Best Practice & Research Clinical Obstetrics and Gynaecology 33 (2016) 86–101

Contents lists available at ScienceDirect

Best Practice & Research Clinical Obstetrics and Gynaecology

journal homepage: www.elsevier.com/locate/bpobgyn

2

Chemotherapy in pregnancy

Siew-Fei Ngu, MBBS, MRCOG, Clinical Assistant Professor *, Hextan Y.S. Ngan, MD, FRCOG, Professor

Department of Obstetrics and Gynaecology, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Keywords:
chemotherapy
pregnancy
cancer
malformation

Cancer diagnosed during pregnancy is uncommon, complicating between 0.02% and 0.1% of all pregnancies. Nonetheless, due to increasing age of childbearing, the incidence of cancer during pregnancy is likely to increase due to higher incidence of several age-dependent malignancies. The most common malignancies include breast cancer, cervical cancer, malignant melanoma and lymphoma. One of the key challenges in the management of cancer in pregnancy is treating the women with standard chemotherapy regimen, without compromising the safety of the developing foetus. Exposure of chemotherapy in the first trimester is associated with an increased risk of major birth defects, whereas use in the second and third trimesters is associated with intrauterine growth restriction, low birthweight and stillbirth. In this article, we review available data regarding the use of chemotherapeutic agents in pregnancy, and we summarise the neonatal outcomes, including malformations, perinatal complications and long-term follow-up. In addition, the management plan during pregnancy is also discussed.

Introduction

Cancer diagnosed during pregnancy is uncommon, complicating between 0.02% and 0.1% of all pregnancies [1,2]. Nonetheless, due to increasing age of childbearing, the incidence of cancer during pregnancy is likely to increase due to higher incidence of several age-dependent malignancies. The

* Corresponding author. 6/F Professorial Block, Department of Obstetrics and Gynaecology, The University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong Special Administrative Region. Tel.: +852 2255 3111; Fax: +852 2855 0947.

E-mail addresses: ngusiewf@hku.hk (S.-F. Ngu), hysngan@hku.hk (H.Y.S. Ngan).

http://dx.doi.org/10.1016/j.bpobgyn.2015.10.007
1521-6934/

most common malignancies diagnosed in pregnancy include breast cancer, cervical cancer, malignant melanoma and lymphoma [2–4], accounting for about 70–80% of pregnancy-associated tumours [5,6]. Other cancers that have been reported included mainly leukaemia, ovarian cancer and thyroid cancer.

Diagnosis of cancer during pregnancy poses a great challenge to the pregnant women, her family and the medical team. The benefits of cancer treatment for the women and the potential adverse effects to the developing foetus must be carefully considered before commencing treatment. Nonetheless, the health and interests of the women should usually prevail over that of her foetus. Some women may decline treatment even in life-threatening situations due to concern for adverse effects of the treatment on their foetus. Therefore, it is paramount that the women and her family be provided with adequate information, support and sufficient time to allow informed decision.

In order to minimise the risk of foetal exposure, comprehensive and updated information about pregnancy-related risks must be conveyed to women undergoing cancer treatment. As approximately 50% of pregnancies are unplanned, they would have been exposed to the teratogens by the time the pregnancy is confirmed [7]. Therefore, women who are diagnosed with cancer during their reproductive years should be counselled about the use of effective contraception to avoid unplanned pregnancy. Moreover, health-care providers including the woman's family physicians, oncologists, haematologists, obstetricians and gynaecologists should actively initiate discussions regarding the women's sexual activity and pregnancy intention, and to avoid any assumptions about the women's pregnancy plans. For women who are contemplating pregnancy, detailed information should be given on potential teratogenic and reproductive risks associated with the use of antineoplastic drugs in pregnancy.

There are controversies concerning whether pregnancy alters the prognosis of cancer. Several studies have reported that pregnant women tend to have a worse outcome than non-pregnant women [3,8]. Some have suggested that the changes in hormonal status during pregnancy may adversely affect outcome. However, according to the literature available, it appears that pregnancy does not have a significant adverse effect on maternal survival when compared with non-pregnant women [2]. In this article, we review available data regarding the use of chemotherapeutic agents in pregnancy, and we summarise the neonatal outcomes, including malformations, perinatal complications and long-term developmental follow-up. In addition, the management plan during pregnancy is also discussed.

Teratology

Teratogenesis is defined as the process by which congenital malformations are produced in an embryo or a foetus. Generally, exposures that cause irreversible damage to the structure, function or normal development of an embryo or a foetus are teratogenic [9]. Teratogens include environmental factors such as radiation, therapeutic drugs such as thalidomide, chemicals such as alcohol and certain viruses such as rubella [10]. Teratogenic effects can be variable in range and severity, and they comprise death (miscarriage or stillbirth), malformations, impaired organ function and impaired fertility [7]. In the general population, congenital abnormalities including defects in the structure or function of an organ occur in 1–3% [10]. Among the major abnormalities, around 25% are due to genetic factors and 65% are due to unknown factors. Defects that are associated with drug treatment account for only 2–3% of the abnormalities [7].

The teratogenicity of a drug is influenced by many factors, such as the timing of exposure, the dose administered, the extent of placental transfer and the duration of exposure. In addition, genetic variability in drug metabolism of the mother and the foetus might explain the different susceptibility of people to the same drugs [11]. In order for the teratogens to result in adverse foetal outcomes, there must be significant amounts reaching the foetus during the critical time period. The majority of drugs reach the foetus through the maternal bloodstream, and the transfer of drugs from the mother to the foetus is enhanced where there is high lipid solubility, loose binding to plasma protein and low molecular weight [11].

Critical periods in prenatal development

The gestational age when exposure occurs is important because the effect exerted by a teratogen is determined by the developmental stage.