MOTHERISK ROUNDS

Diagnostic Radiation in Pregnancy: Perception Versus True Risks

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Abstract

Significant numbers of therapeutic abortions are performed for radiation-exposed pregnant women because of concerns about the teratogenic risk. However, available data suggest that current diagnostic radiation procedures are not teratogenic.

Résumé

Un nombre imposant d'avortements thérapeutiques sont pratiqués chez des femmes enceintes soumises à une radiothérapie en raison du risque de tératogénicité. Toutefois, les données disponibles suggèrent que les procédures diagnostiques courantes en matière de radiothérapie ne sont pas tératogéniques.

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CASE PRESENTATION

The following is not a single case counselled by Motherisk, but a composite that illustrates a typical presentation.

A 26-year-old woman, unaware of her pregnancy of seven weeks' gestation, had an upper gastrointestinal (GI) X-ray series to investigate epigastric pain. She had been on an oral contraceptive for more than two years. After pregnancy was diagnosed, she was told by the radiologist she should terminate the pregnancy because of a high likelihood of malformations. The obstetrician who was asked to perform the pregnancy termination indicated to the patient that this diagnostic procedure does not appear to cause malformations. Unconvinced, she asked to go ahead with the termination but agreed to be counselled by Motherisk. Motherisk calculated that the average fetal radiation exposure could be up to 1.1 mGy.[1] The radiologist in this case estimated it to be 0.9 mGy (1 Gy = 100 rads).

Key Words: Pregnancy outcome, ionizing radiation, imaging, induced abortion, abnormalities

DISCUSSION

It has been estimated that approximately 30 000 fertile women were exposed to an abdominal radiographic diagnostic procedure during the 1980s in the United States.[2] The Health Physics Society's website, Ask the Expert (ATE) receives 600 to 700 consultations each year concerning radiation exposure during pregnancy, obviously only a small sample of the number of occurrences. Newer radiological techniques such as computerized tomography (CT) and therapeutic uses of radiation and radionuclides can expose the fetus to greater than 50 mGy. Handbook 54 of the National Council on Radiation Protection (NCRP) established the 50 mGy level in 1977 for two reasons: first, that most diagnostic radiological procedures do not exceed 50 mGy, and second, that the threshold for birth defects during the most sensitive period of embryonic development is > 200 mGy.[3,4] Furthermore, protraction and fractionation of radiation decreases the radiation's teratogenic potential,[5,6] so that lengthy procedures, multiple procedures separated by hours or days, or use of radionuclides have a lower reproductive risk than an acute exposure.[4]

The Motherisk Study

A cohort of pregnant Canadian women who contacted the Motherisk program between 1999 and 2002 inquiring about exposure to a radiographic diagnostic procedure underwent prospective follow-up.[7] They were exposed to various radiographic diagnostic procedures that involved ionizing radiation. Excluded from the study were women exposed to radiation therapy for conditions such as cancer or for

Table 1. Average fetal dose from X-ray procedures (from Health Canada)[1]

Diagnostic study type	Average dose (mGy)	Diagnostic study type	Average dose (mGy)
Dental	< 0.01*	Barium meal (upper GI fluoroscopy)	1.1
Chest	< 0.01	Barium enema (fluoroscopy)	6.8
Mammography	< 0.05*	Head CT	< 0.005
Pelvis	1.1	Chest CT	0.06
Abdomen	1.4	Lumbar spine CT	2.4
Lumbar spine	1.7	Abdominal CT	8.0
Natural background radiation (entire pregnancy)	0.5*	Pelvis CT	25

*Estimates made by Health Canada.

CT: Computerized tomography.

Table 2. Characteristics of pregnant women who were exposed to a radiographic diagnostic procedure and their controls

Variable	Radiation (n = 198)	Control (n = 198)	*P*
Mean maternal age (years) ± SD	32.1 ± 5.2	32.0 ± 4.8	0.81
Gravidity (mean ± SD)	2.57 ± 1.7	2.36 ± 1.8	0.72
Parity (mean ± SD)	1.97 ± 1.3	1.96 ± 0.8	0.35
Weight gain (mean ± SD)	14.71 ± 8.6	15.26 ± 9.8	0.64
Delivery method			
Vaginal	125 (71.8%)	134 (69.8%)	0.75
Caesarean section	33 (19%)	33 (17.2%)	0.76
Vaginal w/assist	16 (9.2%)	25 (13%)	0.32

SD: Standard deviation.

thyroid ablation therapy, as well as women simultaneously exposed to known teratogenics (e.g., anticonvulsants, heavy use of alcohol or tobacco, or retinoids).

The primary outcome measure of the study was the frequency of major birth defects, defined as structural abnormalities requiring surgical or cosmetic correction or functional abnormalities with major impact on a child's life quality.[8] Details of radiation exposure included the type, location, gestational age at the time of the procedure, indication, number of sessions, and the use of protective shielding.

Data on radiation dose were taken from Health Canada guidelines[1] where average values of fetal dose are presented for different types of procedures (Table 1). Each value assumes the actual amount of radiation, taking into account an average number of exposures.

Data from a control group were retrieved from the Motherisk database and compared with data from the selected cohort. The women in the control group were not exposed to a radiographic diagnostic procedure, cancer therapy, thyroid ablation, or any other teratogen during pregnancy and were queried by Motherisk on exposure to non-teratogenic medications. This group of women was matched with the radiation-exposed group for maternal age, gravidity, and parity.

Characteristics of pregnant women who were exposed to a radiographic diagnostic procedure and of their controls are shown in Table 2. We completed follow-up on 198 women who were exposed to radiographic diagnostic procedures in their pregnancy. Most (77.2%) of the diagnostic imaging procedures were performed in the first trimester of pregnancy.

Radiation data

The fetal dose (average ± standard deviation) following exposure to a radiographic diagnostic procedure was 2.3 ± 0.59 mGy (range 0.01–68.0 mGy). The average gestational age of exposure was 9.1 ± 0.7 weeks (range 1–38 weeks). The average number of views per pregnancy was 2.7 ± 0.2

Table 3. Radiation data

		Number (% within group)
Diagnostic study type	Dental	100 (50.8)
	Chest	31 (15.7)
	Mammography	8 (4.0)
	Upper GI fluoroscopy	6 (3.0)
	Barium enema	2 (1.0)
	Abdomen	7 (3.5)
	Lumbar spine	15 (7.6)
	IVP	1 (0.5)
	Pelvis	1 (0.5)
	Head and neck CT	10 (5.1)
	Extremities CT	11 (5.6)
	Abdominal CT	4 (2.0)
	Lumbar spine CT	1 (0.5)
	Non-specified	1 (0.5)
Indication (n = 196)	Pain	98 (50.0)
	Routine	86 (43.9)
	Infection	8 (4.1)
	Combination	4(2.0)
Multiple X-ray views	Yes	120 (60.6)
	No	78 (39.4)
Shielding (n = 188)	Yes	165 (87.8)
	No	23 (12.2)

CT: Computerized tomography.

(range 1–20 views), and 89.8% of the views were obtained in one session. The radiation data are shown in Table 3.

No direct exposure to the embryo or fetus occurred in 149 of the patients out of the 198 who sought counselling. However, even dental X-rays expose the embryo to very low doses from scatter radiation.

Pregnancy outcome

The reported major anomalies in the radiation and control groups are listed in Table 4. All newborns with major birth defects were exposed to a dose of less than 0.1 mGy.

Eleven women in the radiation-exposed group chose to terminate pregnancy compared with none in the control group. Six of those women stated that they terminated their pregnancy because of radiation ($P = 0.04$). These women were exposed in the first trimester to a radiographic diagnostic procedure involving radiation level of 0.01–5.6 mGy. None of them had an underlying condition that indicated a termination was medically appropriate. The outcomes of pregnancies in the exposed and control groups are shown in Table 5. The rate of major anomalies among offspring of women who were exposed to radiation in the first trimester was 2.6% versus 3% in the control group.

A subgroup analysis of patients exposed to a relatively low dose of radiation (≤ 1.0 mGy) versus a higher dose (≥ 1.1 mGy) was performed (Table 6). The reason for this cut-off point was apparent dose exposure distribution. The high-dose group had significantly more miscarriages (18.6%) than the low-dose group (2.6%). However, logistic regression revealed that the only parameter that was significantly associated with miscarriage rate was the mothers' gestational age of contact with Motherisk. Mothers in this subgroup who were exposed to a higher dose contacted Motherisk earlier in pregnancy than the low-dose group, suggesting that the high-dose group were observed over a longer period of time with more potential for miscarriage.

No anomaly was observed in the high-dose group. The rate of live births was significantly higher in the low-dose group, probably because of the high rate of miscarriages.

Exposure to a radiographic diagnostic procedure during the first trimester of pregnancy led six out of 149 women (4%) to choose to terminate an otherwise wanted pregnancy.

Table 4. Major congenital anomalies in the radiation-exposed and control groups

Group	Type of anomaly	Magnitude and timing of exposure	Procedure
Radiation*	Trisomy 18	0.04 mGy week 1	Extremities X-ray
Radiation	Extra toe	0.01 mGy week 3	Head CT
Radiation	Pyloric stenosis	0.06 mGy week 4	Extremities X-ray
Radiation	Down syndrome	0.06 mGy week 14	Dental X-ray
Control	Cleft palate	–	–
Control	Club foot	–	–
Control	Inguinal hernia surgically corrected	–	–
Control	ventricular septal defect	–	–
Control	Undescended testes surgically corrected	–	–
Control	Pyloric stenosis	–	–

*Major anomalies that were observed in first trimester exposure to radiation (n = 149).

CT: Computerized tomography.

Table 5. Pregnancy outcomes of women exposed to radiation versus controls

Variable	Radiation	Controls	*P*
Live births	173/198	192/198	0.001
Miscarriages	12/198	6/198	0.23
Elective termination	11/198	0/198	0.001
Elective termination due to radiation	6/198	0/198	0.04
Stillbirth/Fetal death	2/198	0/198	0.48
Major malformations*	4/149	6/198	0.79
Birth weight (g) ± SD	3498 ± 566	3515 ± 605	0.79
Prematurity	12/173	24/190	0.1

*Only those who were exposed in the first trimester.

SD: Standard deviation.

Those women were reassured by Motherisk counsellors during positively framed advice that no harm was expected to their fetus following such a low dose of radiation. Moreover, in this cohort, the rate of major anomalies was within the anticipated range of 1% to 3% and similar to the rate of major anomalies in the matched control cohort. Other outcome measures of this study were also similar between the two groups. Subgroup analysis of the radiation-exposed group did not show any adverse effect following a higher radiation dose.

To date, guidelines regarding radiation exposure in pregnancy rely mostly on animal studies and extrapolation of data retrieved from years of research on survivors of atomic bomb detonations. Because of the fear of radiation, women tend to misinterpret the risk of teratogenicity and overestimate an effect on the fetus even when reassuring evidence-based data are provided for them.[9,10] Animal studies dealing with the reproductive effects of ionizing radiation are significantly different from teratology studies in animals using drugs and chemicals.[3,4,11–16] Drugs and chemicals have to be absorbed, possibly metabolized, and transported via the placenta to the implantation site, embryo, or fetus. There can be species differences in mammals for each of these functions. Ionizing radiation, on the other hand, has its effect directly on the fetus. There are no concerns about differences in metabolism, absorption, or placental transfer between an animal model and the human. Many studies indicate that deleterious effects including birth defects occur only if the fetus is irradiated.[11,17–22]

The United States National Council on Radiation Protection (NCRP) states that a radiation exposure of less than 50 mGy has no measurable increased reproductive effect on the fetus.[4,11,23] However, clinical studies examining the actual effect of low-dose radiation associated with

Table 6. Subgroup analysis of radiation-exposed women with low-dose versus high-dose diagnostic radiation exposure

Variable	≤ 1.0mGy (n = 151)	≥ 1.1mGy (n = 43)	*P*
Live births	137 (90.7%)	32 (74.4%)	0.01
Elective termination	5 (3.3%)	0	0.51
Elective termination due to radiation	4 (2.6%)	2 (4.6%)	0.96
Miscarriages	4 (2.6%)	8 (18.6%)	< 0.001*
Stillbirths	1 (0.7%)	1 (2.3%)	0.92
Major anomalies†	4 (2.6%)	0	0.64

* Gestational age at first maternal contact was significantly earlier in higher exposed group.

† Major anomalies that were observed in first trimester exposure to radiation.

radiological diagnostic procedures were rarely performed. Kinlen and Acheson who studied this issue did not find an increased rate of malformations or spontaneous abortions.[24] In contrast, Jacobsen and Mellemgaard reported some eye anomalies in children exposed in utero to low-dose radiation.[25] Bohnen and colleagues showed an association of decreased head circumference with low-dose radiation (< 3 mGy) in the second and third trimesters.[26]

There are significant differences in radiation dose depending on techniques and equipment. For example, fluoroscopy time (usually recorded by the technician) may vary, as may the use of digital radiography equipment. These variables were not available to us.

The tendency to misinterpret the risk of drug teratogenicity and overestimate a drug effect on the fetus even when reassuring data are available is also shown to be the case with respect to very mild alcohol drinking[10] and cocaine use.[27] The misperception of teratogenic risk was investigated by Motherisk with respect to diagnostic radiation in 1991.[28] Regardless of reassuring information and a position statement from an authoritative agency in the US,[23] the fear of harm from low-dose radiation exposure in pregnancy still exists.

A large number of animal studies indicate that the reproductive effects of teratogenesis, growth retardation, embryonic death, and stillbirth are deterministic effects (threshold effects) and that the threshold for these effects are 200 mGy at the most sensitive period of mammalian embryonic development (22nd–40th day postconception in the human). The threshold for these effects is even higher beyond the period of early organogenesis. This means that the 50 mGy limit set by the NCRP is very conservative and that exposures between 50 mGy and 100 mGy, for example, are also without measurable reproductive risks.[3,29] Other confounders might come into play and affect the rate of major malformations and the mother's decision to terminate pregnancy. Other possible effects of radiation, including minor malformations and effects on neurodevelopment, were not assessed in this study.

Lack of information among the public regarding the safety of low-dose radiation exposure may lead to misperception of the risk and to termination of an otherwise wanted pregnancy. Motherisk patients were reassured during counselling. It is conceivable that the rates of pregnancy termination are higher among pregnant women who do not receive appropriate counselling. Therefore, an attempt should be made to increase awareness of the safety associated with low-dose radiation, and thus to prevent termination of otherwise wanted pregnancies.

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