Paternity Balancing

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Key Words

Ethics · Fetal karyotype · Fetal reduction · First-trimester pregnancy · Genetics · In vitro fertilization · Multifetal pregnancy · Multiple gestation · Multiple pregnancy

Abstract

Background: Gestational carriers and egg donors have been used by 'traditional' and now increasingly, gay couples. Three gay male couples, all using egg donors and gestational carriers with semen from both partners, had triplets. All desired reductions to twins for the standard medical indications, but requested, if reasonably possible, to have twins with one fathered by each partner. **Methods:** Following our usual clinical protocol, we performed chorionic villus sampling at 12 weeks on all fetuses obtaining FISH and karyotype. For paternity analysis, 14 polymorphic molecular markers on villi were compared to DNA samples from the two men to include or exclude each. **Results:** Standard assessments were all normal. Paternity testing showed that one partner fathered two of the triplets, and the other one. In all cases, one of the 'twins' was reduced with good clinical outcomes ensuing. **Conclusions:** Paternity balancing increases options for satisfying family planning desires of gay male couples. We believe it comparable to gender preferences in reductions, i.e. it can be considered but only completely

subservient to any clinical criteria. Paternity balancing raises similar ethical issues as reduction with gender preferences, but may increase patient autonomy and mainstream acceptance of stable, gay families.

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Introduction

There is a natural evolution of technologies with radically new approaches being reserved initially for 'life or death' situations. Gradually, as experience builds and costs and benefits become apparent, indications often expand such that 'quality of life' concerns often emerge as the predominant indications for a given approach [1]. Examples of this transition process have included fetal surgery going from congenital diaphragmatic hernia to meningomyelocele, cesarean section utilization, reconstructive to plastic surgery, and fetal reduction (FR) procedures [2, 3].

In vitro fertilization (IVF) has been used for infertility therapy for over 30 years with over 2 million babies born worldwide. A well-known complication, however, has been the generation of multiple pregnancies with a large literature on its sequelae, complications, and management options including ethical implications [4–7]. While there are guidelines as to the number of embryos trans-

ferred, these are not ‘law’ in most countries, and are not always followed [8].

When we and others began FR procedures in the 1980s and we had little data upon which to rely, those procedures were limited to very high-risk patients [9, 10]. We and other groups have seen the practice evolve over 25 years with a better understanding of specific risks and benefits in differing situations [6, 11–15]. The most common starting number has fallen from quadruplets to triplets, and now twins to singleton constitute about 1/3 of cases performed by us [6, 11]. Concomitantly, use of genetic testing by chorionic villus sampling (CVS) prior to FR has become our basic practice included in about 85% of all cases [6, 11]. Our data show this approach improves outcomes by allowing us to improve the chance of keeping fetuses without serious genetic disorders beyond that possible by ultrasound alone. As part of obtaining overnight FISH results looking for aneuploidy of chromosomes 21, 13, 18, X, and Y, we also learn fetal gender. Over time, FISH will certainly be replaced by other molecular techniques that should be cheaper and potentially faster. Technology advancements have also allowed older women to be candidates triggering fertility, medical, and genetic issues simultaneously [12]. Likewise, the experience of IVF and its uses has set precedents for how outcome data are sought, collected and distributed [13].

For the first 15 years or so of our experience, we would not entertain gender preferences. Given the pattern of strong male preference of those couples who did express gender selection interest that we saw in the 1990s, we felt that that it was unethical towards women [9]. As such, we chose not to participate [6]. As expansion of parental interest in gender grew to patients across all ethnic groups, and we have seen an apparent equalization of interest of having boys and girls, we have modified our position to include but not be bound by patient’s gender preferences. We will consider such preferences only provided there are no abnormalities or suspicious findings that dictate our course of action.

More than 30 years ago, we (M.I.E.) published an article in JAMA speculating on the medicolegal implications likely to emerge from IVF just as it was emerging as a viable clinical technique. We envisioned many hitherto unforeseen situations emanating from four areas: rights of the embryos, rights of the parents, rights and exposures of the physicians and hospitals, and public policy questions. We predicted issues involving decision making authority, surrogate motherhood, and inheritance conflicts. All of these have played out over time [14]. However, we did not envision the circumstances below.

We recently have added a new application of genetic testing and coin a new term ‘paternity balancing’ as part of our experience with FR patients. We report on three gay male couples using surrogates – each of whom had triplet pregnancies. They desired genetic testing and FR to maximize pregnancy outcome, but they also requested if reasonable to continue with one fetus fathered by each of them. Their situation highlights, generically, the ability of new technologies to address hitherto societal roadblocks in controversial situations.

Methods

Our general clinical approach incorporates genetic counseling concerning the risks of multiple pregnancies and options for prenatal screening and testing including thorough ultrasound and CVS as appropriate [15]. As with any surrogate situation in the USA, only the pregnant woman has an official ‘vote’ as to decisions and consents. While surrogacy contracts are highly variable in content, enforceability, and economics from state to state, surrogates have generally agreed, a priori, to the concept of genetic testing and FR as appropriate [16, 17]. To be clear, our center (Comprehensive Genetics) does not perform any infertility treatments including IVF. While we occasionally get inquiries from couples undergoing IVF about the possibility of reduction, we are never involved in decisions about how many embryos to transfer and with very few exceptions only see patients after they are pregnant.

We generally perform CVS on one more fetus than the couple is planning on keeping [6, 11, 15]. This approach virtually ensures normal fetus(es) – at least in terms of ultrasound and major chromosomes, and can then possibly give a gender choice option if all are normal. When we receive the appropriate lab information (usually FISH analysis the day after CVS), we can perform the FR – almost always that second afternoon.

Our approach to deciding which fetus(es) to reduce/keep has been prioritized as follows:

- (1) Do we find a problem?
- (2) Are we suspicious about something?
- (3) If nothing else above matters, then we can consider gender preferences.

We have described the above extensively elsewhere, and it will not be repeated further here [6, 11].

After consulting with the first of the three couples (described below), we decided to treat paternity preference according to the same principles as gender preference. Also, whereas the basic FISH analysis for 13, 18, 21, X, and Y can be accomplished within a day, the paternity polymorphisms would require at least a week, thus necessitating a second trip to our center for those from out of town.

All three couples expressed the strong preference to have twins with one from each father, but they understood that such would be considered only if medically there were no significant differences among the fetuses in terms of health as described above. Since we did not have the genotypes of the egg donors, we expressed to the couples that there could be some hesitation about clarity of results, and just as with gender preference could never guarantee that there would be a choice possible.

Table 1. Paternity analysis: probability of fatherhood

	Fetus A	Fetus B	Fetus C
Father 1	99.99%	0%	0%
Father 2	0%	99.99%	99.99%

Determination of paternity using 14 polymorphic markers showing clear differences in paternity likelihood.

Routine FISH and karyotype were performed by usual methods. Paternity analysis was also performed in common fashion using 14 highly polymorphic markers that are used to maximize the chance of segregating by possible fathers.

Results

Couple 1

Partner A is a 40-year-old Caucasian man with no children. Partner B is a 44-year-old Caucasian man with no children. This couple used two egg donors; partner A's sperm was used to fertilize eggs from both donors. Partner B's sperm was used to fertilize eggs from only one egg donor. Their surrogate was a 30-year-old, G₄P₃₀₀₃ Caucasian female. Molecular analysis on CVS showed that all were disomic for chromosomes 13, 18, 21, and sex chromosomes. Paternity analysis revealed that one partner fathered two of the fetuses, and the other one (table 1). Ultrasound showed no concern for any of the fetuses per se, and thus by our criteria first established for gender preference, the same principles were applied here. Reduction was performed leaving one fetus fathered from each partner. Since we did not have any genotype information on the egg donors and it was felt to be inconsequential, no assessment of 'maternity' was conducted.

Couple 2

Partner A is a Caucasian male with no children. Partner B is a Caucasian male with no children. This couple used a single egg donor. Their surrogate was a 35-year-old, G₅P₄₀₀₅ Caucasian female. CVS and molecular analyses were performed as per couple 1 with the same results of two normal fetuses from one partner and one from the other. Reduction left one from each.

Couple 3

Partner A is a 50-year-old Caucasian male with no children. Partner B is a 47-year-old Asian male with no children. This couple used a single egg donor. Their sur-

rogate was a 40-year-old, G₃P₂₀₀₂ Caucasian female. CVS and molecular analyses were performed as per couple 1 with the same results of two normal fetuses from one partner and one from the other. Reduction left one from each father.

In all three cases, we were able to leave euploid twins with one genetically from each father. In one case in which there was a further gender preference (but subservient to the paternity question), we were able to accommodate that preference as well. All procedures went smoothly. One pregnancy has successfully delivered, and the other two are progressing well.

Discussion

The technical performance of triplet CVS and molecular diagnosis in triplets is routine for our program, and as such is unremarkable per se [6, 15, 16]. The particular base pair sequences used to distinguish the two fathers are standard. However, this particular application opens a new venue for equalization of parental aspirations in gay couples that previously has been taken for granted in 'old fashioned' conceptions or even IVF for heterosexual couples.

The first question often asked about the above cases is: why were three presumably healthy embryos transferred into a gestational surrogate when guidelines would generally suggest only one or two? The primary answer given by the couples is financial. These couples have commonly spent well over USD 100,000 between surrogacy agreements and infertility treatments which are not covered by their insurance. They stated they would rather put the risks on the generation of multiples, which can be addressed, rather than potentially needing additional, expensive cycles to achieve a pregnancy. None expressed to us the primary desire for twins with paternity balancing although the desire for twins has been documented in the literature [12]. It was an afterthought beyond first achieving a pregnancy. However, just as many heterosexual couples have stated a preference for twins to have one pregnancy complete their family planning needs – despite increased risks of such pregnancies, it is not surprising that some gay or lesbian couples might have the same preference.

The desire to have children of one's own genetic make-up is a long appreciated preference seen for all types of couples. We have seen many lesbian couples who use sperm from a male relative of one partner and the eggs of the other [17]. In the USA, there are over 15,000 egg do-

nations per year (10% of IVF cases), which has doubled over the past decade [18]. Sperm donations statistics are not accurate, but are manifold higher. Definitions of parenthood have many components. In the USA, the woman giving birth, regardless of genetics, is the legal mother and the only one who can give medical consent during pregnancy. The reason many gestational surrogate programs now use IVF with donor eggs rather than the surrogate's own which would only require artificial insemination, is to minimize the chance that the surrogate will decide *ex post facto* to keep her own child [14]. The consent for reduction is signed by the surrogate and sometimes witnessed (with no legal standing for decision making) by the genetic father(s). As always for our program, the ultimate choice of which fetus(s) to reduce/keep belongs to the doctor based upon our criteria described above, but in our experience, surrogates over the past 25+ years have never requested input as to which fetus(es) were being kept or reduced.

As a practical matter, we view using procedural and laboratory technologies for 'paternity balancing' to be in the same category as gender determination and preferences in multiples. We came to believe in the acceptability of gender preference options in FR cases only after nearly two decades of experience in which we would not consider such. We came to that conclusion as previously seen biases (towards male preference in general and highly in certain ethnic groups) have tended to evaporate with now equal acceptance and preferences for boys and girls in our experience. However, we often have to disappoint some couples who have gender preferences because of genetic analysis showing anomalies, concerns, or no differences among fetuses. The same will undoubtedly occur for paternity balancing.

We know that for many people 'in the middle' and some religious and social conservatives who have voiced opposition including suggesting laws against it that even allowing gay couples to have genetic families by using surrogates is hard to accept, and this application perhaps even more so. However, for much of society the management of triplets with CVS and reduction is already well established and routine [6]. We see paternity balancing as a logical extension using technology for ancillary issues when already indicated by substantial medical concern.

From a sociologic perspective, paternity balancing is both a venue for equalization of parental aspirations and a moral quality-of-life dialog. The space for this dialog is created by at least two aspects of these situations. First, choices are not dictated by purely medical concerns re-

garding risk. Secondly, it is created by how parents 'frame' FR decisions [19, 20]. We have previously described the use of 'framing' in patient's choices about reductions and how they share information with friends and family about those choices [19, 20]. Others have argued that for women who consider reductions to be ethical, the beneficence-based obligations of the physician are somewhat mitigated with respect to the number of embryos to transfer in IVF procedures [18–22]. We have shown empirically that women who have less decision difficulty in FR are usually operating from a medical frame which prioritizes the statistics regarding the risks of carrying multiples and the extent of risk reduction with selective reduction. They can also come from a lifestyle frame (marked by a belief that a balance of children and career has normative value) [19, 20]. Patients who do not believe in FR often come from a deontological frame that does not permit them to consider such interventions [19, 20].

Paternity balancing broadens the consideration of what a lifestyle frame is, and it does so in a manner that is not even remotely identifiable as a slippery slope driven by the new eugenics or pushed by market forces. Paternity balancing does not entail choosing fetuses in terms of hair color or potential contribution to society. Just as with gender preference, paternity balancing should be viewed within the context that a reduction is being performed to improve medical outcomes. The only question concerns the choice of which fetus to reduce. Furthermore, it represents such a small percentage of multi-FR cases that market forces are essentially irrelevant. We believe that what is relevant is respecting the autonomy of the fathers in this new type of cases. Given the heightened awareness of gay couple issues as argued before the US Supreme Court in 2013 and reflected in increasing acceptance of gay marriage in the USA, we believe that using technology in helping gay couples have their own 'genetic' offspring can only further strengthen such relationships.

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Disclosure Statement

None.

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