Parenthood with Exposure to Mycophenolic Acid Products

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Abstract

Successful pregnancy outcomes have been reported in all solid-organ transplant recipients on a variety of immunosuppressive medication regimens. In October 2007, the FDA pregnancy category of mycophenolic acid products (MPA) was changed from category C to D, based on registry and post-marketing data which revealed a higher incidence of spontaneous abortions and structural birth defects. The purpose of this abstract is to describe pregnancy outcomes with exposure to MPA and pregnancies fathered by male transplant recipients conceived while taking MPA. Data were collected by the National Transplantation Pregnancy Registry (NTPR) via questionnaires, telephone interviews, and medical records. There were 152 conceptions in female recipients with exposure to MPA (discontinued <6 wks prior to conception or with use during pregnancy). Outcomes included: 78 live births, 70 spontaneous abortions, 3 stillbirths and 1 therapeutic abortion. Among the live births, there were 14 malformations reported for an incidence of (18%) compared to the incidence of malformations in transplant recipients not exposed to MPA, which is approximately 4.9%. There were 146 male recipients who have fathered 199 pregnancies with 202 outcomes (including twins). Outcomes included: 188 live births, 14 spontaneous abortions, and no therapeutic abortions or stillbirths. Among the live births there were 6 malformations reported, for an incidence of 3.2%. Conclusions: Reports to the NTPR reveal an increased incidence of non-viable outcomes and a pattern of structural malformations in pregnancies exposed to MPA in female transplant recipients compared to those without exposure to MPA. Those pregnancies fathered by male recipients appear similar to that of the general population. Healthcare providers are encouraged to report all pregnancy outcomes in transplant recipients to the NTPR.

Background

In October 2007, the FDA pregnancy category of mycophenolic acid products (MPA) was changed from category C to D, based on registry and post-marketing data which revealed a higher incidence of spontaneous abortions and structural birth defects.

Purpose

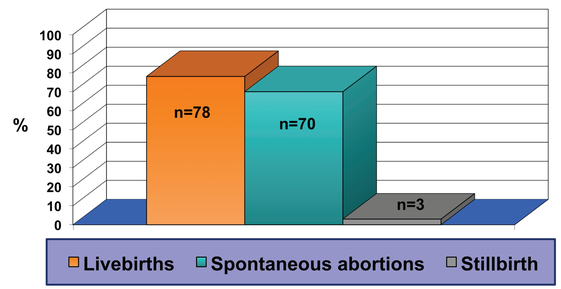
The purpose of this study was to describe pregnancy outcomes with exposure to MPA and pregnancies fathered by male transplant recipients conceived while taking MPA.

Methods

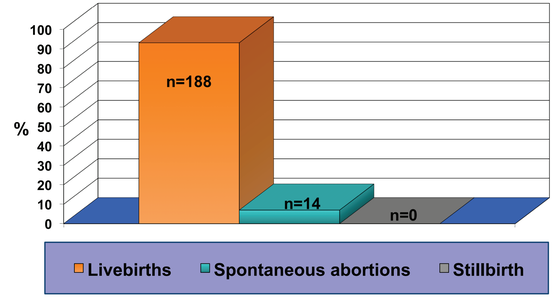
Data were collected via questionnaires, telephone interviews, and medical records.

Pregnancy Outcomes

152 conceptions in Female Transplant Recipients with Exposure to MPA (discontinued <6 wks prior to conception or with use during pregnancy)



146 Male Recipients who Fathered 199 Pregnancies with 202 Pregnancy Outcomes



Structural Malformations Female Recipients Exposed to MPA - Heart

Case	Malformations	Infant Death	Maternal Regimen
1	Facial malformations	N	MMF and Gengraf®
2	Duodenal atresia, atrioventricular canal defect and tetralogy of fallot	N	MMF and TAC
3	Bicuspid aortic valve	N	MMF and TAC
4	Laryngomalacia	N	EC-MPS, TAC, Pred

Structural Malformations Female Recipients Exposed to MPA - Liver

Case	Malformations	Infant Death	Maternal Regimen
1	Total anomalous pulmonary venous return	N	MMF and Neoral®
2	Multiple anomalies (heart lesions, cleft lip and palate, microtia)	Y (neonate)	MMF and TAC
3	Multiple anomalies (congenital heart disease, microtia, bilateral cleft lip)	Y (infant)	MMF, TAC, Pred

Structural Malformations Female Recipients Exposed to MPA - Kidney

Case	Malformations	Infant Death	Maternal Regimen
1	Hypoplastic nails, short fifth fingers	N	MMF, TAC, Pred
2	Cleft lip and palate, microtia	N	MMF, TAC, Pred
3	Syndactyly, microtia	N	MMF, TAC, Pred
4	Microtia type III	N	MMF, TAC, Pred
5	Ventricular septal defect	N	MMF, TAC, Pred
6	Multiple anomalies (diaphragmatic hernia, undeveloped right lung)	Y (neonate)	EC-MPS, TAC, Pred
7	Multiple anomalies (cleft lip and palate, microtia, congenital heart defects)	Y (neonate)	MMF, TAC, Pred

Structural Malformations Fathered Pregnancies with Exposure to MPA

Case	Malformations	Infant Death	Paternal Regimen
1	Tongue-tied	N	MMF, TAC
2	Ventricular septal defect	N	MMF, CsA, Pred
3	Diaphragmatic hernia	Y (neonate)	EC-MPS, TAC, Pred
4	Pyloric stenosis	N	MMF, TAC
5	Club foot	N	MMF, TAC
6	Prader- Willi syndrome, tongue tied	N	MMF, TAC, Pred

Abbreviations

MMF = mycophenolate mofetil
TAC = tacrolimus
Pred = prednisone
EC-MPS = enteric coated mycophenolate sodium
CsA = cyclosporine

Comparison of Structural Malformations

- Among the live births born to female transplant recipients exposed to MPA, there were 14 malformations reported for an incidence of (18%), compared to the incidence of malformations in transplant recipients not exposed to MPA, which is approximately 4.9%.
- Among the live births fathered by male recipients there were 6 malformations reported, for an incidence of 3.2%.
- In the general population structural birth defects are reported in the range of 3-5%.

Craniofacial Dysmorphology

Le Ray et al. Obstet Gynecol 2004; 103(5): 1091

Jackson P et al. Am J Med Genet Part A 2009; 149A(6): 1231

Conclusions

- Reports to the NTPR reveal an increased incidence of non-viable outcomes and a pattern of structural malformations in pregnancies exposed to MPA in female transplant recipients compared to those without exposure to MPA.
  - Structural birth defects consisting of microtia (ear deformity) and facial defects suggest a pattern of malformations.
- Those pregnancies fathered by male transplant recipients appear similar to that of the general population.

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