We describe our experience with the use of embryo biopsy and fluorescent in-situ hybridization (FISH) in order to sex embryos for the purpose of family balancing in a private IVF clinic in India from April 1999–April 2001. Embryos were biopsied and analysed on day 3, cultured in sequential media, and then transferred on day 4 or day 5 after morphological selection of the best embryos. From a total of 42 cycles started, we achieved 14 clinical pregnancies and have had nine live births so far with five ongoing pregnancies. This is the first report of the use of preimplantation sex selection for family balancing in India, where couples place a premium on having baby boys, and the social and ethical aspects of the use of this technology in this setting are discussed.

Key words: blastocyst transfer/embryo biopsy/family balancing/fluorescent in-situ hybridization (FISH)/sex selection

Our experience

Preimplantation genetic diagnosis (PGD) enables the identification of genetic diseases in the embryo before pregnancy is established, and eliminates the need for possible pregnancy termination after prenatal diagnosis of a genetically affected fetus. Determining the sex of the embryo to avoid X-linked disorders remains a common indication for PGD, and the vast majority of such cases are carried out using fluorescence in-situ hybridization (FISH) with DNA probes derived from the X and Y chromosomes (Griffin et al., 1994; Münne et al., 1994; Staessen et al., 1999; ESHRE Preimplantation Genetic Diagnosis Consortium, 1999). While the application of this technique to prevent sex-linked genetic disorders is now widespread, this method can also be used for preimplantation sex selection for social reasons (family balancing), and we report our experience with this technique for this purpose in India.

Thirty-six couples who desired preimplantation sex selection were treated at Malpani Infertility Clinic, Mumbai, India, between April 1999 and April 2001. The preference for sons in India is based on long standing cultural beliefs, and not surprisingly, these couples (all of whom were of Indian origin) desired a baby boy. Some couples underwent more than one treatment cycle and a total of 42 sex selection cycles was started. All couples already had at least one daughter. Many couples had previously used fetal sex determination followed by selective female feticide, even though this has been illegal in India since 1996. We transferred 106 embryos (all of which were determined to be XY by FISH), and achieved 16 biochemical and 14 clinical pregnancies (determined by the presence of fetal heartbeat). Of these, six have delivered so far, and there have been nine live births (three singletons and three sets of twins). The gender was confirmed by gross anatomical examination of the baby at birth, and all nine babies born so far have been boys. Of the ongoing pregnancies, three are singletons and the remainder are twin pregnancies. Two patients suffered an early pregnancy loss (anembryonic pregnancy). The pregnancy rate per transfer was 35.8% (14/39); and the implantation rate (fetal hearts/number of transferred embryos) was 19.8% (21/106).

Discussion

Despite the fact that there are now many hundreds of babies born after PGD (ESHRE Preimplantation Genetic Diagnosis Consortium, 2000), the process remains technically challenging and a number of problems with current procedures remain unresolved including the limited time available for diagnosis, the poor survival of non-transferred embryos following cryopreservation and the limited amount of cellular material available for diagnosis. Despite these problems, we have demonstrated that it is possible for a small IVF centre to use these methods to provide preimplantation embryo sexing, and to achieve ongoing pregnancy and delivery rates comparable with published figures from large well-established centres (ESHRE Preimplantation Genetic Diagnosis Consortium, 1999; Staessen et al., 1999). This may be because the FISH sexing technique (as opposed to aneuploidy screening) is becoming somewhat standardized, and commercially available DNA probes and IVF culture media are of high quality.

Current FISH protocols for sexing can be completed in very little time, and embryos can be transferred on the same day the biopsy is performed (day 3). However, the procedure of
embryo biopsy can compromise development in some embryos, and culturing the embryos in vitro for an additional 24–48 h may allow selection of the embryos which have withstood the procedure with the least damage (Grifo, 1998). An additional observation period of 24–48 h after the biopsy allows identification of the embryos which have continued to cleave after the biopsy, and have the greatest implantation potential. Preimplantation FISH diagnosis is the most accurate method today for sex selection, and is far more reliable than sperm sorting using flow cytometry (Fugger, 2000). However, the use of embryo biopsy for sex selection for family balancing in a country like India where couples have a marked preference for baby boys raises many questions and ethical issues which need to be addressed (Benagiano and Bianchi, 1999; Sureau, 1999). Couples have always wanted to be able to choose the sex of their children, and there is a preference for having baby boys in India, for social and cultural reasons. Rather than use unethical techniques such as prenatal diagnosis for sex determination followed by selective female feticide (illegal in India since 1996), preimplantation sex selection provides a much more acceptable technique to allow couples to choose the sex of their child. Since this is a very personal decision, couples should be free to make up their own minds, and exercise reproductive autonomy. As Stock says so eloquently, ‘We enter a dangerous realm when we regulate so personal and intimate an aspect of our lives as reproduction because of fuzzy claims about sexism or nebulous fears for the health of yet-to-be-conceived children’ (Stock, 2001). In the crusade to protect the health of unborn children who are just a gleam in their parent’s eyes, we should not trample on the rights of the parents themselves (Robertson, 2001; Savulescu, 1999). A common criticism of using embryo biopsy for social sex selection is that it will produce an unbalanced sex ratio. Such arguments have recently been debated in the literature (Pennings, 1996; Malpani, 1998; Sureau, 1999; Benagiano and Bianchi, 1999; Simpson and Carson, 1999). However, the expense, limited availability and comparative inefficiency of sexing by embryo biopsy make this technique an unlikely source of a significant gender skew in any country. In India where this is a major concern, one simple safeguard would be to restrict its use only for couples who have at least one child, and who desire a child of the opposite sex. This approach would lead to more balanced sex ratios rather than the opposite.

The ESHRE Task Force on Ethics and Law states, regarding the ethical concerns related to the technique of PGD: ‘... we are aware of the risks of abuse for non-medical reasons. Information and consent of the couple, public transparency and the respect of professional guidelines will limit abuse.’ (ESHRE Task Force on Ethics and Law, 2001). These are strong words from a committee which has chosen to take the moral high ground, without bothering to explain why they feel using these techniques for non-medical reasons (such as sex selection for family balancing) is an abuse if the couple requests it! Do they feel that using plastic and reconstructive surgery for cosmetic reasons is an abuse of surgical skills? We believe that if we allow people to choose when to have babies; how many to have; and even to terminate pregnancies if they inadvertently get pregnant, then they should be allowed to select the sex of their child if they would like to do so. The basic purpose of all technology is to give people more control over their destiny than they have had in the past, and we need to allow people to make their own choices for themselves.

Surprisingly little has been written about the clinical use of preimplantation genetic diagnosis for social sex selection. Even though a growing number of clinics worldwide offer this service, few publish their data, presumably because this is not considered to be politically correct by Western standards (Ethics Committee of the American Society of Reproductive Medicine, 1999). This is unfortunate because the merits and ethical aspects of this approach need to be discussed and debated in a public forum. These data and experiences could also provide useful information which could be used to help improve pregnancy rates with PGD when used for strictly medical indications.

References


