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Use of antidepressants by pregnant women: Evaluation of perception of risk, efficacy of evidence based counseling and determinants of decision making

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Summary

Background: The World Health Organization predicts that by 2012, depression will be the number one disease in the world. Thus, many women who become pregnant will require treatment with antidepressants. We are aware that women and their health care providers remain hesitant to prescribe and take these drugs during pregnancy, despite evidence of the relative safety.

Objectives: 1) To determine perception of risk of antidepressant drugs by pregnant women with depression, 2) to determine the efficacy of evidence-based counseling, and 3) to identify determinants that influence women in their decision making regarding the continuation/discontinuation of antidepressants during pregnancy.

Methods: Women who called The Motherisk Program requesting information about the safety of an antidepressant during pregnancy were compared with two other groups: 1) Women who called about antibiotic use (i.e., non-teratogenic drugs used short-term) and 2) women who called about gastric medications (i.e., non-teratogenic drugs used long-term). Their perception of risk was measured before and after evidenced-based information was given and determinants of decision making was also evaluated.

Results: We recruited 100 women taking antidepressants during pregnancy and 100 in each comparison group. Despite receiving evidence-based reassuring information, 15% of antidepressant users, compared to 4% using gastric drugs and 1% using antibiotics, chose to discontinue their medication. The main determinants of decision making were based on: information received prior to calling Motherisk, family and friends advice, the internet, sequence of advice given and if a women was undecided at the time of call.

Conclusions: Women continue to fear taking antidepressants during pregnancy, more so than non psychiatric drugs, however, evidence based counseling can lower this fear, although not totally. Deciding whether to continue to take a medication or not during pregnancy, is a complex decision for women and their healthcare providers to make.

Keywords: Pregnancy; antidepressants.

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Background

Since the thalidomide disaster of the 1960s, there has existed the general view that every drug has teratogenic potential, and that women should refrain from taking any medications at all during pregnancy. As a result, pregnant women are commonly advised to avoid all pharmacotherapy for fear of causing fetal malformations. However, with the number of published epidemiologic studies to date documenting the relative safety of antidepressants, (Pastuszak et al., 1993; Chambers et al., 1996; Kulin et al., 1998; McElhatton et al., 1996; Nulman et al., 1997; Einarson et al., 2001a, 2003). It appears that women who are depressed and require an antidepressant during pregnancy should be treated. Despite this reassuring information, it has been documented that women have abruptly discontinued their antidepressant upon confirmation of pregnancy (Einarson et al., 2001b).

The issue of not treating depression during pregnancy is emerging as an important issue which requires addressing. A study found that untreated depression during pregnancy may have deleterious effects on peripartum

and neonatal outcomes, such as more cesarean sections and a greater number of admissions to neonatal intensive care units (Kurki et al., 2000; Chung et al., 2001). A woman who is depressed may also make other poor decisions during her pregnancy, such as drinking alcohol and not attending her obstetrician's appointments, etc. (Zuckerman et al., 1989). In addition, a woman who is depressed may also have difficulty bonding with her child after birth and may experience other adverse attachment behaviours (Orr and Miller, 1995; Bosquet and Egeland, 2001).

Up to 25% of women of childbearing age suffer from depression, as this disorder has a peak prevalence between 25 and 44 years of age (Marcus et al., 2003). In addition, as it is known that at least 50% of all pregnancies are unplanned, (Mathews et al., 2003) it is likely that a substantial number of women will be taking an antidepressant when they become pregnant.

Due to this high prevalence and the risks of untreated depression during pregnancy, there exists a need to evaluate misconceptions about antidepressant use during this period in a woman's life. Understanding women's perceptions and decisions about taking antidepressants during pregnancy is crucial if women and their health care providers are to be empowered to make informed decisions about their health and the health of their babies. However, despite the frequency of depression in pregnancy and the relative wealth of reassuring epidemiologic studies available in the scientific literature, this information does not appear to have filtered down to the general population. Consequently both women and their health care providers have little guidance with which to make an informed decision regarding treatment.

Thousands of women and their healthcare providers call our line each year requesting information about exposures in pregnancy, a substantial number of them (12%) regarding antidepressants. We have not and neither (to our knowledge), has any other group examined how these women perceive teratogen risk, compared to other women. As well, we have not examined how the information dispensed by us influences them in making informed decisions, nor have we identified the determinants behind their decision-making. There is therefore a need to investigate how pregnant women make decisions about antidepressant use, both to prevent abrupt discontinuation of the drug and to develop strategies for more effective counseling.

Our objectives were to: 1) To determine perception of risk of antidepressant drugs by pregnant women with depression, 2) to determine the efficacy of evidence-based counseling and 3) to identify determinants that influence women in their decision making, regarding the continuation/discontinuation of antidepressants.

Methods and participants

The Motherisk Program is a teratogen-information counseling service for women and their health care professionals regarding the safety/risk of drugs, chemicals, radiation or infections during pregnancy and lactation. It is a multidisciplinary group of health professionals, who offer evidence-based information to callers. We receive approximately 35,000 calls per year, 67% regarding pregnancy, with the remainder of the calls dealing with breastfeeding. Of the 150–200 women who call daily, approximately 30 of them present with questions concerning antidepressant drugs. In fact, we have estimated that approximately 12% of all calls concern antidepressant use.

Our study was comprised of 3 groups of participants: 1) women taking antidepressants, that have been found not to elevate the baseline rate for malformations. 2) women with a chronic gastric condition that required medication during gestation that had not been found to be teratogenic, and 3) women taking short-term antibiotics for an infection, which have also been found not to elevate the baseline rate of major malformations. All of the women had to be currently taking the drug and were either pregnant or planning a pregnancy.

Group 1: Antidepressants

Women with an active diagnosis of depression comprised the antidepressant group. Women were included only when the diagnosis was confirmed by her physician. The medications included the tricyclics, SSRIs and SNRIs. Callers who were taking antidepressants for which safety data were not available were excluded from study. Women were also excluded if they were taking the antidepressant for any other reason than depression.

Group 2: Gastric medications

Women in the gastric condition group were taking proton pump inhibitors (PPIs) or H2 blockers, both groups of which have been found to not elevate baseline risk for major malformations (i.e., omeprazole, cimetidine, ranitidine, etc.). These medications have a long-term use profile similar to those of antidepressants, thus representing chronic use for comparison purposes.

Group 3: Antibiotics

Women using antibiotics with established fetal safety profiles (i.e., cephalosphorins and penicillins) were also enrolled. The average period of therapy for an antibiotic is 5–7/days, so these drugs represented short-term medication use, also representing a suitable group for comparison purposes.

Motherisk callers inquiring about antidepressants (or medications in the comparison groups) who met the inclusion criteria were informed of the study by the counselors. After agreeing to participate in the study, were transferred to the study coordinator without receiving any further information about their drug of concern. Callers were then asked for study participation consent after the protocol was explained to them in detail. If a woman declined to participate, she still received evidence-based information about her current drug in the form of standard Motherisk counseling.

Using a structured intake form, all data pertaining to reproductive risks, including complete medical status, family history of birth defects, gravidity, parity, previous spontaneous or therapeutic abortions, comorbidities (e.g., anxiety, obsessive compulsive disorder, eating disorders, etc.), concurrent medications, vitamin use, nutrition, use of recreational drugs, tobacco and alcohol use were documented. Gestational age at time of call (in weeks), last menstrual period, whether or not the pregnancy was planned, and any pregnancy complications, were recorded. The history of her current condition (i.e., depression, GI condition, or infection), was also documented. The dosage of the current medication and duration of use were also recorded. Also noted were the specialty of the treating physician (i.e., family physician, obstetrician/gynecologist, or psychiatrist) and the advice received during in pregnancy. The CES-D was administered to each caller in each of the three groups at the initial interview.

This study used a specially designed structured questionnaire, created to evaluate perceptions and perceptual choices. The survey was designed to evaluate changes in risk perception as a result of an intervention (counseling), and to evaluate determinants involved in women's decision-making. As both the survey and the interview in which it is administered are only semi-structured, often women's answers appeared in the form of volunteered information and dialogue. The questionnaire asked for information on all sources of advice the woman received 'in favor' and 'against' taking the medication, in pregnancy. In addition, participants were asked if they had spoken to anyone else about the use of this medication and what those individuals said about its' safety during pregnancy. As well, they were asked if they had done their own research on the internet or had seen anything about their medication in the media. They were asked which piece of information had affected their decision the most. If they decided to stop using their medication, they were asked how bad their condition (depression, GI condition, infection) would have to get, for them to consider using the medication during pregnancy. The questionnaire also asked for the women's own views (expressed as open-ended answers) about medication use in pregnancy. She was also asked about the self-rated efficacy of her medication, and the self-rated severity of her condition (depression, GI condition, infection). The questionnaire was administered before the woman was given any information, to eliminate any bias.

Following completion of the intake form and questionnaire, it was explained, in language and terminology that were well understood by the lay public, evidence-based information about the safety in pregnancy of the medications of inquiry. After they had been given all the information available, it was explained that in every pregnancy there is always a baseline risk in the population of having a baby with a malformation, whether they have taken any medication or not and that their exposure would not likely increase this risk.

Before and after the evidence-based counseling, women were asked to complete the Risk Perception Analogue Scale which measured her perception of risk from zero (no risk) to 100 (risk in every case), and their present predisposition or tendency to continue or discontinue the drug in question. They were also asked about their perception of teratogenic risk in the general population as well as their own perceived risk of the medication they were taking.

Two weeks after the initial interview, a follow-up interview was conducted to ascertain if the woman continued or discontinued her drug therapy and to identify determinants that may have affected her decision.

The instruments used for assessment included an analogue scale, 7-point Lickert scale, and the CES-D tool. The analysis of the data was conducted in several stages: We initially compared the perception of teratogenic risk among women receiving antidepressants before and following evidence-based counseling, using the Student's paired t-test or the Wilcoxon signed ranks test, depending on the normality of the data. Patients scored their perception of teratogenic risk using the Analogue Scale (AS).

Similar analyses were conducted with comparison groups. Subsequently, using ANOVA or Kruskal-Wallis tests, we compared the initial and post counseling AS scores among the depression and comparison groups. The main outcomes that were measured, was whether or not women in each group continued or discontinued their prescribed pharmacotherapy, and what determinants influenced that decision. The effectiveness of Motherisk counseling was also evaluated, with effectiveness measured by her decision to continue the medication.

Results

We were able to complete interviews with 100 women in each group, for a total of 300 responses. There were no statistical differences between groups in maternal demographics, which also included socioeconomic and educational status with all the women calling Motherisk when planning a pregnancy or within the first 6 weeks of gestation. Of those who participated, 99% made the decision as to whether or not to use the medication within the two weeks between calls, while one woman (in the antidepressant group) required a longer period to make a decision. 98% of the women planning a pregnancy became pregnant within the study duration and there was a planned pregnancy rate of 51% in all three groups.

Of the women who were approached to participate, there were 11 refusals in the antidepressant group, 9 in the gastric medication group and 14 in the antibiotic group (Chi square = 1.26, P = 0.53). The brand of antidepressants and dosages are described in Table 1.

Table 1. Antidepressants used during pregnancy by the women in this study

Antidepressant	Number n = 100	Mean dose used (mg)	Range of doses (mg)
Amitrityline	1	50.0	25–300
Fluoxetine	4	25.0	20–60
Sertraline	2	50.0	50–200
Citalopram	12	27.5 ± 14.2	20–60
Paroxetine	69	18.7 ± 1.3	20–60

Table 2. Impact of Motherisk counseling on perception of teratogenic risk

Perception of risk (pre-counseling)*	Perception of risk (post-counseling)	P value
87% of depressed women rated risk of antidepressants as greater than 1–3%	12% of depressed women rated risk of antidepressants as greater than 1–3%	<0.001
56% of women with gastric problems rated risk of medications as greater than 1–3%	4% of women with gastric problems rated risk of medications as greater than 1–3%	<0.001
22% of women with infections rated the risk of medications greater than 1–3%	2% of women with infections rated the risk of medications greater than 1–3%	<0.001

* Actual baseline rate for major malformations in the general population is 1–3%.

Table 3. Differences in continuers and discontinuers of antidepressants in pregnancy

Measure	Discontinuers (n = 15)	Continuers (n = 85)	p-value
Severity of depression by CESD	24.1 ± 10.7	19.1 ± 9.2	0.05
Severity of depression by self-rated score	3.1 ± 2.1	2.6 ± 1.7	0.57
Initial risk perception (from AS)	52.7 ± 24.2	39.4 ± 27.2	0.04
Final risk perception (from AS)	49.9 ± 33.7	7.1 ± 12.5	<0.001
# of sources consulted in addition to MR	3.0 ± 0.9	3.13 ± 1.2	0.98
# of positive advice received	1.1 ± 0.5	1.6 ± 0.8	0.02
# of negative advice received	3.0 ± 2.2	1.3 ± 1.2	0.05
Duration of depression (years)	2.6 ± 2.6	3.4 ± 3.9	0.67
Duration of depression treatment (years)	1.4 ± 1.3	1.9 ± 1.9	0.42
Physician concern (scale of 1–7)	3.0 ± 1.7	4.4 ± 2.0	0.01
How likely (%) to use medication prior to counseling	9.0 ± 15.6	42.3 ± 33.3	<0.001
How likely (%) to use medication after counseling	11.0 ± 20.4	87.6 ± 21.6	<0.001
Efficacy of medication (scale of 1–7)	4.1 ± 1.7	3.5 ± 1.4	0.18

Perception of risk before and after counseling in all three groups, is described in Table 2. High initial risk perception was associated with less chance of continuing the medication. Despite receiving reassuring information, of those women using antidepressants, 15/100 (15%) chose to discontinue their medication regardless, compared to 4/100 (4%) of gastric medication users and 1/100 (1%) of antibiotic users (Chi square = 17.5, $P < 0.001$). All discontinuers reported that the first source that they discussed the safety of the medication use with in pregnancy, was negative and advised discontinuation. A greater proportion of continuers reported that the first source they consulted gave a reassuring opinion. Consequently, it appears that the sequence of advice received was important to those women in their decision making. Differences between continuers/discontinuers of antidepressant medications are described in Table 3.

In those women who discontinued their antidepressants, 47% had initially decided to discontinue, while 40% had not made a firm decision at the time of call. The remaining 13% had decided to continue their medication, but contacted Motherisk for further reassurance. Of the continuers, 10% rated the risk of antidepressants as greater than baseline following reassuring counseling, but continued taking the medication despite this opinion. This included one woman rating the risk of her antidepressant as 100% likely to cause birth defects. In the discontinuer group, 12 out of 15 (80%) still rated the risk of antidepressants as greater than baseline following counseling. Counseling had the greatest impact (in terms of risk perception change) on women who were originally undecided in their course of action, and the least impact on discontinuers. The only determinants that appeared to correlate with a woman's final decision, were the number of positive and negative sources received, and the initial risk perception. Higher numbers of negative sources were associated with less likelihood of continuing the medication during pregnancy (Pearson correlation coefficient $r = -0.201$, $P < 0.05$). Higher numbers of positive sources was associated with a higher likelihood of continuing the medication during pregnancy (Pearson's $r = 0.391$, $P < 0.01$). The number of overall sources consulted did not correlate with final decision. High initial risk perception was associated with less chance of continuing the medication. Level of education, socioeconomic status, marital status, maternal age, gravity, parity, GA

Table 4. The main determinants of overall decision-making

Determinant	Antidepressant users (n = 100)	Comparison group (n = 200)
Info from friends and family	3 (3%)	41 (20.5%)
Physician/pharmacist/other	6 (6%)	15 (7.5%)
Internet, media, television, etc.	5 (5%)	10 (5%)
Personal beliefs	20 (20%)	22 (11%)
The Motherisk Program	66 (66%)	112 (56%)

at time of call, brand of drug used dosage and year of market appearance), and planned versus unplanned pregnancy, did not correlate with the decision outcome. Description of the main determinants of decision making are described in Table 4.

There was no difference in scores between all three groups in their self-rating of risk-taking ability, concern for the well-being of their baby, ability to cope with their condition without medication, or value of the physician. The comparison groups did not believe more strongly than antidepressant users that short term medications or smaller doses of medications represented a safer pregnancy alternative. Women in the comparison groups agreed significantly less that all medications are harmful during pregnancy ($p < 0.001$), and significantly less that the potential consequences of taking their medication during pregnancy were too great to take a chance ($p < 0.001$). There were no statistical differences between the groups in any of the other questions that were asked.

Discussion

To our knowledge, this is the first study that examined risk perception of pregnant women in three comparison groups, who were taking different types of medications. In addition, we also examined the efficacy of counseling, following reassuring evidence-based information and the determinants involved in women's decision making regarding whether or not they would continue their antidepressant medication during pregnancy.

As the women in the three groups did not differ in socioeconomic status, GA at time of call, education, gravidity, parity martial status, or on other demographic variables, we felt confident that these groups were well matched with respect to those variables, thus facilitating comparisons.

It was interesting to note that there were more losses to follow-up in the antibiotic group. This may be because antibiotics users were less invested in the information received, due to being less apprehensive initially about the use of their medications in pregnancy.

It was also interesting to note that after antidepressant users were initially diagnosed with depression, they appeared to wait for a substantial period of time before starting an antidepressant. Antibiotic and gastric medication users, in contrast, began their medications immediately after diagnosis. This may be due to the fact that a stigma still exists surrounding psychotropic drug use and women may be less receptive to the idea of psychotropic agents, when compared to somatic agents, and therefore spend more time deliberating whether to use them or not.

It was also interesting to note that physician counseling did not affect a woman's decision to continue or to discontinue antidepressants. In fact, many of the women described their physicians' lack of direction or advice in this matter, and they were mostly instructed to call Motherisk or consult other sources.

In the recent Motherisk case series of women who abruptly discontinued their antidepressant medications, evidence-based counseling was only partially effective in re-instituting antidepressant medication. In that 2001 study, despite reassuring counseling, 33% of women did not restart their antidepressants (Einarson et al., 2001b). In comparison, this current study showed evidence-based counseling to be twice as effective, as 85% of antidepressant users chose to continue their antidepressant. However, the major difference in these two studies was that the women in the previous study had already discontinued their antidepressant prior to calling Motherisk and in this study, they were all still taking their drugs. This current study also had a higher success rate (defined as the percentage of users continuing their antidepressant), however that may only be due to the fact that it may be easier to successfully encourage continuation of a medication when the individual is already taking it, rather than when discontinued. The women in the previous study had all discontinued their antidepressant prior to calling and with 70% of them experiencing severe abrupt discontinuation syndrome. Thus, this traumatic experience may well have affected their decision to not re-start the medication.

Two of the women in the antidepressant group felt they had to make a choice between the pregnancy or the medication, despite the fact that they received reassuring counseling that it was safe to be pregnant and take the medication. Subsequently, they chose to take the medication rather than to become pregnant, which confirms to us that there continues to be a strong fear of psychotropic drug use in pregnancy. Some women decided to lower their dose of medication following evidence-based counseling, or to avoid the medication altogether in the first trimester. This was an interesting decision because this advice was certainly not part of the counseling received

from Motherisk. This reinforces the concept that the information one receives first is difficult to erase, especially when the information is frightening.

An unexpected finding, where counseling appeared to have been 100% effective, was in the 13/100 (13%) of antidepressant users who had considered terminating an otherwise wanted pregnancy due to fear of teratogenic risk prior to calling us. Subsequently, none of them followed through with a termination. Of note, there were no women in either of the comparison groups who considered termination, which appears to confirm the statements of the women in all three groups that psychotropic drugs are more harmful to use in pregnancy than are other drugs. To the women, this probably appears to be logical, as psychotropic drugs function on the central nervous system, thereby possibly harming their baby's developing brain.

We had hypothesized that continuers would show significantly higher depression scores when compared to discontinuers, yet this difference was not observed and we found that risk perception and final decision making was independent of severity of depression. When a woman had already made up her mind prior to receiving evidence-based counseling, she was more likely to disregard any information that contradicted her decision. We also found that when women were undecided in what course of action to take, counseling was the most effective.

All of the women consulted many informational sources when making a decision about antidepressant use during pregnancy. However, more of the women in the comparison groups consulted Motherisk as a single source, whereas the antidepressant users consulted multiple sources, as they tended to look for 'second', 'third', and 'fourth' opinions before making a decision. More than likely this was because they probably needed more reassurance than the women in the comparison groups.

Risk perception is complex and even when women could recall and repeat reassuring information they had received, they still opted to discontinue their antidepressant. Women using antidepressants often reported feeling guilty about doing so, and stated a preference for other treatments such as herbal medications. In some cases there was cognitive dissonance in women using antidepressants, i.e., their risk perception of the drug did not match their decision making. Two examples included the woman who believed her antidepressant was 100% teratogenic but decided to continue taking it, and the woman who stated that it was safe, but still discontinued.

It cannot be underestimated how important friends and relatives are in the determinants of decision making. A substantial number of the women identified this person as more important to the decision-making process than the Motherisk information they received.

We found that the sum total of the amount of negative and positive advice received by a woman determines her decision. This is understandable, as advice that is reaffirmed or reiterated by several independent people, is more likely to be believed. Women were also more likely to remember negative advice, and they described being unable to discard it.

These results revealed to us that there is clearly more to reassuring a woman that a drug is safe to take in pregnancy, than simply providing evidence-based information. Often the perceived risk does not match the communicated risk and women can take away a message that is strikingly different than what was intended. Aside from information received, personal feelings, intuition, values and beliefs appear be a powerful determinant of risk perception and medical decision making. The importance of factors that are not easily quantified, such as personal beliefs and ''gut'' feelings should not be ignored. Women also place great value on the advice received from friends and family that have had similar experiences.

The main limitation of this study is that this group of women may not be representative of the population of depressed pregnant women. These were women who were excessively worried and called Motherisk, compared to women in the general population who either may be comfortable with taking an antidepressant during pregnancy or who are unaware of Motherisk and do not seek further information.

In summary, women remain anxious about using psychotropic medications in pregnancy, more so than somatic drugs, however, evidence based counseling can lower this fear, although not entirely. Deciding whether to continue to take a medication or not during pregnancy, is a complex decision for women and their healthcare providers to make.

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