The prescription of anthracyclines during pregnancy in haematology: case reports and literature review

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Introduction

- Anthracyclines is one of the most important group of drugs used nowadays in cancer chemotherapy.
- Chemotherapy is essential in the management of haematological malignancies.
- When acute leukemia (AL), aggressive non-Hodgkin lymphoma (NHL) or Hodgkin lymphoma (HL) occurs during pregnancy, chemotherapy is an emergency but fetal risk must be considered.

» Our objective is to evaluate fetal and maternal outcomes associated with anthracyclines prescriptions in pregnant women with haematological malignancies.

Materials and Methods

- Literature review was performed in Pudmed and Embase databases until May 2012
  - keywords: pregnancy, acute leukemia, Hodgkin lymphoma, non-Hodgkin lymphoma, cancer chemotherapy, doxorubicin, daunorubicin and idarubicin
  - selection criteria of articles: diagnosis of haematological malignancy and anthracycline prescription during pregnancy, fetal outcome
- Cases of pregnant women with AL, NHL or HL treated by anthracyclines were collected from Teratogenic Agent Information Centre (CRAT), a French reference centre providing specialized information for clinicians about drug use in pregnancy.

Results

- Literature review: 81 articles

134 cases of pregnant women with haematological malignancies treated by anthracyclines during pregnancy

<table>
<thead>
<tr>
<th>Haematological malignancy</th>
<th>Prescribed anthracycline at standard dosage</th>
<th>Trimester of treatment/exposure initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL</td>
<td>Doxorubicin n=69</td>
<td>1st trimester n=30, 2nd trimester n=69, 3rd trimester n=2</td>
</tr>
<tr>
<td>NHL</td>
<td>Daunorubicin n=40</td>
<td>1st trimester n=9, 2nd trimester n=27, 3rd trimester n=12</td>
</tr>
<tr>
<td>HL</td>
<td>Idarubicin n=25</td>
<td>1st trimester n=1, 2nd trimester n=3, 3rd trimester n=11</td>
</tr>
</tbody>
</table>

Normal neonatal outcomes (100/134)

- Depending on haemopathy
  - NHL: 90% normal newborns
  - HL: 85% normal newborns
  - AL: 84% normal newborns

- Depending on anthracycline
  - Doxorubicin 68% normal newborns
  - Daunorubicin 80% normal newborns
  - Idarubicin 40% normal newborns

- Depending on trimester
  - 1st trimester: 5% normal newborns
  - 2nd trimester: 77% normal newborns
  - 3rd trimester: 78% normal newborns

Maternal outcomes

- 77% remissions
- 7% progressions, relapses or deaths
- 16% unknown

Fetal toxicities (34/134)

- 20 deaths
- 8 growth retardations
- 6 congenital abnormalities

- only idarubicine was associated with fetal cardiomyopathy

Case reports from CRAT

5 cases of pregnant women with haematological malignancies treated by anthracyclines

- chemotherapy in early 3rd trimester
- doxorubicin or daunorubicin at standard dosage
- 5 normal newborns (but 2 preterms)
- 3 maternal complete remission
  (2 unknown maternal outcomes)

Conclusions

Embryo-fetal toxicity depends on gestational age, anthracycline and haematological malignancy.

- 2nd or 3rd trimester exposures were mainly associated with favorable neonatal outcomes.
- Idarubicin was specifically associated with risk of fetal cardiotoxicity, probably due to its lipophily, facilitating placental transfer.
- Unfavorable fetal outcomes more frequent in AL compared to lymphomas (NHL, HL), probably reflect that chemotherapy can never be delayed post partum in AL.

» Anthracyclines prescription for haematological malignancies is possible in 2nd and 3rd trimesters of pregnancy with minimal risk to the developing fetus and then must be conducted by a multidisciplinary team.