Pre-implantation Genetic Diagnosis/HLA-selection/In vitro fertilisation in Fanconi Anaemia

Why might we consider Pre-implantation Genetic Diagnosis/HLA-selection/In vitro fertilisation?

Most children affected by Fanconi Anaemia will require a bone marrow transplant at some point, either for bone marrow failure, or following the development of leukaemia. The outcome is best if the (HLA-) matched donor is a brother or sister of the affected child, both in terms of surviving the bone marrow transplant, and also because of the lower risk of graft versus host disease and subsequent chance of head & neck cancer. About 20% of families will be in the position of having a brother or sister who is suitably HLA-matched. The results of bone marrow transplantation in Fanconi Anaemia using an unrelated HLA-matched donor have significantly improved over recent years but overall are not yet as good as from a sibling matched donor. In addition, a proportion of Fanconi Anaemia affected children will neither have a matched sibling donor nor a matched unrelated donor. Bone marrow transplantation in such circumstances is very high risk. Some families may choose to pursue Pre-implantation Genetic Diagnosis/HLA-selection/In vitro fertilisation (PGD/HLA-selection/IVF or 'saviour sibling') as a means of both having a further Fanconi Anaemia unaffected child and a HLA-matched donor for their Fanconi Anaemia affected child. Successful PGD/HLA-selection/IVF for Fanconi Anaemia was first reported in 2001.

What exactly does PGD/HLA-selection/IVF involve?

The procedure of PGD/HLA-selection/IVF is complex and involves cutting-edge technology. Similar to 'traditional IVF', the father's sperm fertilizes the mother's egg in the 'test-tube' to make an embryo. The embryo is allowed to grow for about three days until it is made up of about eight or more cells. One of these cells is then removed for complex molecular biological analysis for both Fanconi Anaemia and also for HLA-typing. The removal of one of the embryo cells is not thought to be of long-term harm. For each IVF cycle, there may be up to a dozen embryos. Not all of these embryos will survive. For each embryo analysed, there is a three out of sixteen chance it will be both Fanconi Anaemia unaffected and a HLA-match. Further detailed information is provided on providers' websites (see below).

Is PGD/HLA-selection/IVF an easy thing to do?

Choosing to embark on PGD/HLA-selection/IVF is not an easy road. Some families may struggle with PGD/HLA-selection/IVF as a choice from a religious or philosophical perspective. Some families will have had the diagnosis of Fanconi Anaemia made too late in terms of fertility of the mother for PGD/HLA-selection/IVF to be an option (ideally, the mother should be 35 years of age or younger). For others, PGD/HLA-selection/IVF may prove to be unaffordable. PGD/HLA-selection/IVF can be about £7000 per cycle with parents going through at least half a dozen cycles.

Typically, parents may go through about two to three cycles per year over a period of two to three years. The chances of success with each cycle are not high and it is possible that the whole process may be unsuccessful with respect to a saviour sibling although an FA-unaffected child is likely. There is a small risk to the mother as with any type of IVF. The PGD/HLA-selection analysis is not fool-proof. There is one FA family in the US who went through PGD/HLA-selection/IVF only to have twins both Fanconi Anaemia affected. It is emotionally stressful, but those who do embark on it may feel as if they are doing something positive, both for their Fanconi Anaemia affected child and their family.

Are there any other issues we need to think about if embarking on PGD/HLA-selection/IVF?

You may wish to think twice about who you discuss your decision with if you choose to embark on PGD/HLA-selection/IVF. Some people, even relatives, may have strongly-held negative opinions concerning the process and may as a result be insensitive to the situation you and your family find yourselves in.

Is PGD/HLA-selection/IVF permitted in the UK?

PGD/HLA-selection/IVF for Fanconi Anaemia is legal in the UK. However, any provider of PGD/HLA-selection/IVF in the UK has to make application to the Human Embryonic and Fertilisation Authority (www.hfea.gov.uk) for a licence for each family it takes on. This licence application takes about three months.

Will the NHS pay for PGD/HLA-selection/IVF?

PGD/HLA-selection/IVF is variably funded by the NHS. Successful funding is more based on a 'postcode lottery' rather than by any systematic approach. A funding application has to be made to the Primary Care Trust (PCT) that covers the area in which the family reside. The funding application should be made by both the haematologist and geneticist together. Some PCTs will fund one to three cycles of PGD/HLA-selection/IVF. Some will refuse funding altogether. There is an Appeals process that parents may choose to engage in if the initial funding application is rejected.

Do we need to have any tests done before we can be referred for PGD/HLA-typing/IVF?

If a family wishes to undergo PGD/HLA-selection/IVF, complementation group analysis must be completed on their Fanconi Anaemia affected child, and ideally mutation analysis also on their affected child and both parents. PGD/HLA-selection/IVF can still be performed if one or both gene mutations are not found as long as the complementation group, i.e., the specific Fanconi gene affected, has been identified. In addition, if both parents are from a population group in which other genetic disorders are more frequently seen, then both parents should be checked by the geneticist for their carrier status, e.g., cystic fibrosis for Caucasians.

Where could we have PGD/HLA-selection/IVF performed?

There is currently only one healthcare-provider in the UK that offers PGD/HLA-selection/IVF for Fanconi Anaemia with both embryo biopsy and the single-cell PGD/HLA-selection analysis done on site, that is, CARE Fertility in partnership with Cooper Genomics (Genesis Genetics, see Genesis Genetics Institute below), at Nottingham (http://www.carefertilityweb.co.uk/pgd/pgd.shtml). One of the most experienced providers of PGD/HLA-selection for Fanconi Anaemia in North America is Cooper Genomics, Detroit, (https://www.coopergenomics.com/).

What should we do next if we wish to pursue PGD/HLA-selection/IVF?

A family wishing to explore the possibility of PGD/HLA-selection/IVF should discuss this option with their geneticist and haematologist. The geneticist and haematologist will be aware of PGD/HLA-selection/IVF but may not have any direct experience, as PGD/HLA-selection/IVF has only very recently become available in the UK. Following the appropriate genetic analysis of both parents and their Fanconi Anaemia affected child, the geneticist or haematologist should make the referral onwards to the appropriate PGD/HLA-selection/IVF provider on the request of the parents. The geneticist and haematologist should also make a joint application to the family's Primary Care Trust for funding.

This information sheet has been prepared by Dr Thomas Carroll, an FA affected parent and medical doctor, using the available evidence from the medical literature and also having sought appropriate professional opinions.

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