident with maternal depression), and when treatment is not implicated. Another study done by Mulder et al. (2011) found an increased risk of fetal neurobehavioral development and abnormal sleep patterns in utero with SSRI exposure.

A possible life threatening complication of pregnancy is preeclampsia. Preeclampsia causes decrease blood flow to the placenta, which causes a decrease in oxygen and nutrients to the fetus (Mayo Clinic, 2011). Initial signs and symptoms of preeclampsia are elevated blood pressure and protein in the urine. Kurki et al. (2000) evaluated the incidence of preeclampsia and found women with depression had a 2.5% higher risk for preeclampsia versus women without depression. Another study by Qiu, Sanchex, Lam, Garcia, & Williams (2007) found that moderate depression had a two times greater risk and severe depression had a three times greater risk of preeclampsia. This would be reason for additional evaluation and blood pressure screenings in women with depression as well as feasible basis to treat depression versus leaving untreated.

Head circumference is measured at birth and compared with nationally set growth charts to provide data on brain development. The measurements can indicate brain swelling (large head) or that the brain is not growing appropriately (small head) (Mannheim & Zieve, 2011). There is conflicting data about the effects of SSRIs on head circumference. While Colvin et al. (2011) found a slight decrease in head circumference in infants exposed to SSRIs in utero, other studies found no difference between infants exposed versus not exposed to SSRIs (Lund et al, 2009; Wisner et al, 2009).

Existing data has provided a link between decreased bone mineralization and frail bones with SSRI exposure. Studies done on adults who take SSRIs have shown a two times increased risk of bone loss compared to individuals who did not take SSRIs (Oregon Health & Science University, 2011). Colvin et al. (2011) studied bone mineralization of newborns by ultrasound to determine bone density. The data revealed no variation of bone density between infants exposed and not exposed to SSRIs. The reliability of this data is somewhat low due to the study's small sample size. Even though there may be a bone loss risk in adults who take SSRIs, this may not be true for neonates even though SSRIs cross through the placenta to the fetus.

Strengths

A number of strengths in each study increased their validity and reliability. Nine studies (Dubnov-Raz et al., 2011; Kornum et al., 2010; Latendresse & Ruiz, 2011; Lund et al., 2009; Mulder et al., 2011; Oberlander et al., 2006; Roca et al., 2011; Wisner et al., 2009; Suri et al., 2007) were approved by a hospital or research site which supported the study and its validity. Six studies (Kurki et al., 2000; Latendresse & Ruiz, 2011; Mulder et al., 2011; Roca et al., 2011; Wisner et al., 2009; Suri et al., 2007) required the participants to sign an informed consent which increased the study's validity. Six studies (Kulin et al., 1998; Li et al., 2009; Lund et al., 2009; Mulder et al., 2011; Oberlander et al., 2006; Pedersen et al., 2009) had a large number of participants (over two hundred and fifty) in their sample size to make the study reliable.

A widely used, dependable, and well-known screening tools was utilized in eight studies (Huot et al., 2004; Kurki et al., 2000; Latendresse & Ruiz, 2011; Li et al., 2009; Mulder et al., 2011; Roca et al., 2011; Wisner et al., 2009; Suri et al., 2007) which improved the study's reliability. Some of the depression screening tools used were Beck Depression Inventory, Center for Epidemiology Studies Depression Scale, Hamilton Depression Rating Scale, and Diagnostic

and Statistical Manual of Mental Disorders. Eight studies (Colvin et al., 2011; Dubnov-Raz et al., 2011; Kornum et al., 2010; Latendresse & Ruiz, 2011; Lund et al., 2009; Oberlander et al., 2006; Pedersen et al., 2009; Wisner et al., 2009) obtained data from national or local databases, national registries, or hospital records which supported the data's reliability.

A blind assessment evaluation of either the mother or newborn was utilized in three studies (Mulder et al., 2011; Wisner et al., 2009; Suri et al., 2007) Compliance with SSRI therapy was confirmed in two studies which supported the validity of the study (Pedersen et al., 2009; Wisner et al., 2009). Toxicology tests were performed on participants to rule out ingestion of other medications, illicit drug use, and alcohol to improve the study's reliability in two studies (Wisner et al., 2009; Suri et al., 2007). Factors that could affect the study's results were adjusted in two studies (Kornum et al., 2010; Pedersen et al., 2009) to allow to increased reliability of the study. The type of SSRI used during pregnancy was disclosed in seven studies (Colvin et al., 2011; Kornum et al., 2010; Kulin et al., 1998; Mulder et al., 2011; Pedersen et al., 2009; Roca et al., 2011; Suri et al., 2007) which allowed for comparison between medications as well as being able to rule out if one medication could alter the overall results in regards to this class of medication. The SSRI dose was disclosed in six studies (Dubnov-Raz et al., 2011; Kornum et al., 2010; Kulin et al., 1998; Mulder et al., 2011; Roca et al., 2011; Suri et al., 2007) which allowed evaluation of adverse effects that could have been dose dependent.

Limitations

Reliability of a study is related to its sample size as a small sample size would not provide enough data to make the study reliable. There were four studies (Kurki et al., 2000; Latendresse & Ruiz, 2011; Roca et al., 2011; Suri et al., 2007) that had a small sample size (less than two hundred and fifty) which could affect the study's reliability.

Location was not disclosed in one study (Huot et al., 2004) which could potentially alter the study's validity as location is pertinent to data validity. There were nine studies (Colvin et al., 2011; Dubnov-Raz et al., 2011; Kornum et al., 2010; Kurki et al., 2000; Lund et al., 2009; Mulder et al., 2011; Oberlander et al., 2006; Pedersen et al., 2009; Roca et al., 2011) that were located out of the United States. This could affect the reliability of the study as each country has their own standards of medical care.

Validity was affected in six studies (Colvin et al., 2011; Huot et al., 2004; Kulin et al., 1998; Kurki et al., 2000; Li et al., 2009; Pedersen et al., 2009) as the studies were either not approved by the research site/hospital or did not disclose if they had been. Reliability was affected in one study (Mulder et al., 2011) as not all participants completed all three ultrasounds before delivery as the researchers allowed participants to join at different times and in another study (Latendresse & Ruiz, 2011) as not all participants completed all the questionnaires. Three studies (Kurki et al., 2000; Li et al., 2009; Lund et al., 2009) assessed maternal depression one time during pregnancy which could affect the reliability of depression affecting the neonate as additional data is needed.

Four studies (Colvin et al., 2011; Lund et al., 2009; Mulder et al., 2011; Oberlander et al., 2006) only allowed a specific time of SSRI exposure compared with SSRI exposure during entire length of pregnancy. The type of SSRI was not included in the participant's data in eight studies (Dubnov-Raz et al., 2011; Huot et al., 2004; Kurki et al., 2000; Latendresse & Ruiz, 2011; Li et al., 2009; Lund et al., 2009; Oberlander et al., 2006; Wisner et al., 2009) which could alter the results if one SSRI was responsible for exposure effects. The use of medications other than SSRIs was included in three studies (9Lund et al., 2009; Oberlander et al., 2006; Roca et al., 2011) which decrease the reliability of the data and alter the study's results. One study (Lund et

al., 2009) did not exclude other psychiatric disorders which could alter how a diagnosis other than depression could affect the mother and fetus. Duration of depression was not assessed in four studies (7,9,11,12). Potential participant bias was found in only one study (Li et al., 2009). The most reliable measurement tool was not used in one study (Dubnov-Raz et al., 2011) as researchers did not want to expose the infants to radiation. This is why an ultrasound was used to measure bone density versus a DEXA scan.

Other factors that could possibly affect the results of the study were not taken into account in four studies (Dubnov-Raz et al., 2011; Huot et al., 2004; Kornum et al., 2010; Kulin et al., 1998) which could affect the study's reliability. One study (Kulin et al., 1998) only used information from the mother regarding her pregnancy and neonatal outcome in which it was difficult to show the data as factual. One study (Kurki et al., 2000) only allowed Caucasian and nulliparous mothers. All of the studies included singleton pregnancy except one study (Suri et al., 2007) included a set of twins in their data.

All of the articles reviewed were observational studies. Some studies randomly chose their participants, for example from hospital databases, however the use of SSRIs and/or depression during pregnancy was already evident, which makes it difficult to have randomly controlled studies. Since pregnancy is a difficult topic to study, it is only possible to study the effect of a medication after the mother has chosen to take the medication as it is unethical to ask mothers to take medications to determine neonatal outcomes.

Summary

Overall, SSRI exposure is linked to a slight increase in neonatal withdrawal symptoms (such as restlessness and irritability), preterm birth, lower birth weight, longer hospital stay or neonatal intensive care admission, abnormal in utero sleep patterns, fetal neurobehavioral

development, and PPHN. There was conflicting data with persistent pulmonary hypertension in newborns, congenital malformations, and birth defects; however, a slight increase in congenital malformations was found with Paroxetine. There was no variation between SSRI exposure with Apgar scores, head circumference, and neonatal bone density. Depression without antidepressant treatment is linked to a slight increase in preterm birth, Apgar scores, lower birth weight, atypical neonatal temperament, neonatal stress, and preeclampsia. There was no variation in congenital malformations with depression. Pregnant women or women of childbearing age need to be aware of the risks and benefits of SSRIs as well as the effects of untreated depression on their unborn child. Education needs to be provided in order for patients to be able to make an informed decision regarding the treatment of their depression.

A brochure was created in order to highlight the current data on SSRI use and depression during pregnancy as well as their risks and benefits. A copy is attached in appendix A.

Discussion

Interpretation

The objective of this project was to give providers current evidence about SSRI use during pregnancy so that they would be able to help patients make informed decisions about their care. The brochure includes information about the benefits and risks of SSRI use as well as the risks of maternal depression. The brochure's key points were definition of SSRIs, informational websites, pregnancy categories of SSRIs, SSRI affects to baby, maternal depression affects to baby, and what to do about depression. The information pertained to the pregnant mother, their fetus in utero as well as neonate after birth.

Outcome and Dissemination

An educational brochure was created and presented to eight healthcare providers and one medical student who provide care to pregnant women and women of childbearing age. The specialties of the providers included: internal medicine, family practice, and obstetrics-gynecology. The brochure was presented along with an explanation of this project. The providers were given an opportunity to ask questions about the brochure and copies were left with them to allow time for use with patients. All providers were told that a follow-up visit would take place in order to get feedback about the brochure and if it benefited their practice and patients.

A follow up visit with providers took place approximately one week after the brochures were disseminated in order to gain feedback. All of the providers knew of some type of adverse effect with SSRI use, however four of them were not aware of the most current research and ACOG recommendations regarding SSRI use during pregnancy. The providers unanimously felt the objectives of the presentation were met and that current evidence was provided. All of the providers felt the brochure had an attractive design and the facts were clear, easy to read, and to the point.

A couple providers stated the brochure was helpful in their practice as they were able to have all the benefits and risks as well as ways to cope with depression during pregnancy all in one printout. They were able to use the brochure to educate patients so that patients along with their provider were able to make an informed decision in managing their depression during pregnancy. Providers who did use the brochure with patients indicated that the patients were appreciative to have the risks and benefits laid out in front of them to compare.

Overall, they all felt treatment options for depression during pregnancy need to be individualized, but that they now feel more comfortable prescribing SSRIs after being given

current evidence. A number of providers asked for additional information on a newer SSRI, escitalopram (lexapro), however it was explained that limited research is available.

Implications for Nursing

The need for further research is quite evident as SSRI use during pregnancy has not been well investigated and the data that is available is limited and somewhat conflicting. Due to the nature of the studies needed, it can be difficult to accurately assess teratogenic effects of a medication during pregnancy as it is unethical to ask patients to partake in a study. There are also a number of limitations to studying pregnancy as there are a number of other factors that can affect the results. The severity of depression, underlying conditions, and characteristics of individuals can alter results and make it difficult for studies to provide accurate results. Additional studies with large sample sizes are needed to increase what is known, explain conflicting results, and to determine differences.

Education is an essential part of an advanced practice nurse's role. Patients need to know the risks and benefits of treatment options that can affect their health. This becomes an even larger focus when a patient is pregnant as their unborn child's health is also at stake. As a provider, it is vital to know current evidence and guidelines when caring for patients. Not only so providers can be better informed but also so patients can be provided current data in order to make informed decisions. This is why knowing the most current data becomes crucial as guidelines and recommendations are always changing.

Reputable organizations publish current evidence based research so that providers are able to safely recommend treatment options for patients. It is important to stay current with evidence-based research so that providers are able to give their patients proper care and education. With the data given by reputable organizations, providers should ultimately follow the guidelines to ensure they are practicing safely and efficiently. Through a trusting

relationship with patients and a thorough assessment, providers will be able to use their skills by providing patients with the best care possible.

Conclusion

Safely managing depression during pregnancy can be difficult as the risks and benefits of SSRI use as well as the risks of depression are at stake. Providers need current, evidence based data and guidelines to be able to provide their patients with the appropriate education and treatment options. Providers need to have the trust of their patients, as it is not only the patient's health at risk, but also their unborn baby. A plan needs to be formulated between the provider and the patient to determine the best treatment for their depression and to prevent relapse.

This project addressed SSRI use during pregnancy by providing current literature on its safety. Even though the data is limited and at times conflicting, current recommendations state that SSRIs should be used when the benefits outweigh the risks. Proper education should always be done so the mother is able to make an informed decision regarding the treatment of her depression.

SSRIs are one of the best treatment options for depression. During pregnancy, the adverse effects can cause a women to not want to continue antidepressant treatment. While further research is needed, the results found in this project show that SSRI use can be used during pregnancy, but the benefits need to outweigh the risks.

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