At the coalface: medical ethics in practice

Pregnancy, autonomy and paternalism

Gillian M Lockwood *Oxford Radcliffe Hospital, Oxford*

Abstract

Modern medicine is increasingly aware of the significance of patient autonomy in making treatment choices. This would seem to be particularly important where the therapy requested was "voluntary" as in fertility treatment or cosmetic surgery. However, the Hippocratic doctrine "Primum non nocere", seems especially relevant where the treatment sought may have a low chance of a successful outcome or even be life-threatening. Mrs A's case demonstrates the difficulty faced by the physician who wants to maximise her patient's autonomy, but "Above all, do no harm".

(*Journal of Medical Ethics* 1999;25:537-540)

Keywords: Reproductive rights; autonomy

Infertility and renal disease

Renal transplantation, the treatment of choice for patients with end stage renal failure, can correct the infertility due to chronic ill health, anaemia and tubal damage generally encountered when these patients are managed by renal dialysis. Currently only one in 50 women of child-bearing age becomes pregnant following renal transplant and it may be that many more would welcome the chance of biological parenthood if their fertility problems could be overcome. The first successful pregnancy, conceived in 1956 following an identical twin renal transplant was reported in 1963.¹

Until recently pregnancy had been thought to present considerable hazards to the transplant recipient. However, some reviews^{2,3} have suggested that pregnancy in the graft recipient, unlike the rare pregnancy in patients undergoing dialysis, is usually likely to lead to a live birth⁴ and the pregnancy may have little or no adverse effect on either renal function or blood pressure in the transplant recipient. The current medical consensus is that if, prior to conception, renal function is well preserved and the patient does not develop high blood pressure, then only a minority of transplant recipients will experience a deterioration of their renal function attributable to pregnancy.⁴

It is inevitable that the rapid return to good health enjoyed by the majority of women following successful renal transplantation should encourage them to consider conception. Although only a small proportion of women with a functioning graft become spontaneously pregnant, modern assisted reproductive techniques (ART), especially in vitro fertilisation and embryo transfer (IVF-ET), could theoretically increase this proportion to near normal levels. Pregnancy, especially if ART is required, clearly entails extra risks for the renal transplant recipient, but these are risks that, with appropriate counselling, the patient may be prepared and even eager to take.

In this paper, I shall discuss the ethical dilemmas involved in counselling renal transplant patients seeking pregnancy but requiring ART. I shall begin by reporting my experience of treating a couple with longstanding infertility with IVF-ET where the wife was a renal transplant recipient and her initial renal failure was due to severe, recurrent pre-eclampsia. Pre-eclampsia is a potentially life-threatening condition of late pregnancy causing raised blood pressure and renal complications which can progress to cause fits and cerebro-vascular accidents (stroke) and is associated with severe growth retardation of the fetus and, often, premature delivery.

Case history

Mrs A, a 34-year-old woman was referred to our unit for IVF treatment following eight years of failure to conceive after a reversal of sterilisation operation had been performed.⁵ She had been born with only one poorly developed kidney, but this was not known until, at age 20, she was investigated for very severe pre-eclamptic toxæmia (PET) which she suffered during her first pregnancy. Her baby was born at 26 weeks' gestation and he died shortly after birth from complications of extreme prematurity. A second pregnancy in the following year was also complicated by severe PET, renal damage, premature delivery at 26 weeks' gestation and neonatal death. Sterilisation by tubal ligation was offered

and accepted under these circumstances, in view of the anticipated further deterioration of her renal function with any subsequent pregnancy. There was a significant further advance of her renal disease, necessitating the initiation of kidney dialysis and two years later, a related donor renal transplant (from her mother) was successfully performed. After the transplant, Mrs A remained well and maintained good kidney function on a combination of anti-rejection drugs, steroids and blood pressure tablets. At age 26, a reversal of sterilisation operation was performed because she had become so distressed by her childlessness. Two years later, when pregnancy had not occurred, a test showed that both tubes had, once again, become blocked.

At the time that Mr and Mrs A were referred to our IVF unit, there were no case reports of successful IVF in women with renal transplants, but specialists were becoming increasingly reluctant to advise women with transplants *against* trying for a baby, as medical care for "high-risk" pregnancies was improving dramatically. Following discussion with the transplantation unit and the high-risk pregnancy specialists, we felt that an IVF treatment cycle could be offered to Mr and Mrs A as long as the risks of IVF-ET, over and above those attendant upon a spontaneous pregnancy in these circumstances, were understood and accepted by the couple and minimised, as far as possible, by the IVF team.

An IVF treatment cycle was started using the normal drug regimen, but the patient was given a much lower dose than usual, with the aim of minimising the effect of the hormone stimulation on the transplanted kidney. The IVF cycle was successful and resulted in a twin conception although the pregnancy was complicated at 20 weeks' gestation by a right deep vein thrombosis. The twins were born prematurely at 29 weeks' gestation, but were otherwise well, requiring only minimal resuscitation and respiratory support. After delivery of her babies, Mrs A remained well and her renal graft continued to function normally with no change in medication required.

What are the risks?

Severe pre-eclampsia and eclampsia can result in irreversible damage to the maternal kidney, particularly due to acute renal cortical necrosis. Women who have recurrent pre-eclampsia in several pregnancies or blood pressures that remain elevated in the period following delivery (the puerperium), especially if they have pre-existing renal disease and/or hypertension, have a higher incidence of later cardiovascular disorders and a reduced life-expectancy.⁶

Pregnancy is recognised to be a privileged immunological state and therefore episodes of rejection during pregnancy might be expected to be lower than for non-pregnant transplant recipients. Nevertheless, rejection episodes occur in nine per cent of pregnant women, occasionally in women who have had years of stable renal function prior to conception.

Risks for the fetus and neonate

Immunosuppressive (anti-rejection) drugs are theoretically toxic to the developing fetus, however, maternal health and graft function require continuation of maintenance immunosuppression. Women with impaired renal function are recognised to be at risk of giving birth prematurely and to growth-retarded or small-for-dates babies. A large French study of women with pre-existing renal damage reported a prematurity rate of 17% and a spontaneous or therapeutic abortion rate of 20%, as compared to prematurity and spontaneous abortion rates of eight per cent and 12%, respectively, in the normal population.⁷ In women with renal transplants, pre-term delivery is also common (45-60%) and small-for-dates babies are delivered in at least 20% of cases.

However, the long term health effects of events *in utero* for the offspring of transplanted mothers are harder to quantify and there is animal evidence of delayed effects of immunosuppressive therapies and intrauterine growth retardation.

Balancing autonomy and safety

The decision to accept the couple onto our IVF treatment programme posed significant dilemmas of both a technical (obstetric and renal) and an ethical nature. Severe pre-eclampsia can present as a progressive condition, tending to occur with greater virulence in successive pregnancies: this, after all had been the rationale behind the original decision to sterilise the patient after the death of her second baby, precipitated by pre-eclampsia and extreme prematurity. The successfully functioning transplanted kidney had been donated by the patient's mother and therefore, as an organ, was 30 years older than the patient herself. Hence, there were real concerns that the transplanted kidney could be jeopardised by the strain of a normal pregnancy. The use of donated eggs, which can permit post-menopausal women of 50+ years to become pregnant with IVF-ET has demonstrated a significant incidence of pregnancy associated hypertension and frank pre-eclampsia⁸ suggesting that the aged kidney is less able to withstand the stress of pregnancy.

A recent editorial review⁹ reported that about 35% of all conceptions in renal transplant patients failed to progress beyond the first trimester because of therapeutic (approximately 20%) and spontaneous (approximately 14%) abortions. Problems occur some time after delivery in 11% of women with transplants, unless the pregnancy was complicated prior to 28 weeks' gestation, in which case remote problems can occur in 24% of pregnancies. However, of the conceptions that continue beyond the first trimester, 94% end successfully in spite of a 30% chance of developing hypertension, pre-eclampsia or both. However, distinguishing between time-dependent and pregnancy-induced problems is clearly difficult. Davison¹⁰ cites registry data indicating that ten per cent of mothers who are transplant recipients die within one to seven years of childbirth.

Additional problems

The technique of IVF-ET also poses additional problems for the renal transplant patient. The hormone drug regime involves supra-physiological levels of estradiol and these are associated with a higher risk of thrombotic (blood-clotting) episodes than in normal pregnancy. Access to the ovaries may be compromised by the positioning of the transplanted kidney in the pelvis, although ultrasound scanning does permit the kidney to be readily visualised. Successful pregnancy rates per embryo transfer in IVF-ET have tended to depend upon multiple embryos being transferred at ET, but a multiple pregnancy (seen in 25%+ of all IVF pregnancies following a three embryo transfer) would exert greater strain on the kidney than a singleton, is more likely to be associated with the development of pre-eclampsia and has increased risks of premature delivery of the babies.

The ethical aspects of undertaking IVF and embryo transfer in these circumstances are possibly harder to quantify and yet more contentious. It is recognised that even under optimum circumstances, at the most effective units, the probability of a successful pregnancy with a single treatment cycle of IVF-ET is only about 25%. Was it acceptable to expose Mrs A to all the risks of an IVF cycle that was four times as likely to fail as to succeed? Even where the IVF is successful in establishing a pregnancy, there is still the non-negligible risk that renal function may deteriorate and the patient may be safely delivered, but again become dependent upon renal dialysis. The Human Fertilisation and Embryology Act of 1990 laid great stress on the importance of obtaining true informed consent from patients undertaking procedures such as IVF: in cases such as this it is

particularly important that the patient and her husband were made aware of the risks associated not only with the failure of IVF-ET but also with its success.

Arguments that could be advanced against offering fertility treatment to renal transplant recipients, such as whether it is in the best interests of the patient to be helped to achieve a state as a result of which she may suffer chronic ill health or even early death, have also been advanced against permitting "old", ie post-menopausal, women to become pregnant via the technique of egg-donation IVF. In both instances, one could argue that, as long as the risks associated with fertility treatment and pregnancy were thoroughly explained to, and accepted by, the woman (and her partner), then to refuse treatment on the sole ground that her health may deteriorate is unacceptably paternalistic on the part of the clinicians involved. Mrs A stated that if she had not agreed to the sterilisation (which she claimed she had been placed under undue pressure to accept at the time of the diagnosis of her renal failure), then she would not only have been able, but would definitely have tried to achieve a further pregnancy, as she did after the reversal of sterilisation was performed.

Scarce resources

The Human Fertilisation and Embryo Act (1990) also places great emphasis on the "interests of the child" who may be born as a result of procedures such as IVF-ET. This emphasis has been interpreted by some authorities as encouraging fertility units to feel justified in refusing treatment to women with significant health problems or to post-menopausal women as it would, so they claim, not be in "the interests of the child" to be born to a mother with a reduced life-expectation due to chronic ill health or advanced age. Society readily countenances *men* becoming fathers at an age when their life-expectancy is reduced irrespective of whether assisted reproductive techniques are required and the medical profession is heroic in its efforts to assist women with serious health problems who become pregnant *spontaneously*. It is unquestionably in the interests of the child who will *only be born if* his or her transplanted mother is offered fertility treatment, that she should be offered such treatment, even if he or she loses his mother at an early age or has to deal with the consequences of her ill health, as otherwise, *he or she* won't exist! However, when the issue of the allocation of scarce resources is so much at the forefront of medical decision making, clinicians may need to consider the possibility that pregnancies achieved under these exceptional cir-

cumstances may be associated with increased risks of prematurity and handicap.

The desire to bear a child may be just as strong, or even stronger, in a woman with chronic ill health or reduced life-expectancy than in healthy women. This is seen in the readiness with which women who are HIV-positive or have multiple sclerosis deliberately conceive even though they know that pregnancy may accelerate their disease. The desire to achieve the normality of pregnancy and motherhood, if only for a short while, can be overwhelming and must be recognised and treated sympathetically by physicians working in this field. As this case has shown, a carefully controlled IVF cycle can offer the chance of pregnancy to the renal transplant patient and ensure that the benefits of one major medical advance are not jeopardised by the pursuit of another. Even without the benefit of hindsight, I feel we would not have been justified in withholding that chance.

Gillian M Lockwood, BM, BCh, MA, is Clinical Research Fellow in Fertility at the Nuffield Depart-

ment of Obstetrics and Gynaecology, Radcliffe Hospital, Oxford.

References

- 1 Murray JE, Reid DE, Harrison JH, *et al.* Successful pregnancies after human renal transplantation. *New England Journal of Medicine* 1963;269:341-3.
- 2 Sturgiss SN, Davison JM. Effect of pregnancy on long-term function of renal allografts. *American Journal of Kidney Disease* 1992; 9:167-72.
- 3 Davison JM. Pregnancy in renal allograft recipients: problems, prognosis and practicalities. *Baillieres Clinical Obstetrics and Gynaecology* 1994;8:501-25.
- 4 Lindheimer MD, Katz AI. Pregnancy in the renal transplant patient. *American Journal of Kidney Disease* 1992;19:173-6.
- 5 Lockwood GM, Ledger WL, Barlow DH. Successful pregnancy outcome in a renal transplant patient following in-vitro fertilization. *Human Reproduction* 1995;10,6:1528-30.
- 6 Chesley LC, Annitto JE, Cosgrove RA. The remote prognosis of eclamptic women. Sixth periodic report. *American Journal of Obstetrics and Gynecology* 1968;124:446-9.
- 7 Jungers P, Forget D, Henry-Amar M, *et al.* Chronic kidney disease and pregnancy. In: Grunfeld J, Maxwell M, Bach J, *et al.*, eds. *Advances in nephrology*. New York: Year Book Inc, 1986:103-41.
- 8 Antinori S. Fetal and maternal morbidity in menopausal women age 45-63 years. *Human Reproduction* 1995;10:464-7.
- 9 Davison JM, Redman CWG. Pregnancy post transplant. *British Journal of Obstetrics and Gynaecology* 1997;104:1106-7.
- 10 Davison JM. 1992 Renal disease. In: De Swiet M, ed. *Medical disorders in obstetric practice*. Oxford: Blackwell Scientific Publications, 1992.

News and notes

Journal of Medical Ethics - <http://www.jmedethics.com>

Visitors to the world wide web can now access the *Journal of Medical Ethics* either through the BMJ Publishing Group's home page (<http://www.bmj.com>) or directly by using its individual URL (<http://www.jmedethics.com>). There they will find the following:

- Current contents list for the journal
- Contents lists of previous issues
- Members of the editorial board
- Subscribers' information
- Instructions for authors
- Details of reprint services.

A hotlink gives access to:

- BMJ Publishing Group home page
- British Medical Association website
- Online books catalogue
- BMJ Publishing Group books.

The web site is at a preliminary stage and there are plans to develop it into a more sophisticated site. Suggestions from visitors about features they would like to see are welcomed. They can be left via the opening page of the BMJ Publishing Group site or, alternatively, via the journal page, through "about this site".