

THE WAY WOMEN PERCEIVE TERATOGENIC RISK

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Because of increased anxieties of drug-induced congenital malformations, women and physician alike fear drug therapy in pregnancy even in life-threatening situations. The goal of counseling women on their teratogenic risk is to present to them an accurate, up-to-date estimate of their benefit to risk ratio. However, the same data may be received and interpreted very differently by different patients, leading them to individual conclusions and finally to the decision to continue or terminate pregnancy.

In both North America and Europe there are high rates of elective abortions^{1,2} and while pregnancies are terminated for a variety of reasons, incorrect perception of a teratogenic risk may be an important factor. Most women who have been made aware of major malformations or chromosomal aberrations through ultrasound or amniocentesis choose to terminate pregnancy.³ As documented by the Greek experience after the Chernobyl disaster, even an unbiased suggestion of adverse fetal outcome may prompt women to terminate pregnancy “to be on the safe side”.⁴

This phenomenon has been painfully demonstrated in the case of radio diagnostic procedures performed during pregnancy. Many associate “radiation” with the effects of the atomic bomb and other nuclear disasters that have come about in world history. Usually, radio diagnostic procedures involve fetal exposures to low doses of ionizing radiation in the realm of less than 5 rad. This level of exposure is not considered to be teratogenic.⁵ In spite of this many pregnant women exposed to such radiation are rather concerned and consider termination of their pregnancy. Even after information is provided in regards to the safety of specific radio diagnostic procedures, their perception of teratogenic risk remains well above the baseline population risk.⁶

Special attention and consideration should be given when counseling pregnant women exposed

to low-dose ionizing radiation. At Motherisk, we have been continuously impressed by the number of cases of misperception and distorted information regarding the potential teratogenic risk of drugs and chemicals. In particular, we felt that many women tend to assign an unrealistically high risk to medications not known to be teratogenic. In some cases, this misperception has led to termination of pregnancy.

In an attempt to objectively quantify women’s perception of their teratogenic risk, we created a 10 cm visual analog scale. After collection of patient’s data, and before delivering our view of the apparent risk, women are asked to assign to their perceived risk for major malformations a number between 0% and 100%. We also ask what, in their opinion, is the risk for major malformations in the general population, because their knowledge of baseline risk is crucial for their perception of their own risk. In addition, patients are asked to quantify from 0% to 100% their tendency to terminate or continue pregnancy.

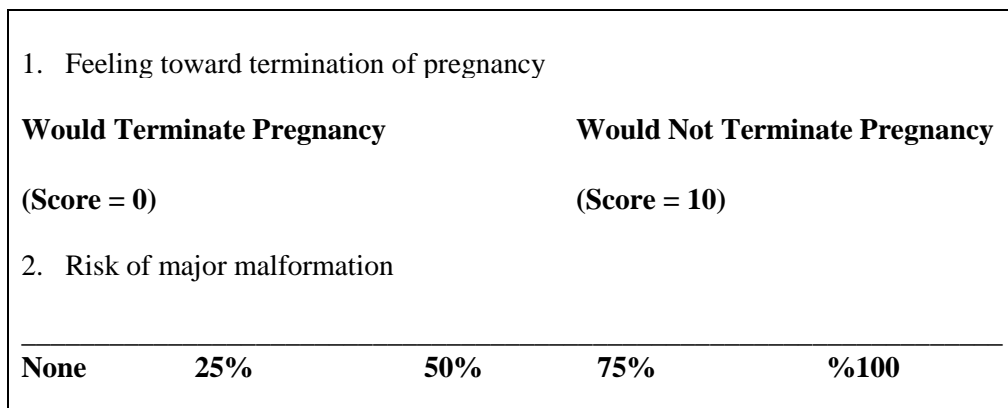
The completion of this questionnaire is followed by informing the patient of all known information about the exposure(s) in question. Subsequently, the questionnaire is repeated. Patients are urged to express their own views and not to answer the questionnaire in a way they might think would please the interviewer. Analysis of the first 80 cases on which the visual analog scale (VAS) was used between September and December 1986 reveals the power of this tool in detecting misperception and misinformation.⁷

Before receiving up-to-date information about the specific exposure, women exposed to nonteratogens assigned a mean risk of $24 \pm 2.8\%$ for major malformations. After the interview, however, the risk was perceived as lower ($14.5 \pm 3\%$, $p < 0.01$). The risk for major malformations in the general population was estimated as $5.6 \pm 1.3\%$, which is comparable to the real figure in the

literature. The perceived risk before and after our intervention was significantly different from that estimated by the patients for the general population. The tendency for continuation of

pregnancy showed a significant change following the interview (from 7.9 ± 0.3 to 8.7 ± 0.3 in the analog scale, $p < 0.01$).

FIG. 1 Visual Analog Scale



Eleven patients were exposed to medications known to be teratogenic. Their perceived teratogenic risk was unchanged ($36.2 \pm 11.7\%$ before and $36.7 \pm 15.6\%$ after the interview). Their tendency for termination/continuation of pregnancy did not change following the interview. Three of them did decide to terminate pregnancy within a few weeks of the consultation.

Eleven of our patients were single mothers. Although they did not perceive their risk differently from married women, those who had been exposed to nonteratogens showed a significantly higher tendency to terminate pregnancy before the interview (4.7 ± 1.2 on VAS units single mothers vs. 8.1 ± 0.4 married, $p < 0.05$). Following the intervention, their perception significantly changed, being less likely to terminate their pregnancy (7.4 ± 1.2 , $p < 0.05$) but the VAS was still different from married women.

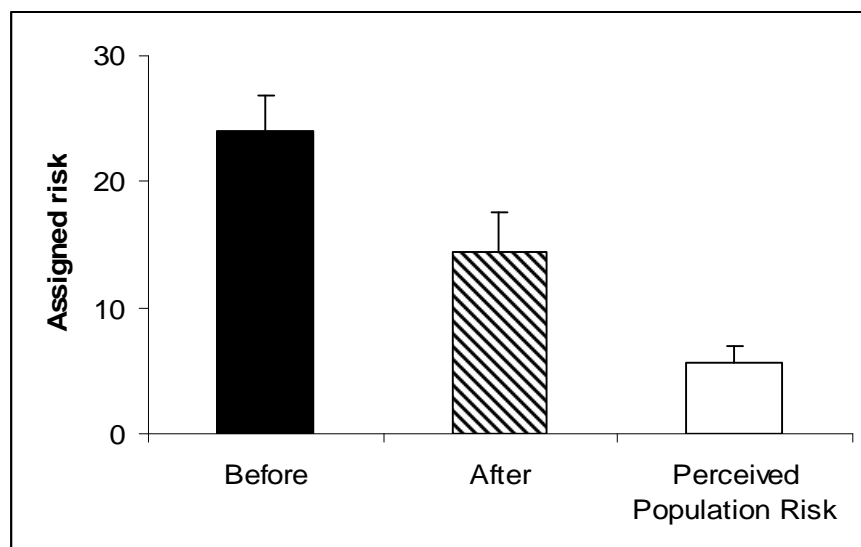
No correlation was found between estimation of risk (or tendency to terminate/continue pregnancy) and number of preparations consumed by the woman, age, parity, or socioeconomic status. No differences in perception of risk were detected between women referred by physicians and those who were self-referred. This analysis highlights that pregnant women exposed to nonteratogenic agents believe they have a risk of 1

in 4 of having a child with major malformations. This figure is very close to the known risk of thalidomide.⁸ Importantly, these women estimated the risk in the general population to be 5%, which is similar to the real figure of 4-5%.⁹ This means that the concept of teratogenic risk was well understood and that women were all informed about the risk in the general population. In addition, it lends clinical significance to the unrealistically high risk assigned by these women to their nonteratogenic exposures.

This phenomenon was well described in our study where women with nausea and vomiting of pregnancy (NVP) in their first trimester were prospectively followed. Over three-quarters of the 260 women enrolled initially believed that pharmacologic treatment of NVP increased their teratogenic risk. After having been counseled in regard to the extensive literature on the safety of anti-emetics (other than thalidomide which is the only medication ever to have been positively proven to cause birth defects), these women were followed up at 20 weeks' gestation. The risk perceived decrease significantly after counseling.¹⁰

Two basic reasons can be put forward to explain the unrealistically high teratogenic risk assigned by pregnant women: misinformation and misperception.

FIG. 2 Patient-assigned risk of major malformation for parents not exposed to teratogens



Misinformation

Advisories on potential teratogenic risk appear constantly in the lay media, usually to stress risks, and very rarely to address the safety of specific drugs. Analysis of 15 different popular magazines disclosed poor scientific standards and a clear tendency to be misleading or inaccurate.¹¹ There was a tendency to alarm readers without justification. In addition, popular books dealing with pregnancy often tend to assign risk to drugs not proven to be risky.

For example the author of, *Will My Baby Be Normal?* states, "Do not take any aspirin or medication that include aspirin if you think you might be pregnant. Midline body defects have been attributed to this drug".¹² Such defects are not believed to be associated with salicylates in humans. In yet another instance, J. Elkington entitled his book on reproductive toxicology, *The Poisoned Womb*, although most of the data discussed do not prove poisoning in humans.¹³ Possible sources of misinformation are the *Physicians' Desk Reference* and the *Martindale*, which includes warnings on exposures during pregnancy that are no longer correct. Reference books dealing with drug use in pregnancy have been published^{9,14,15} and should be used by physicians caring for women in pregnancy.

Another source of misinformation is physicians. We have dealt with more than a few cases in which physicians advised women to terminate pregnancy despite non teratogenicity (Figure 3). This may reflect a defensive approach in the current litigious atmosphere, or the possibility that physicians themselves are misinformed. Our data indicate that women referred by physicians did not have a more accurate perception of risk than self-referred patients.

A prime example of physician misinformation is seen with the use of cocaine. To date, there has been really no evidence to suggest that cocaine increases teratogenic risk in any meaningful way above the population baseline. However, a survey administered by us¹⁶ revealed that the majority of participating physicians felt that malformations were associated with cocaine use. These same physicians would also wish to terminate a pregnancy where exposure to cocaine occurred during the first 8 weeks of gestation. This is alarming, as physicians' erroneous perceptions may lead them to offer women unjustified terminations of pregnancy. Fortunately the same analysis showed that, in most cases, counseling pregnant women exposed to cocaine are successful in changing their tendencies towards termination.

FIG. 3 Letter of a Motherisk patient who had been advised by other physicians to terminate pregnancy

“Last December, I sought your help regarding a couple of tranquilizers I had taken within the first few weeks of my pregnancy. The prescribing doctor and a well-respected obstetrician had suggested that I abort the pregnancy.

As a result of your advice, my husband and I are the ecstatic parents of a beautiful, healthy baby girl. I cannot thank you enough. The work you are doing is a wonderful necessity. If there is anything I can do for your program on a volunteer basis, I would be more than happy to be of assistance”.

Misperception

Our experience shows that even after we had advised women that medications taken by them did not increase their risk of having a malformed child, their own *perceived* risk was significantly higher than their *perception* of risk in the general population.

It is conceivable that during pregnancy there is an increased sensitivity to this issue, leading to a distorted perception of risk. Of special interest is the approach of single mothers: while assigning a teratogenic risk similar to married women before receiving our advice, they were much less ready to continue pregnancy with such a risk. Single mothers may have a variety of psychological, moral, and socioeconomic reasons to discontinue pregnancy. For them, a distorted perception of teratogenic risk may be the last straw in the decision to terminate pregnancy.

Our intervention appears to have significantly changed the perception of women exposed to nonteratogenic agents in terms of estimating the risk as well as in the tendency to terminate/continue. This tendency was best documented in the subgroup of single mothers, in which some of the women who were already booked for dilatation and curettage decided to carry on the pregnancy.

If post-interview assessment still revealed an unrealistically high perception of risk or tendency to terminate pregnancy, we would spend additional time to explain to the woman that her apparent risk, based on current knowledge, is lower than the one perceived by her. We have recently shown that appropriate counseling can empower the majority of women who discontinued their psychotropic drugs to resume their use.⁷

It may be argued that women contacting a consultative service such as Motherisk are a selected group of patients with a higher degree of concern, and therefore their perception does not accurately represent the total population of pregnant women. Yet, it is such individuals who are more likely to decide to terminate pregnancy based on wrong information.

It is also possible that some women who are ambivalent about continuing their pregnancy seek a legitimate medical reason for termination. In both cases, accurate information will help the woman and her family to make a knowledgeable decision.

The Impact of Risk Perception on Women’s Decision to Continue Pregnancy

In an attempt to assess the relevance of the risk perception as measured by us in predicting women’s apparent decision about their pregnancy, we analyzed the 123 women who expressed a tendency of 50% or more to terminate their pregnancy between September 5, 1986 (the date the VAS was first introduced) and January 29, 1988 (Table 1).

TABLE 1 Study Population

Women who tended \geq 50% to terminate their pregnancy prior to information	123
Women who tended \geq 50% to continue their pregnancy	246
EXCLUSIONS	
Prospective cases (not yet pregnant)	5
Refusals to follow-up	3
Lost for follow-up	7
Had not reached EDC	30
STUDY COHORT (N=78)	
Decided to continue pregnancy (CP)	61^a
Decided to terminate (TA)	17

^aOutcome as follows: 57 normal infants, 4 miscarriages

At the time of the consultation all 123 women verbally expressed serious consideration of terminating their pregnancy and documented this on the VAS. Of these, the following were excluded from further analysis: 5 came for prospective advice and did not become pregnant until the analysis of the data; 3 refused to participate in the telephone follow-up; 7 could not be reached at the contact telephone numbers; and 30 had not yet reached their expected date of confinement (EDC). Thus, our study group consisted of 61 women who decided to continue their pregnancy despite their initial tendency and 17 who chose to terminate their pregnancy.

The two groups [continued pregnancy (CP), n=61, and therapeutic abortion (TA), n=17] did not differ statistically in their mean age, number of pregnancies, number of previous live births, therapeutic or spontaneous abortions, or number of exposures in the pregnancy of question, where "exposures" included every medical preparation, chemical, or radiation reported during the consultation.

The tendency to terminate pregnancy before receiving the relevant medical information did not differ significantly between the CP and TA groups ($34.3 \pm 2.5\%$ vs. $24.8 \pm 5.4\%$, respectively, $p>0.05$). Following the interview, however, there

was a highly significant difference in the response of the two groups: women who eventually terminated their pregnancies had a non significant increase in the tendency to continue pregnancy and in most cases did not pass the 50% point ($24.8 \pm 5.4\%$ to $45.1 \pm 9.8\%$) ($p>0.1$). Their tendency to terminate pregnancy after the counseling process was significantly different from the CP group ($p<0.0001$).

Of 61 women in the CP group, 4 had a miscarriage between 8 and 12 weeks of gestation. The other 57 women had normal pregnancy outcomes, with no apparent major malformations or developmental delay up to 9 months of postnatal age. Table 2 presents the analysis of the 17 women who chose to terminate their pregnancy. In two cases, women were exposed to drugs known to have adverse fetal outcome (BCNU for mycosis fungoides and warfarin for prosthetic valve), and in a third case an amniocentesis done because of maternal age (>35 years) tested positive for Down's syndrome.

Of interest, one woman exposed to non teratogens claimed in the follow-up interview that her decision to terminate pregnancy was based on the information she received during the Motherisk consultation; however, the summary letter sent to her physician clearly stated that she did not have an increased teratogenic risk. One woman attributed her decision to advanced age and poor gynecological history, and another had an increased genetic risk for major malformations. In two cases, the women claimed that their obstetricians encouraged them to terminate pregnancy owing to a high teratogenic risk (up to 80%) despite our advice of no such increased risk. Eight women who perceived their teratogenic risk as high despite our advice indicated that this was their main reason for termination; four of them were unmarried.

Of the 78 evaluable pregnancy patients who intended to terminate their pregnancy prior to our consultation, it is probable that we reversed the tendency in 61 (57 normal healthy babies and 4 miscarriages). Although it is impossible to prove that all these pregnancies would have been terminated without our intervention, it is conceivable that this might have been the case, since most women who showed a greater than 50% tendency to terminate pregnancy after our intervention eventually did so. The two groups,

TA and CP, did not differ in a large number of characteristics and had very similar rates of drug exposures. However, most of the 17 cases in the TA group expressed obvious explanations, unrelated to the exposures in question, as factors that led them to decide to terminate their pregnancy. Four of them were unmarried; in the analysis above we have shown that single mothers, despite estimating their teratogenic risk in a similar manner to married women, have a significantly higher tendency to terminate their pregnancy.

TABLE 2 Analysis of reasons for therapeutic abortion as indicated by the women

REASON	Number of Cases ^a
Exposure to drug with potential adverse fetal effect	2
Down's syndrome detected in amniocentesis	1
Advanced age with poor gynecological history	1
Higher genetic risk for major malformations	1
Advised to terminate pregnancy by obstetricians despite exposure to nonteratogens	2
Unmarried women	4
Fears of higher teratogenic risk despite Motherisk advice	8
Claimed termination was according to Motherisk advice (not confirmed by summary letter)	1

^aTotal exceeds 17 (the number of women who chose to terminate their pregnancy) because some women had more than one reason for termination

After confirming the clinical relevance of the VAS, we now use the information collected not only for epidemiological endpoints, but also for individual cases. For example, if after the interview the woman has a tendency of termination higher than 50%, it is probably that she will not continue her pregnancy. If we are impressed that the teratogenic risk is the main reason for her tendency, and not other social, psychological, or personal reasons, we extend the interview to explain again the lack of risk associated with her exposure. The same insight is

employed to counsel women exposed to teratogenic agents, if their perception does not reflect realization of an increased risk.

Empowering Pregnant Women to Take Medications

There are situations where women avoiding taking medications can have a major effect on their health, and even life-threatening. Such is the case with severe depression, where we have recently shown that appropriate counseling can empower the majority of depressed women who discontinued their psychotropic medications “cold turkey” to resume therapy. Prior to restarting their medications, many of the women had severe worsening of their symptoms.¹⁷

In a novel initiative, a Canadian manufacturer has introduced a silhouette of a pregnant woman as indicia to morning sickness tablets (Figure 4). In an observational, cross sectional study, perception of teratogenic risk among volunteer women was compared between a plain white tablet versus a white tablet with an image of a pregnant woman. The difference in teratogenic risk perception was highly significant ($p < 0.0001$). In the survey group of 132 pregnant women, the mean perception of teratogenic risk was decreased by 23.4% when viewing tablets imprinted with the image of a pregnant woman. (Unpublished data)

While these findings must await more studies in pregnant women, this may be an important means to increase compliance and hence effectiveness of medications in pregnancy, with a parallel decrease in morbidity and need for hospitalization.

FIG. 4 Example of indicia used on a tablet to encourage women to use the product in pregnancy



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