Best Practice & Research Clinical Obstetrics and Gynaecology 28 (2014) 191–199

Contents lists available at ScienceDirect

Best Practice & Research Clinical Obstetrics and Gynaecology

journal homepage: www.elsevier.com/locate/bpobgyn

1

Reducing multiple births in assisted reproduction technology

Siladitya Bhattacharya, MD, FRCOG [a,*], Mohan S. Kamath, MS, DNB [b]

[a] Division of Applied Health Sciences, University of Aberdeen, Obstetrics and Gynaecology, Aberdeen Maternity Hospital, Foresterhill, Aberdeen AB25 2ZD, UK
[b] Reproductive Medicine Unit, Christian Medical College, Vellore, India

Keywords:
assisted reproduction technology
in-vitro fertilisation
multiple pregnancy
elective single embryo transfer

Multiple pregnancy, a complication of assisted reproduction technology, is associated with poorer maternal and perinatal outcomes. The primary reason behind this is the strategy of replacing more than one embryo during an assisted reproduction technology cycle to maximise pregnancy rates. The solution to this problem is to reduce the number of embryos transferred during in-vitro fertilisation. The transition from triple- to double-embryo transfer, which decreased the risk of triplets without compromising pregnancy rates, was easily implemented. The adoption of a single embryo transfer policy has been slow because of concerns about impaired pregnancy rates in a fresh assisted reproduction technology cycle. Widespread availability of effective cryopreservation programmes means that elective single embryo transfer, along with subsequent frozen embryo transfers, could provide a way forward. Any such strategy will need to consider couples' preferences and existing funding policies, both of which have a profound influence on decision making around embryo transfer.

Introduction

Assisted reproductive technology (ART) includes procedures that involve in-vitro handling of human gametes or embryos for purposes of establishing a pregnancy [1]. The past 3 decades have witnessed a dramatic increase in the number of women undergoing ART treatment worldwide, with

* Corresponding author. Tel.: +44 1224 438419; Fax: +44 1224 438486.
E-mail address: s.bhattacharya@abdn.ac.uk (S. Bhattacharya).

1521-6934/$ – see front matter
http://dx.doi.org/10.1016/j.bpobgyn.2013.11.005

more than 5 million children conceived by means of this treatment [2]. Ovarian stimulation has traditionally been used in ART to produce a number of oocytes, and has the involved replacement of more than one embryo to maximise pregnancy rates. This has led to an increase in the number of twins and higher order multiple pregnancies [3]. Although initially seen as an acceptable outcome of ART, concerns have increasingly been raised about the consequences of such a policy on the health of women and children. Compared with singleton pregnancies, women carrying twins and other multiples are at increased risk of maternal complications, such as preeclampsia, preterm premature rupture of membrane, and caesarean section [4]. A fivefold increase in neonatal mortality occurs after twin delivery compared with singleton delivery, and this risk is higher in higher order multiples [5].

In many parts of the world, a conscious effort has been made to reduce the rates of iatrogenic multiple pregnancy by means of legislation and policy changes. A favourable downward trend in multiple pregnancy rates has resulted from the introduction of single-embryo transfer (SET) policies in some countries, but this is by no means a universal phenomenon [6,7]. In this chapter, we review various strategies for reducing multiple pregnancies in in-vitro fertilisation (IVF), including legislative and policy changes.

Burden of the problem: risks of multiple pregnancies after assisted reproductive technology

Data from 376,971 European IVF treatment cycles in 2007 show a multiple birth rate of 22.3% (21.3% twins and 1% triplets), similar to rates in 2005 and 2006 (21.8 and 20.8%, respectively) [8]. Figures from the Society for Assisted Reproduction Technology (SART) registry in the USA, based on 108,130 ART cycles, revealed a multiple birth rate of 35.4, of which 31.8% were twin, 3.5% were triplets, and 0.1% were higher order multiple [9].

In the UK, data published by the Human Fertilisation and Embryology Authority (HFEA) for the years 2009 and 2010 show a multiple pregnancy rate of 25.4 and 22.2%, respectively. In 1992, for every 100 deliveries after successful ART treatment, 28 were multiple births, whereas the multiple births figures stood at 23 per 100 deliveries after ART treatment in the year 2006.

Risks associated with multiple pregnancies

Multiple pregnancy increases the risk of maternal mortality, estimated to be 14.9 out of 100,000 compared with 5.9 out of 100,000 for singleton births [10]. The incidence of complications of pregnancy, such as pregnancy-induced hypertension, is also increased, and the risk of anaemia is doubled; uterine atony, dystocia, increased operative deliveries, and postpartum haemorrhage are all associated with multiple pregnancy [11], as is the incidence of depression [12].

Prematurity occurs in nearly one-half of all multiple pregnancies, and is the main cause of neonatal morbidity and mortality; 42% of twins and 8% of singletons are born before 37 completed weeks [13,14]. Twins face a six-fold and triplets a 10–20-fold increase in risk of mortality compared with singletons [15].

Gestational age and birth weight are inversely related to the number of fetuses. The mean gestation for twins, triplets and quadruplets is 35, 33 and 29 weeks, respectively. Ninety per cent of triplets and higher order multiples weigh less than 2500 g compared with only 6% of all singletons; 78% of triplets and higher order multiples, and 48% of twins will need admission to neonatal intensive care units compared with 15% of singletons [16].

Higher rates of congenital anomaly in children conceived through ART have been reported and are more common in multiple pregnancies; the risk of cerebral palsy is increased three- to seven-fold in twins and ten-fold in triplets [11,17]. Long-term behavioural problems have been found to be higher in children born after multiple births compared with children born as singletons [18]. Prenatal screening poses additional difficulty, and leads to increased anxiety during the antenatal period for women carrying multiples [19]. Multiple gestation requires more frequent clinical and ultrasonographic monitoring compared with singleton pregnancies.

Maternal and neonatal complications in multiple pregnancies are presented in Tables 1 and 2.

Healthcare costs rise four-fold in twins and ten-fold in triplets compared with costs associated with singleton pregnancies. The health risks associated with preterm birth are important contributors to