Critical Reviews in Oncology/Hematology 104 (2016) 52–64

Contents lists available at ScienceDirect

Critical Reviews in Oncology/Hematology

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

Management of hemopoietic neoplasias during pregnancy

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Contents

ARTICLE INFO

Article history:
Received 27 July 2015
Received in revised form 12 March 2016
Accepted 10 May 2016

ABSTRACT

Hemopoietic neoplasias are unique cancers generally affecting bone marrow, and requires a special attention for disease control and also their complications. When these neoplastic disorders accompany to pregnancy there are many risks both for mother and foetus. Diagnostic difficulties due to the limited use

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http://dx.doi.org/10.1016/j.critrevonc.2016.05.006

Keywords:
Hemopoietic neoplasia
Pregnancy
Chemotherapy
Radiation therapy
Supportive care
Leukemia
Lymphoma
Myeloproliferative neoplasia
Fertility preservation

of imaging modalities is essential in pregnant women. On the other hand suboptimal using of the anti-neoplastic drugs and their higher toxicity in mother and foetus must be considered in the management of these neoplastic disorders. Due to the lack of therapeutic guidelines in these cases, team approach is essential and therapy requires to the use the art of medicine.

1. Introduction

Hemopoietic neoplasia (HN) during pregnancy causes severe risks for mother and foetus. Diagnosis is difficult due to the overlap of disease and pregnancy related symptoms and relatively limited use of imaging modalities in pregnant women (Brenner et al., 2012; Lavi et al., 2014). On the other hand, data about the toxicity and the efficacy of anti-neoplastic chemotherapy (ANC) in cases with HN accompanying pregnancy is retrospective (Brenner et al., 2012).

Management of medical problems during pregnancy is complex, has challenges and requires skill and to use the art of medicine. Essential point is to provide a balance between to maximize the cure chance and survival of the mother and to minimize the treatment related toxic effects to the foetus and also if possible for future pregnancies (McGregor and Das-Gupta, 2015; Rizack et al., 2009). However primary goal of the treatment must be health of the mother. For this reason, termination of the pregnancy is the most important choice in early trimester to allow the adequate therapy for mother. In 2nd and 3rd trimester ANC is generally reasonable in spite of some risks (Brenner et al., 2012; Lavi et al., 2014). It is very well known that human physiology changes during pregnancy and pregnant patients are almost excluded from standard clinical trials. Therefore specific interventions have been extrapolated from the non-pregnant population. In this situation maternal health is essential importance, but the health of foetus should be considered. It must not be forgotten that child is the priority of the mother (McGregor and Das-Gupta, 2015).

2. The influence of physiologic changes during pregnancy on pharmacokinetics of chemotherapy

Early gestation is the time of conception until somatic formation (up to 3 weeks from conception). Embryonic period, between weeks 2 and 8 after conception (4–10 weeks after the 1 st day of last period) is critical for organogenesis and embryo is most sensitive to ANC in this period (Koren and Lishner, 2010).

Physiologic changes developing in pregnancy have been shown in Table 1. Of course increase in plasma volume and changes in hepatic and renal functions affect the pharmacokinetics of the drugs (Weisz et al., 2004; Cardonick et al., 2010). ANC can inhibit the migration and proliferation of trophoblasts in 1 st trimester in human placenta. This may cause to low birth weight (LBW) babies and close monitoring of the foetus whose mother receiving ANC is mandatory (Brenner et al., 2012).

3. Decisions for the management of the pregnant woman with hemopoietic neoplasia

Management of the pregnant woman with HN requires multidisciplinary team approach and good collaboration. This team must cover the hemato-oncologist, obstetrician, neonatologist, clinical nurse specialist and anaesthesist (Ali et al., 2015). Fig. 1 shows the team members managing pregnant woman with HN. This team must be familiar with the effect of maternal neoplasia and ANC on the foetus for a successfull outcome of the mother and baby. On the other hand all the team members must be keep in mind the preferences of patient and her family (Lavi et al., 2014; Rizack et al., 2009; Eyre et al., 2015). However this is not an easy job, ethical dilemmas may cause anxiety both for pregnant woman and also for treating physicians (Eyre et al., 2015). Key points for clinical decision have been shown below.

Table 1
Physiologic changes in pregnancy.

*Increase in plasma volume
*Amniotic fluid as third space
*Hepatic oxidation
*Decreased albumin
*Enhanced hepatic detoxification of drugs
*Increased hepatic clearance
*Diminished gastric motility
*Increased renal clearance

Key points for clinical decision
• Natural history of the disease,
• Wishes and expectations of the mother,
• Local and general ethical issues,
• Physiological and religious beliefs,
• Personal and social security status.

Therapy should be similar to that of non-pregnant women but some factors are important in decision making: 1-Gestational age, 2-stage of the HN, 3-nature of the disease (aggressive, indolent), 4-choice/priority of the pregnant woman (Lavi et al., 2014).

Detrimental effects of the ANC on the foetus are; 1-fetal demise, 2-congenital malformations, 3-carcinogenesis, 4-intrauterine growth restriction (IUGR), 5-mental retardation. All of these factors must be reviewed and therapy of pregnant woman with HN should be personalized (Lavi et al., 2014; Rizack et al., 2009). Data about the management of HN in pregnancy is limited and we need international collaboration to reach more useful strategy for these patients. Regular obstetric and hematological evaluation are mandatory in pregnant cases with HNs. Ultrasound scans to detect fetal development is safe and practical tool (Ali et al., 2015).

4. Incidence-epidemiology-etiology

Cancer (Ca) is diagnosed in 0.1% of pregnancies and is the second most common cause of maternal death after gestation related vascular events. It has been thought that the prevalence of Ca will be increased in near future due to the older age for pregnancy, especially in developed countries. Solid tumors are more commonly seen in pregnant women compared to HNs. The most commonly seen 3 malignancies in pregnant women are breast Ca, cervical Ca and malignant melanoma, and these are followed by lymphomas and acute leukemias. Thirty years ago non-Hodgkin lymphoma (NHL) in pregnancy has been estimated as 0.8 cases per 100.000 pregnancies. In recent years NHL has been reported in 1–5