Best Practice & Research Clinical Obstetrics and Gynaecology 26 (2012) 729–738

Contents lists available at SciVerse ScienceDirect

Best Practice & Research Clinical Obstetrics and Gynaecology

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

1

Demographics of infertility and management of unexplained infertility

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

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

Keywords:
unexplained infertility
expectant management
intra uterine insemination
super ovulation
clomifene citrate
in-vitro fertilisation

The cause of infertility is unexplained in about 22–28% of all infertile couples. The prognosis for spontaneous pregnancy in such couples is better than in those with diagnosed causes of infertility. Traditional treatment options in this group have included expectant management, clomifene citrate, intrauterine insemination with (super ovulation plus intrauterine insemination) or without (intrauterine insemination) super ovulation and in-vitro fertilisation. Despite being more expensive, empirical clomifene and intrauterine insemination in an unstimulated cycle do not improve the chances of live birth compared with expectant management. Although unlikely to be more effective than no treatment in couples with a reasonably good prognosis, super ovulation plus intrauterine insemination has been shown to be more effective than intrauterine insemination. Any potential advantage of super ovulation plus intrauterine insemination has to be balanced against the relatively high risk of iatrogenic multiple pregnancy. In-vitro fertilisation remains the treatment of choice in long-standing unresolved infertility and, when coupled with the use of elective single embryo transfer, can minimise the risk of multiple pregnancies. Data from randomised trials confirming the superiority of in-vitro fertilisation over expectant management is limited.

* Corresponding author.
E-mail address: s.bhattacharya@abdn.ac.uk (S. Bhattacharya).

1521-6934/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.bpobgyn.2012.08.001

Introduction

Infertility has been defined as failure to conceive after regular unprotected sexual intercourse for 1 year.[1,2] This definition reflects the prognostic approach to this condition, based on the knowledge that, in a general population, 84% of all women are expected to conceive within 1 year of regular unprotected sexual intercourse. This figure rises to 92% after 2 years, and 93% after 3 years.[3] The term 'unexplained infertility' refers to infertile couples in whom standard investigations, including tests of ovulation, tubal patency and semen analysis, are normal. The prevalence of unexplained infertility has been shown to vary from 22–28%.[4,5] A more recent study puts the prevalence among couples attending a fertility clinic to be 21% in women aged under 35 years, and 26% in women over 35 years.[6]

Standard work-up for infertility

The basic fertility work up needs to balance the cost and invasive nature of currently available investigations against their value in informing clinical decision making. The National Institute for Health and Clinical Excellence in the UK and the American Society of Reproductive Medicine in the USA have recommended the following essential tests: semen analysis, assessment of ovulation and evaluation of tubal patency by hysterosalpingogram or laparoscopy.[7,8] The place of laparoscopy versus hysterosalpingogram continues to be debated, but it is felt that laparoscopy should be considered when severe endometriosis, pelvic adhesions or tubal disease is suspected.[8]

The predictive value of the post-coital test has been questioned, and the result of a randomised-controlled trial has not shown improved pregnancy rates in women undergoing this investigation.[9] Tests of ovarian reserve have been shown to be useful in predicting follicular response to controlled ovarian stimulation in in-vitro fertilisation (IVF), but their role in predicting pregnancy outcomes in infertile women is limited.[10]

Causes of unexplained infertility

Standard fertility investigations are far from comprehensive and unable to identify subtle abnormalities in the reproductive pathway. The cause of unexplained infertility is, therefore, likely to be heterogeneous, with proposed causes ranging from endocrinological, immunological and genetic factors.[11] In addition, compromised ovarian reserve is a factor which, while not always captured in the diagnostic pathway, can be responsible for a diagnosis of unexplained infertility in older women.

Some investigators have questioned the validity of the term 'unexplained infertility', as it is sensitive to the number, nature and quality of the tests used.[12] Others have argued that the limited number of treatment options, and the overwhelming dependence on assisted reproduction, means that increasing the number of expensive and invasive tests is unlikely to change the treatment strategy in these couples.[13]

Prognosis

Couples with unexplained infertility have a higher chance of spontaneous pregnancy than those where definite barriers to conception have been identified.[14] A number of prognostic models have attempted to determine factors associated with spontaneous livebirth.[14–16] A synthesis of these models has been produced by Hunault et al.[17–19] and validated in a Dutch population. Prognostic factors are gradually emerging as key to informing clinical decision-making. The chance of pregnancy leading to live birth is influenced by female age, duration and previous pregnancy.[14] For example, a woman aged 28 years with 2 years of unexplained infertility has been shown to have a 36% chance of conceiving over the next 12 months.[14] The decision to treat a couple with unexplained infertility should, therefore, take into account their chances of spontaneous conception.