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Contraceptive use in female recipients of a solid-organ transplant

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Abstract

Context—Women of reproductive age account for more than one-third of all solid-organ transplant recipients and are advised against becoming pregnant for 1 to 2 years after their surgeries. The risks posed to the woman, the transplanted organ, and the fetus underscore the importance of systems to ensure that patients receive counseling on family planning, including return to fertility, contraceptive use, and when pregnancy can be safely considered, and highly effective methods of contraception.

Objective—To investigate use of contraceptives among women after solid-organ transplant and to identify opportunities to improve care.

Design—A cross-sectional survey study.

Setting—An urban academic medical center.

Patients—Women 18 to 50 years old who have received a kidney, pancreas, and/or liver transplant within the past 1 to 24 months.

Intervention—Participants completed self-administered questionnaires regarding their menstrual pattern, pregnancy history, contraceptive use before and after transplant, and counseling on family planning issues.

Main Outcome Measures—Contraceptive use.

Results—The most common contraceptive method used in both the year preceding transplant and the year after transplant was condoms. Participants desired more counseling on highly effective contraceptive methods, such as intrauterine devices. Participants would like to receive contraceptive counseling from an obstetrician/gynecologist or transplant care team provider.

Conclusion—Female recipients of solid-organ transplants want more counseling on highly effective methods of contraception.

Women of reproductive age make up 37% of the transplant recipients in the United States, with 10817 women receiving organ transplants in 2013.¹ Of these women, 35% were between 18 and 49 years old; thus, female reproductive health is an important issue among transplant recipients.¹ Women with end-stage renal disease may experience reduced fertility,

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but fertility may be restored after transplant.² Pregnancies in organ transplant recipients are high risk because of potential complications such as preeclampsia, preterm delivery, and low birth weight.³ Higher rates of birth defects in pregnant transplant recipients have been attributed to certain immunosuppressive medications, such as mycophenolate.⁴⁻⁸ The American Society of Transplantation recommends avoiding pregnancy for at least 1 year after receiving a solid-organ transplant.⁹

These risks underscore the importance of using highly effective contraception, defined as methods with a failure rate less than 1%, to avoid an unplanned pregnancy.¹⁰ Health care providers should counsel transplant patients on the potential return to fertility, contraceptive options, and when pregnancy can be safely considered. The goals of this study were to assess contraceptive counseling and use of various contraceptive methods among female recipients of solid abdominal organ transplants. In addition, this study explores patients' preferences for contraceptive counseling.

Methods

This study was conducted at the transplant clinic of UC San Diego Health System, an urban academic health system from June 2012 to August 2013. Women of reproductive age between 18 and 50 years old who came to the clinic 1 to 24 months after receiving a kidney, pancreas, and/or liver transplant were approached to participate in the study. Additional inclusion criteria were being sexually active with men and speaking English. Women were excluded from the study if they were currently pregnant or had a history of hysterectomy or bilateral oophorectomy. Each participant was provided a \$10 gift card as an incentive and written informed consent was obtained. This study was approved by the University of California, San Diego, Human Research Protection Program's institutional review board.

The questionnaire was adapted with permission from Guazzelli et al¹¹ from a prior study in Brazilian kidney transplant recipients. It was then reviewed for readability by the institution's patient education coordinator. The self-administered questionnaire used in this study had 6 demographic questions and 21 multiple-choice questions on medical history, menstrual history, pregnancy history, contraceptive use, and contraceptive counseling. Demographic information, including details of organ transplant(s), concurrent medical conditions, and current immunosuppressant medications, was verified against the medical record. The questionnaire took approximately 15 minutes to complete. Data were entered into Microsoft Excel for descriptive statistical analysis.

Results

A total of 32 women were approached to participate. Nine of these women did not meet the eligibility criteria because more than 24 months had elapsed since the transplant, they were not sexually active with men, they had a history of hysterectomy, or they did not speak English. Of the 23 women who met the eligibility criteria, 21 consented to participate in the study. Two women declined to participate because of concerns about the release of protected health information.

Data for all 21 solid-organ transplant recipients of reproductive age were analyzed. Characteristics of the study participants are summarized in Table 1. Participants were a mean age of 34 years old (range, 23–50 years) and a mean of 9 months (range, 1–24 months) had elapsed since the transplant surgery. The most common immunosuppressant medications were prednisone (95%), tacrolimus (90%), and mycophenolate formulations (57%).

Participants were asked about the frequency of menses before and after transplant. One participant selected multiple frequencies, 3 participants did not respond to the posttransplant question, and 2 participants did not respond to either the pretransplant or posttransplant question. Those responses were not included. Before transplant, nearly half of the participants had menses every 28 days (n=7, 47%), followed by every 29 to 35 days (n = 3, 20%), more than every 35 days (n=3, 20%), every 21 to 27 days (n=1, 7%), and less than every 21 days (n = 1, 7%). After transplant, participants had menses less than every 21 days (n=5, 33%), every 21 to 27 days (n=4, 27%), every 28 days (n=4, 27%), and every 29 to 35 days (n=2, 13%).

Fifteen (71%) of the study participants had a history of pregnancy before transplant. Of the 42 total pregnancies, 23 (55%) were unplanned and 19 (45%) were planned. Most pregnancy outcomes were live births of term infants of more than 37 weeks (n = 23, 55%). The other outcomes were live births of preterm infants of less than 37 weeks (n = 10, 24%), miscarriage (n=5, 12%), termination (n=3, 7%), and ectopic pregnancy (n=1, 2%). No pregnancies occurred among the participants after transplant.

Two-thirds of the participants (67%, n=14) received counseling on when it would be safe to become pregnant, and many (n=11, 52%) received this counseling from a transplant physician. Fewer participants were counseled by a transplant nurse (n = 7, 33%) and/or a pharmacist (n = 3, 14%). This counseling occurred in the clinic before transplant (n=9, 43%), in the hospital after transplant (n = 7, 33%), and/or in the clinic after transplant (n = 9, 43%). Almost one-third reported never receiving such counseling (n = 6, 29%). Participants reported being told various waiting periods before becoming pregnant. One-third reported being told to wait 1 year (n = 7, 33%) and others reported being told to wait 2 years (n = 5, 24%). One-third of participants were not sure what the recommended waiting period was (n = 7, 33%). Nearly all (90%) were aware of potential risks of birth defects associated with their posttransplant medications.

Participants reported receiving counseling on a variety of contraceptive methods. Most received counseling on condoms (n = 8, 38%), oral contraceptive pills (n = 7, 33%), and/or intrauterine devices (IUDs, n=5, 24%). Some patients also were counseled on sterilization (n = 3, 14%), injection (depot medroxyprogesterone acetate, n=2, 10%), and/or spermicide (n=2, 10%). Patients received contraceptive counseling exclusively from the transplant care team, including a transplant physician (n=11, 52%), a transplant nurse (n=10, 48%), and/or a pharmacist (n=8, 38%). No patients had received contraceptive counseling by an obstetrician/gynecologist. When participants were asked about when contraceptive counseling was provided at the various phases of care, half indicated receiving counseling in the clinic before transplant (n = 10, 48%), fewer in the hospital after transplant (n=9, 43%), and more than half in the clinic after transplant (n = 11, 52%). The contraceptive methods

used by participants before and after transplant are presented in Table 2. In both the year before transplant and the year after transplant, the predominant contraceptive method used was condoms. One patient changed from a highly effective method to a less effective method (IUD to abstinence), and another participant changed from a less effective method to a highly effective method (condoms to IUD).

Nearly half of the participants indicated an interest in receiving counseling on intrauterine methods (n = 10, 48%), followed by oral contraceptive pills (n = 7, 33%), condoms (n = 4, 19%), injection (depot medroxyprogesterone acetate, n = 4, 19%), and/or sterilization (n = 1, 5%). Participants indicated that they would like to receive contraceptive counseling from a transplant physician (n = 10, 48%), obstetrician/gynecologist (n = 9, 43%), transplant nurse (n = 8, 38%), and/or pharmacist (n = 3, 14%). Participants indicated that they would like to receive contraceptive counseling in the transplant clinic before transplant (n = 8, 38%), in the transplant clinic after transplant (n = 7, 33%), during a referral visit to an obstetrics and gynecology clinic after transplant (n = 5, 24%), during a referral visit to an obstetrics and gynecology clinic before transplant (n = 4, 19%), and/or in the hospital after transplant (n = 3, 14%).

Discussion

The results of this study reveal that after transplant, women are not using highly effective contraceptive methods (ie, methods with a typical failure rate <1%), despite recommendations to avoid pregnancy for 12 to 24 months. Most used condoms before and after transplant. Condoms are not highly effective methods of contraception and carry an 18% failure rate with typical use (Table 3).¹² Although a higher level of motivation for pregnancy prevention may be expected after transplant, this study revealed that women are not using highly effective methods of contraception.

We found that most patients are receiving counseling on when it would be safe to become pregnant (67%). In another study of solid-organ transplant recipients, French and colleagues¹³ reported lower rates of counseling about the potential for pregnancy after organ transplant (42% in kidney recipients, 30% in liver recipients). The study by French et al revealed that less than half of transplant recipients were counseled by a health care provider either before (43%) or after (37%) transplant to use birth control. Specific methods were recommended even less often, during only half of those discussions. Oral contraceptive pills were recommended most frequently (52%–57%), followed by condoms (15%–20%) and IUDs (15%–20%). Only about half (48%) of these women were using any method of contraception.¹⁴ Compared with those findings, we found that rates of counseling were higher for condoms, similar for IUDs, and lower for oral contraceptive pills. Another survey of US transplant center physicians indicated that patients are primarily counseled on condom use, followed by oral contraceptive use, which is more consistent with our findings.¹⁴

This study is unique because it reveals the female transplant recipients' perspective on what type of contraceptive counseling they would like to receive, when, and by which health care providers. Participants did not receive any counseling by obstetricians/gynecologists, but these participants would like more counseling on highly effective contraception such as

IUDs and they would like to receive this counseling from obstetricians/gynecologists or transplant care providers. The obstetrician/gynecologist has the added ability to provide the contraceptive methods as well, particularly sterilization, IUDs, or implants. Participants indicated a preference for contraceptive counseling to occur in the transplant clinic before transplant, followed by in the transplant clinic after transplant. These findings could be incorporated into an interventional study to improve use of more effective contraception in this population.

Many of the women in the study were taking a formulation of mycophenolate, which is considered a potentially teratogenic medication and should not be taken without concurrent use of highly effective contraception.¹⁵ Maternal exposure to mycophenolate may result in structural malformations in the offspring.⁴⁻⁸ The other immunosuppressant medications are generally not regarded as teratogenic but have been associated with increased risk of fetal growth restriction, premature delivery, and low birth weight.¹⁶⁻¹⁸ Exposure to a potential teratogen is an important reason for counseling these women about highly effective contraceptive methods.

The Centers for Disease Control and Prevention's US Medical Eligibility Criteria for Contraceptive Use (USMEC) has specific guidance on the safety of each contraceptive method for women who have received solid-organ transplants.¹⁹ These methods are listed in order from most effective to least effective in Table 3, along with the percentage of women who experience an unintended pregnancy in the first year of use for each contraceptive method. Of note, according to the USMEC and available evidence, IUDs are safe to use for most recipients of solid-organ transplants.^{19,20} However, the American Society of Transplantation statement from several years ago recommends against the use of IUDs in transplant patients because immunosuppressants may decrease the effectiveness of IUDs.⁹ Both of these recommendations are based on limited data; however, it is important for these 2 groups to reach a consensus to prevent confusion among providers and patients.

Limitations

The participants are representative of the age and ethnicity distribution among the general population of abdominal organ transplant recipients, although nearly all participants were kidney transplant recipients. A limitation of this study is that it included only English-speaking women; therefore, the perspectives of Spanish-speaking women were not captured. Excluding Spanish-speaking patients may affect the generalizability of the results to predominately Spanish-speaking populations. It is important to note, however, that Hispanic/Latina women comprised one-third of the study population. The other limitation of this study is its small sample size. Participant recruitment was a challenge from a small population of patients at a single clinic. However, given that very few prospective studies on contraceptive use among female solid-organ transplant recipients have been done, the findings of this study do provide further insight into the unique perspectives and needs of this population. Future studies should involve patients from multiple centers.

Conclusion

The results of this study will help inform health care professionals on how to counsel solid-organ transplant patients about contraception in order to prevent unplanned pregnancy after transplant. Women may experience restoration of fertility after transplant; thus, counseling on highly effective contraception is necessary. Women should be counseled about the risks of pregnancy after transplant. Not only should this counseling take place before transplant, but it also needs to continue after the transplant surgery. Future interventions in female recipients of solid-organ transplants may include counseling of patients about highly effective methods of contraception, such as IUDs, and care from an obstetrician/gynecologist experienced in the provision of contraceptives to medically complicated patients.

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Table 1

Participant characteristics (N = 21)

Characteristic	Value
Age, mean (SD); range, y	34 (7); 25–50
Body mass index, ^a mean (SD); range	64 (3); 17–41
Time since transplant, mean (SD); range, months	9 (7); 1–24
Ethnicity, No. (%)	
Hispanic/Latina	7 (33)
White	4 (19)
Asian/Pacific Islander	6 (29)
Black/African American	3 (14)
Other ethnicity	1 (5)
Organ transplanted, No. (%)	
Kidney	16 (76)
Liver	4 (19)
Kidney and pancreas	1 (5)
Number of cigarettes smoked a day, No. (%)	
None	21 (100)
1	0 (0)
Highest level of education, No. (%)	
Less than high school	2 (10)
High school degree	7 (33)
College degree	8 (38)
Graduate degree	4 (19)
Marital status, No. (%)	
Single, never married	8 (38)
Married	11 (52)
Separated	2 (10)
Divorced	0 (0)
Widowed	0 (0)
Immunosuppressant medications, ^b No. (%)	
Azathioprine (Imuran)	2 (10)
Cyclosporine (Gengraf, Sandimmune)	2 (10)
Mycophenolate mofetil (CellCept)	9 (43)
Mycophenolate sodium (Myfortic)	3 (14)
Prednisone	20 (95)
Sirolimus (Rapamune)	0 (0)
Tacrolimus (Prograf)	19 (90)

^a Calculated as weight in kilograms divided by height in meters squared.

^b Values sum to more than 100% because patients indicated all of their immunosuppressant medications (71% were taking 3, 24% were taking 2, and 5% were taking 1 medication).

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Table 2Contraceptive methods used before and after transplant (N = 21)^a

Contraceptive method	No. (%) of patients	
	Before transplant	After transplant
No contraceptive method used	3 (14)	4 (19)
Contraceptive method used	18 (86)	17 (81)
Type of contraceptive method		
Male sterilization	2 (11)	2 (12)
Female sterilization	2 (11)	2 (12)
Intrauterine device	1 (6)	1 (6)
Injectable	1 (6)	0 (0)
Oral contraceptive	3 (17)	1 (6)
Condoms	10 (55)	11 (65)
Withdrawal	3 (17)	0 (0)
Spermicide	1 (6)	2 (12)

^aPercentages total more than 100 because patients indicated all contraceptive methods used, and some used more than 1 method.

Table 3Effectiveness rates and US medical eligibility criteria for contraceptive methods^a

Contraceptive method	Women experiencing an unintended pregnancy within the first year of use, %		Medical eligibility criteria for use in patients following solid-organ transplant ^b	
	Typical use	Perfect use	Complicated	Uncomplicated
Male sterilization	0.15	0.10	NA	NA
Female sterilization	0.50	0.50	NA	NA
Levonorgestrel intrauterine device	0.20	0.20	3 ^c /2 ^d	3 ^c /2 ^d
Copper intrauterine device	0.80	0.60	3 ^c /2 ^d	3 ^c /2 ^d
Progestin-only implant	0.05	0.05	2	2
Progestin-only injectable	6.00	0.30	2	2
Progestin oral contraceptive	9.00	0.30	2	2
Combined hormonal contraception (combined oral contraceptive pill, vaginal ring, transdermal patch)	9.00	0.30	4	2
Male condoms	18.00	2.00	NA	NA

Abbreviation: NA, not applicable.

^aBased on information from Trussell¹² and Centers for Disease Control and Prevention.¹⁹

^bCategories of medical eligibility criteria for contraceptive use: 1, a condition for which there is no restriction for the use of the contraceptive method; 2, a condition for which the advantages of using the method generally outweigh the theoretical or proven risks; 3, a condition for which the theoretical or proven risks usually outweigh the advantages of using the method; 4, a condition that represents an unacceptable health risk if the contraceptive method is used.

^cInitiation.^dContinuation.