

Immunosuppressants Pose Challenge in Pregnancy

Balancing immunosuppression with the health of the woman and fetus requires team approach.

BY KERRI WACHTER
Senior Writer

WASHINGTON — Balancing immunosuppression in a pregnant allograft transplant patient with the health of the woman and her fetus requires a team approach between high-risk obstetricians and transplant physicians, according to one expert speaking at a meeting sponsored by the National Kidney Foundation.

“Pregnancy in the transplant recipient, aside from the issue of renal dysfunction, poses a unique set of considerations, and that’s because of immunosuppressants,” said Michelle A. Josephson, M.D., of the University of Chicago.

None of the immunosuppressants used for transplantation—cyclosporine, tacrolimus, azathioprine, steroids, rapamycin, and mycophenolate mofetil—are rated pregnancy category A, using the Food and Drug Administration classification system. In fact, most are rated category C, meaning there are no data on their use in humans during pregnancy. “All medications used to prevent rejection cross the maternal-placental interface,” she pointed out.

Despite the lack of data and potential risks, a consensus group convened in 2003 by the Women’s Health Committee of the American Society of Transplantation recommended immunosuppression be maintained during pregnancy to avoid rejection.

Graft rejection can be difficult to discern during pregnancy because serum creatinine levels are low during this period, and small changes can be missed, Dr. Josephson said. In addition, abnormalities that turn up on liver function tests can have a number of etiologies. For these reasons, graft dysfunction during preg-

nancy warrants appropriate investigation—by biopsy if necessary.

“If rejection occurs, it can be treated with steroids,” Dr. Josephson recommended. Inadequate immunosuppression, graft instability, and rejection likely affect the graft prognosis. However, age, number of allografts, and repeat pregnancies don’t seem to impact graft function and prognosis.

The consensus group also agreed that a high-risk obstetrician and a transplant physician should manage pregnant transplant patients. Obstetricians should optimize maternal health, maintain normal glycemia, ensure adequate fetal growth, and anticipate preterm birth. The transplant physician should ensure maintenance of graft function and aggressively manage hypertension and preeclampsia. Cesarean section is not indicated except for standard obstetric reasons.

During the conference, experts addressed a number of concerns for this group of patients to develop management recommendations. “We recognized that the risk of prematurity in the population was high. We realized that intrauterine growth retardation is high,” said Dr. Josephson. In addition, during pregnancy renal transplant recipients may have renal insufficiency, hypertension, and preeclampsia.

Traditionally, it was recommended to wait 2 years after transplantation to try to become pregnant. However, newer immunosuppressants have made rejection less of an issue. This opens the possibility for a more individualized approach to timing. The group agreed pregnancy could be attempted once certain criteria had been met:

- ▶ No graft rejection in the year after transplant.

- ▶ Adequate and stable graft function (creatinine level less than 1.5 mg/dL, no or minimal proteinuria).

- ▶ No acute infections that could impact the fetus.

- ▶ Maintenance of immunosuppression at stable dosing.

There are, however, special circumstances that could impact the recommendations:

- ▶ Rejection outcome within the first year (consider further graft assessment with biopsy and GFR).

- ▶ Maternal age.

- ▶ Comorbid factors that may impact pregnancy and graft function.

- ▶ The patient’s history of compliance.

The timing considerations could be met at 1 year post transplant, depending on the individual. ■

Care Varies for Transplant Recipients

A survey of the management practices of allograft transplant recipients who are or wish to become pregnant highlights the lack of consensus on the care of these patients.

Perhaps the most important finding of the survey was that the care of these women generally has been based on experience, patient preference, or center protocol, not on any available evidence, Dr. Josephson said.

“After nearly 50 years and thousands of deliveries, we should know what we’re doing, but do we?” she asked.

The Women’s Health Committee of the American Society of Transplantation sent out a questionnaire to all 257 transplant centers in the United States to determine the current practices for the care of transplant recipients who wish to become or are pregnant. The response rate was 56%.

The respondents had an average of 16 years’ experience in transplant medicine.

A total of 82% said they recommend that their transplant patients not try to become pregnant for some period of time after receiving the transplant.

Most who recommended a waiting period said their patients should wait 1-2

years. Almost 20% recommended that their patients never become pregnant. Most respondents—about three-quarters—did not limit their patients to one pregnancy.

Regarding immunosuppressant therapy in pregnancy, most respondents felt that older drugs—cyclosporine, tacrolimus, and steroids—were probably OK to use. “What I think was really interesting was that with azathioprine—one of the safest medications and actually the one that we have, aside from steroids, the most experience with—there was a little bit of debate,” she said.

Responses varied widely concerning the safety in pregnancy of newer immunosuppressants, such as rapamycin and mycophenolate mofetil.

High-risk obstetricians most commonly managed the pregnancies of transplant recipients, making up 85% of the physicians caring for these patients. Most respondents preferred going ahead with vaginal deliveries, although one-quarter of them recommended cesarean section for these patients.

Two-thirds of respondents advised their patients not to breast-feed.

Extended Prenatal Care Could Help to Better Address Chronic Illness

BY JOYCE FRIEDEN
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WASHINGTON — The term “prenatal care” should be rethought to include much more of a woman’s life cycle, Dawn Misra, Ph.D., said at a meeting sponsored by the Jacobs Institute of Women’s Health.

“We have to go beyond the [typical] prenatal period” of a few months before pregnancy, said Dr. Misra of the University of Michigan, Ann Arbor. When it comes to chronic illnesses that may affect pregnancy, for example, “we have to plan strategies to address these matters across the life course; if we want to fix them, we can’t wait until pregnancy to [address] them.”

Dr. Misra gave hypertension as an example. “There really is no good treatment for hypertension once you’re pregnant,” she said. “You can do some things to try to moderate its effects and lessen its impact, but you can’t fix it. So [instead] we could prevent women from having hypertension and entering pregnancy with

hypertension.” This involves addressing such chronic health problems in the pre-conception period as well as between pregnancies.

She gave several reasons why providers haven’t taken this approach. “Public health and medical professionals are wedded to the notion that prenatal care is fundamental,” she said. “There have been a lot of successes with prenatal care, but I would like to take a step back and think about how prenatal care is not the only answer.”

The health care financing system has encouraged this model of prenatal care by the way it reimburses for care, she continued. As a result, “very few women get no prenatal care, yet we haven’t achieved much improvement in terms of infant outcomes.”

Changing this system of care would

also mean increasing involvement by providers outside the specialty of ob.gyn., such as pediatricians, Dr. Misra said. “Pediatricians are taking care of future mothers. They could spend time from that perspective thinking about chronic illnesses,

keeping [these patients] well, and thinking about what future concerns might be.”

Some of these changes might be fostered by improving medical school training. In addition, people from outside

the medical profession such as coaches and personal trainers could be involved in these types of issues, she said.

Pediatricians could also help provide better record transfer, Dr. Misra noted. “We have young girls moving from the pediatrician to the ob.gyn. or the nurse-midwife. A lot is lost when young girls move to those providers, and we need to

find better ways to relay their health history.” This is a challenge that needs to be met, especially in the wake of a study showing that 25% of pregnant women have a chronic health condition, Dr. Misra added.

On a broader level, public health officials need to rethink their method of separating chronic disease care from maternal and child health programming, Dr. Misra said. “This may require thinking about how future [pregnancy] outcomes are dependent on preventing these kinds of illnesses.”

One audience member commented that although she liked the speaker’s message, “The women’s health movement has been struggling for a long time to get away from thinking about women’s health merely in terms of maternity and reproduction,” she said. “I think we need to reword language like ‘preconceptional.’ When we’re sitting in this room, we know what we’re talking about, but many people out there still think of women as reproductive machines.” ■

The women’s health movement has been struggling to get away from thinking about women’s health only in terms of maternity and reproduction.