



Mini Review

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Is it Ethical to Offer ART in Transplant Patients?



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Abstract

Numerous medical and surgical innovations have improved transplant recipient outcomes and this improved survival has led to an increased focus on their quality of life issues. This renewed focus includes controlling fertility and breeding. However, not all reproductive-age transplant recipients are able to conceive naturally. For this women in fertility is considered a threat to their quality of life. The decision to use Assisted Reproduction Techniques (ART) to help solid organ transplant female patients become pregnant raises unique medical and ethical concerns.

Introduction

Solid organ transplantation can prolong the life of individuals with end stage disease [1]. Numerous medical and surgical innovations have improved transplant recipient outcomes and this improved survival has led to an increased focus on their quality of life issues [1,2]. This renewed focus includes controlling fertility and breeding [3]. However, not all reproductive-age transplant recipients are able to conceive naturally. For this women, infertility is considered a threat to their quality of life [1,4]. An important question for this matter and that we should introduce at these point is: Is it lawful to offer these patients infertility treatments? And if so, how should the selection of these patients be made? Shall we use the same drug protocols and in the same dosages? Unfortunately, there is not a direct answer to these questions. We know that for women, both organ transplantation and IVF are independently associated with increased risks of preterm birth (PTB), low birth weight (LBW), small for gestational age babies (SGA) and perinatal mortality [4-6]. However, there is limited published data on pregnancy, delivery and the effect of ovarian stimulation on the graft, following ART, and so this is a controversial subject [1-7].

Discussion

Menstrual irregularity is common in women with chronic diseases. Nevertheless, normal menstrual and ovulatory function resumes the majority of them following successful organ transplantation, leaving many women with newly potential to conceive [1-3,8]. However, not all reproductive-age transplant recipients are able to conceive naturally. The decision to use Assisted Reproduction Techniques (ART) to help

solid organ transplant female patients become pregnant raises unique medical and ethical concerns. A multidisciplinary team is required to address the complex medical, ethical and psychosocial issues involved in treating infertile transplant recipients [1-3,9-15]. Only a few case reports and small studies have previously been published regarding women with solid organ transplantation, which have delivered children after ART [3-6,16].

When reproductive specialists consider touse ART in transplant recipients they must first determine patient eligibility. Transplant recipients should be in good health and, ideally, graft function should be good to excellent, stable and rejection-free before attempting pregnancy [4]. In general, most transplant centres recommend a delay of pregnancy until 1 to 2 years following transplant [4,5,17,18]. Also, all comorbidities should be well controlled, the immunosuppressive regimen should be at the lowest dose and, if the underlying disease is genetically transmitted, it should be available a pre implantation genetic diagnosis (PGD) [1-5].

There are several ART techniques and the decision to perform one over other will depend on the fertility status of each couple. Usually, if the cause is an ovulation, the first technique to be performed is ovulation induction (OI), which is an easy process, normally achieved with the use of clomiphene citrate (CC), letrozole (LTZ) or low doses of gonadotropins [19,20]. When OI does not work, a step up in ART is to try intra-uterine insemination [1,19,20]. This technique is simple, hardly invasive and the higher risk to the transplanted patient is only related

to the drugs used. When these two techniques are not enough or when the couples do not meet the requirements for their use (ex. if there is a tubal obstruction), the ART technique to use is in vitro fertilization (FIV) or intracytoplasmic sperm injection (ISCI) [19,20].

During the cycle, the oocyte retrieval is this step where the risks are substantially larger in organ transplanted patients [2,21]. As these patients have multiple co-morbidities, general anaesthesia for oocyte retrieval has increased risk of complications. Therefore, at the beginning of the cycle a pre-anaesthetic appointment should be scheduled in order to fully assess the risk and prevent morbidity. 2 During retrieval there is an actual risk of injuring the transplanted organ, when the organ is in the pelvic cavity, as it happens in renal transplanted patients. In these patients we also need to keep in mind other possible complications like thromboembolism (TE) due to the OHSS, oestrogens and surgical intervention [14,21]. Nonetheless, routine TE prophylaxis is not recommended [1,2]. After being approved and determined their eligibility, couples can begin the process on an Assisted Reproductive Unit, where they will start the usual ART study.

The goal of ART is to achieve a healthy child from an uncomplicated pregnancy, delivered at term, avoiding multiple gestations and ovarian hyper stimulation syndrome (OHSS), without detriment to maternal health [1,2]. Traditionally, in Europe, couples should choose to transfer one or two embryos, with the acquaintance that if two embryos are transferred there is a higher probability of a multiple pregnancy and all the risks inherent to it. For this matter, the trend nowadays is to do a single embryo transfer (SET) at the blastocyst stage [19]. This issue should be specially considered in solid organ transplanted patients who already have an increased risk of hypertension in pregnancy, pre-eclampsia, PTB and delivery SGA babies and do not need to overlap the increased risks of a multiple pregnancy [2-5]. For doctors, few data in the literature is available regarding the effect of ovarian stimulation or its complications on solid transplanted organs.

In this regard, it is not clear whether ovarian stimulation should be modified in any way [7]. Special care should be taken to avoid ovarian hyper stimulation and it is advisable to be conservative with the number of embryos transferred to avoid the risk of a high-order multiple pregnancy in an already high-risk medical condition [3,21]. Due to the lack of available data, the reproduction management of organ transplant recipients has been mostly extrapolated from renal transplantation evidence-based guidelines and experience, although care providers should always have in mind the differences between the transplanted organs [2].

Conclusion

A multidisciplinary approach is required to fully assess the advisability of proceeding ART in transplant recipients [1].

This approach has led to better candidate selection, treatment surveillance and improved outcomes, while decreasing complications [2]. This careful selection of patients will, hopefully, result in outcomes comparable to those in women who undergo solid organ transplantation and have a spontaneous conception [4]. A careful thought has to be made about the number of embryos to transfer and probably SET in solid organ transplanted patients probably should be the rule [21].

Nonetheless, to all that was said before, the couple should be made fully aware, through reliable information, of the potential risks associated with pregnancy and the use of ART in order to give appropriate informed consent before starting the techniques [3,4]. The couples should know that nowadays there is little experience with the subject that literature is scarce but it is possible to conceive in safety using assisted reproductive technology, when certain requirements are fulfilled. Reporting the use of ART in these couples may help to create the necessary guidelines, forestall potential problems and allow couples to make an informed decision before undergoing treatment [7].

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