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The evidence base regarding the experiences of and attitudes to preimplantation genetic diagnosis in prospective parents

Jenny Cunningham, MSc, Midwife*, Lesley Goldsmith, PhD, Research Fellow, Heather Skirton, PhD (Professor of Applied Health Genetics)

University of Plymouth, School of Nursing and Midwifery, Faculty of Health, Education and Society, Drakes Circus, Plymouth PL4 8AA, United Kingdom

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ABSTRACT

Baackground: Preimplantation genetic diagnosis was developed as an alternative to prenatal diagnosis for couples with a family history of genetic disease. After in vitro fertilization, the embryos can be analysed to ensure that only healthy embryos are transferred to the uterus. Past studies have suggested that couples who wish to avoid having a child with an inherited genetic condition look favourably on preimplantation genetic diagnosis as it prevents the need for termination of pregnancy following prenatal diagnosis of an affected fetus. However, it is important to understand the experiences of couples who have used or consider using this technique.

Methods: To ascertain the current evidence base on this topic, we conducted a mixed methods systematic review. Four databases were searched for relevant peer-reviewed papers published between 2000 and 2013. Of 453 papers, nine satisfied the inclusion criteria and were assessed for quality. Results of nine papers were analysed and synthesised using a narrative approach.

Findings: Three main themes emerged: (1) motivating factors; (2) emotional labour; (3) choices and uncertainty. The review has identified an emotional and difficult journey for couples pursuing preimplantation genetic diagnosis. While use of the technique gives hope to families who wish to prevent transmission of a genetic disease this is not without hard decision-making and periods of uncertainty. Lack of information was perceived as a barrier to access this reproductive option.

Implications for practice: Recommendations include: training and education in genetics for midwives who are the first point of contact for pregnant women; clinics to use a decision-making tool to emphasise the uncertainty involved in PGD and improved communication and psychological support to couples.

Introduction

Preimplantation genetic diagnosis (PGD) was developed in the 1980s as an alternative to prenatal diagnosis (PND) for couples with a family history of genetic disease (Braude et al., 2002). Before this technology was available, many couples at risk of having a child affected by an inherited genetic condition had a number of reproductive choices. These included taking the risk of having an affected child (or children), having PND followed by the option of termination of pregnancy (TOP) for an affected child, remaining childless, or having a child through adoption or gamete donation (Thornhill et al., 2005). The advent of PGD made it possible for some couples for whom PGD was available to avoid both the risk of having an affected child and the need to make a decision about termination of an affected pregnancy.

Preimplantation genetic diagnosis was made possible by the development of in vitro fertilisation (IVF) and development of methods for genetic diagnosis at the single cell level (Geraedts and De Wert, 2009). Following IVF or intra cytoplasmic sperm injection (ICSI), a single cell (or cells) is (are) removed from a human embryo on the third day after fertilisation and analysed for a specific genetic abnormality (Braude et al., 2002). Only unaffected embryos are transferred to the uterus.

Indications for PGD

Single-gene disorders

The ten most common single-gene diseases diagnosed through PGD has been unchanged in recent years (Geraedts and De Wert, 2009). Geraedts and De Wert (2009) state that these disorders make up about 80% of all PGD cycles for monogenetic disorders using PCR. Single-gene disorders can be either autosomal recessive, autosomal dominant or X-linked recessive (see Table 1).

In recent years, there has also been an increase in PGD for a variety of cancer predispositions, such as hereditary non-polyposis

* Corresponding author.
E-mail addresses: jennymidwife@googlemail.com (J. Cunningham), lesley.goldsmith@plymouth.ac.uk (L. Goldsmith), heather.skirton@plymouth.ac.uk (H. Skirton).

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Table 1
The ten most common single-gene disorders diagnosed through PGD (taken from Geraedts and de Wert, 2009).

Autosomal recessive conditions 1 in 4 pregnancies of two carrier parents affected	Autosomal dominant conditions 1 in 2 pregnancies (if one affected parent affected)	X-linked recessive conditions 1 in 4 pregnancies of carrier mother affected
β-thalassaemia	Huntington's disease	Fragile X syndrome
Cystic fibrosis	Myotonic dystrophy	Duchenne muscular dystrophy
Spinal muscular atrophy	Charcot–Marie-Tooth disease	Haemophilia
Sickle cell disease		

colorectal cancer, and familial breast and ovarian cancers (Harper et al., 2012). Although these are autosomal dominant conditions the penetrance may be variable, meaning not all those who are mutation positive will develop the condition (Menon et al., 2007).

Chromosome abnormalities

Other genetic disorders for which PGD can be offered include chromosome translocations that can be transmitted in an unbalanced form to the embryo. Translocations occur when a piece of one chromosome transfers to another chromosome. Where the chromosomes have been rearranged so that no chromosome material has been lost or gained a person will have a balanced translocation (Braude et al., 2002). The individual with this chromosome arrangement will be almost always phenotypically normal (Braude et al., 2002). When a parent has a balanced translocation this can lead to a baby with a normal, balanced or unbalanced translocation, the latter usually resulting in miscarriage, stillbirth or severe structural and mental disabilities (Franssen et al., 2011). Preimplantation genetic diagnosis can ensure that the embryo has a balanced chromosomal arrangement, although the success rate is low due to the high number of embryos unsuitable for transfer (Harper et al., 2012). Additionally, a systematic review undertaken by Franssen et al. (2011) found that there was insufficient data to demonstrate that PGD improves birth rate in couples with a structural chromosome abnormality and recurrent miscarriage.

Human leucocyte antigen

Preimplantation genetic diagnosis (PGD) is also available to help parents conceive a sibling who is human leucocyte antigen (HLA) compatible with a child suffering from an inherited disease that can be cured through haematopoietic stem cells to repopulate his or her bone marrow (Simpson, 2010). The older child is thus cured of a terminal illness, the baby is born free of genetic disease and the parents subsequently have two healthy children. Simpson (2010) gives the likelihood of a genetically normal HLA-compatible embryo as three in 16, which explains why couples look to PGD to help them.

PGD in practice

The latest synthesis of the European Society of Human Reproduction and Embryology (ESHRE) PGD collaboration data (Goossens et al., 2012) showed the success rates of PGD (see Table 2).

Regulation of PGD

The situation in Europe regarding use of PGD is diverse, with differences in regulation, legislation and technical infrastructure (Soini et al., 2006). Some countries, including Germany, Austria and Switzerland, prohibit the technology (Knoppers and Isasi, 2004). The German debate is focused on the 'eugenic' implications of PGD and the moral status of the embryo, due to the practice of eugenics during Nazi Germany (Borkenhagen et al., 2007). However, due to public demand, the situation in Germany is due to change with legislation being passed to allow PGD in

Table 2
The success rate of PGD (taken from Goossens et al., 2012).

	Chromosome translocations	Single gene disorder	Preimplantation genetic screening	Sexing for X-linked disorders
Childbirth rate (% per OR)	17.1	19.7	16.4	11
Childbirth rate (% per ET)	27.1	26.1	23.1	15

OR=oocyte retrieval (egg retrieval) and ET=embryo transfer.

'exceptional circumstances' (Kullmann, 2013). Both France and the United Kingdom (UK) have regulatory frameworks. In the UK, the Human Fertilisation and Embryology Authority (HFEA) was set up in 1991 as part of the Human Fertilisation and Embryology Act 1990, in order to regulate IVF treatment and human embryo research. There are currently 18 clinics in the UK licensed to carry out PGD (NHS, 2013). In the US there is no regulation of PGD and clinical staff work to their own codes of conduct and can decide how they use PGD (Robertson, 2003).

Context of other studies

A broad literature review into PGD was undertaken as a first step. There were studies which had investigated women's attitudes to PGD, including Pergament (1991) who found that the technology was more acceptable to women who had previous abnormal PND results and that the agreed major advantage of PGD was the avoidance of TOP. Participants in other studies included women at risk of transmitting thalassaemia (Palomba et al., 1994; Chamayou et al., 1998; Farra et al., 2008; Hui et al., 2002). These women generally found PGD preferable to PND with higher rates of approval from women who had experienced TOPs or who had an affected child. The findings of authors of a Scottish study (Miedzybrodzka et al., 1993) were that whilst a high proportion of women indicated they would prefer PGD to PND, previous experiences also influenced choices. Women who had previously undergone PND favoured this method (with the possibility of TOP) over PGD.

The literature also included more recent studies which investigated participants views about PGD for adult-onset diseases with varying penetrance. There was a mixed response to PGD in the studies involving women at an increased risk for hereditary breast and ovarian cancer, which is an autosomal dominant condition. PGD is seen in a positive light in Menon et al.'s study (2007) with the majority viewing it as acceptable, however only 14% would consider it for their own use. This was similar to Staton et al. (2008) who also found the majority of participants were concerned about transmitting the mutation to their children but only 13% said they were likely to use it. There was also ambivalence expressed with respondents questioning the ethics of selecting out embryos with an adult-onset disease (Menon et al., 2007; Staton et al., 2008; Quinn et al., 2009).