MOTHERISK UPDATE

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Cancer chemotherapy during pregnancy

Consortium of Cancer in Pregnancy Evidence

ABSTRACT

QUESTION I have an 8-weeks' pregnant patient who was diagnosed with stage III Hodgkin's disease last week. The oncologist suggests delaying chemotherapy until the second trimester. What are the effects of chemotherapy on a fetus after the first trimester? Where can I find reliable information on the subject?

ANSWER Available data suggest that exposure to chemotherapy during the first trimester of pregnancy is associated with increased risk of major malformations. Exposure during the second and third trimesters does not result in major malformations, but could have nonteratogenic effects, such as low birth weight. The brain develops throughout pregnancy, and it could be affected later in pregnancy.

RÉSUMÉ

QUESTION On a diagnostiqué la semaine dernière la maladie de Hodgkin au stade III chez une de mes patientes enceinte de huit semaines. L'oncologue suggère de retarder la chimiothérapie au deuxième trimestre. Quels sont les effets de la chimiothérapie sur un fœtus après le premier trimestre? Où puis-je trouver des renseignements fiables à ce sujet?

RÉPONSE Les données disponibles font valoir que l'exposition à la chimiothérapie durant le premier trimestre de la grossesse est associée à un risque accru de malformations majeures. L'exposition durant le deuxième et le troisième trimestres ne se traduit pas par d'importantes malformations, mais pourrait comporter des effets tératogènes, comme un faible poids à la naissance. Étant donné que le cerveau se développe durant toute la grossesse, il pourrait être affecté plus tard durant la grossesse.

Diagnosis of cancer during pregnancy is one of the most extreme scenarios in medicine: the creation of a new life might coincide with the mother's death. This situation can put immense stress on pregnant patients, their families, and medical staff. Cancer occurs only rarely during pregnancy; incidence is 0.07% to 0.1%.[1] The current trend to defer pregnancy until later in life might lead to increased incidence of cancer during pregnancy. There is, however, very little information on the effect of pregnancy on cancer and the effects of cancer and its therapy on pregnancy outcome.[2,3] Because chemotherapeutic agents in current use have substantially increased longevity and survival, it is important that physicians ensure optimal treatment for mothers without harming their fetuses.

Most chemotherapeutic agents have been shown to damage rapidly dividing cells, such as bone marrow, intestinal epithelium, and reproductive organs. Animal studies suggest that a fetus would be similarly affected by these agents because fetal tissues have a high growth rate. This damage could result in spontaneous abortions or malformations.[4]

Chemotherapeutic drugs are potent teratogens. Currently, there is very little information on the effect of cancer chemotherapy on fetuses.[5] The risk of malformations when chemotherapy is administered during the first trimester has been estimated at 10% for single-agent chemotherapy and at 25% for combination chemotherapy.[6,7] Thus, chemotherapeutic agents should be avoided during the first trimester.

There is no evidence of increased risk of teratogenesis during the second and third trimesters.[5] A recent report on a small series of breast cancer patients confirmed, prospectively, that chemotherapy is effective and safe when administered after the first trimester.[8] The long-term nonteratogenic

Do you have questions about the safety of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at (416) 813-7562; they will be addressed in future Motherisk Updates. Published Motherisk Updates are available on the College of Family Physicians of Canada website (**www.cfpc.ca**). Some articles are published in *The Motherisk Newsletter* and on the Motherisk website (**www.motherisk.org**) also.

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effects of chemotherapy remain largely unknown. There have been reports of increased risk of stillbirth, low birth weight, and intrauterine growth retardation following treatment in the second and third trimesters.[5,9]

When chemotherapy is administered during pregnancy, delivery of the infant should be timed to avoid the worst chemotherapy adverse effects (ie, on blood cells) and their associated problems. Only a few reports associate chemotherapy administered to a mother with hemopoietic depression in her infant. Hemopoietic depression is self-limiting, but it increases the risk of neonatal infection and hemorrhage.[10]

The very limited available information does not suggest that children born to mothers treated with chemotherapy during pregnancy have impaired mental or physical development or will be infertile.[11] Incidence of second malignancies in these children should be evaluated. To date, only a single case report describes the occurrence of multiple malignancies in the son of a patient with acute lymphocytic leukemia who was exposed in utero to cyclophosphamide and steroids. His twin sister was not affected.[12] Antineoplastic agents administered systemically might reach clinically significant levels in breast milk, so breastfeeding is contraindicated.[13,14]

Use of cytotoxic immunosuppressive drugs for disorders other than cancer is increasing rapidly. These drugs are currently used for rheumatic disorders (especially in young women), after organ transplantation, and for other conditions. When these medications are used for non-malignant conditions, they are used at lower doses than for treating tumours. Alkylating agents (mainly cyclophosphamide) and antimetabolites (6-mercaptopurine and azathioprine) are often used for these conditions.[15]

Although there are some controlled studies on the effects of chemotherapy on fetuses, most literature is based on either case reports or small, uncontrolled series. In an attempt to close the gap and overcome some of the difficulties faced by physicians taking care of pregnant women with cancer, Motherisk has established the Consortium of Cancer in Pregnancy Evidence (CCoPE), an international group of oncologists, obstetricians, pediatricians, pharmacologists, geneticists, and specialists in related fields. The CCoPE has developed up-to-date, evidence-based information on diagnosis, management, prognosis, and effect on fetal outcome of cancer during pregnancy. This information is available in a new section of the Motherisk website at **www.motherisk.org**.

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