CPD Paper 6

Investigating the Infertile Couple

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Abstract

***Introduction**: Investigations play a pivotal role in the workup for infertility. The results must be interpreted carefully as these assess dynamic function. Evidence-based guidelines are useful in the selection of appropriate tests. **Materials and Methods**: A review of current evidence-based guidelines for the investigation and management of the infertile couple is undertaken. **Results**: The main areas that correlate with fecundability are ovulatory function, tubal patency and semen analysis. **Conclusion**: The appropriate selection of investigations based on problem areas identified by history and physical examination would guide the physician in the management of the infertile couple.*

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Key words: Infertility, Investigations, Laparoscopy, Ovulation, Semen, Tubal patency

Introduction

Infertility is defined as the inability to conceive after 1 to 2 years of unprotected intercourse. In general, an estimated 84% of all women would conceive after a year of intercourse. This figure rises cumulatively to 92% after 2 years and 93% after 3 years.[1] Data from historical populations estimated rates of prevalence of infertility to be 5.5%, 9.4% and 19.7% at ages 25-29 years, 30-34 years and 35-39 years, respectively;[2] bearing in mind the effects of age, such definitions would serve as a useful guideline as to when to proceed with evaluation for infertility. However, if there is an obvious cause for infertility in the history, investigations should be initiated earlier.

Ovulation and Ovarian Reserve

The frequency and timing of the menstrual cycle gives an indication if the woman is ovulating regularly. Regular menstrual cycles in the range of 26 to 36 days are usually indicative of ovulation.[3] However, it is possible that up to 9% of regular menstrual cycles are anovulatory.[4]

Anovulation and infrequent ovulation account for about 21% of infertility.[5] The World Health Organisation classifies ovulation disorders into 3 groups: low gonadotrophins and low oestrogen (hypothalamic amenorrhoea, hypogonadotrophic hypogonadism), which account for about 10% of ovulatory disorders; gonadotrophin disorder and normal oestrogen (predominantly polycystic ovarian syndrome), which account for about 85% of ovulatory disorders; and high gonadotrophin and low oestrogen (premature ovarian failure), which account for about 4% to 5% of ovulatory disorders. Hence, in the investigation of anovulation, it is useful to perform the serum follicle-stimulating hormone (FSH), luteinising hormone (LH), testosterone, prolactin and thyroid function tests.

The presence of ovulation can be confirmed by measurement of serum progesterone in the mid-luteal phase on day 22 or approximately 7 days before menses. The values range from 16 nmol/L to 28 nmol/L as the lowest limit indicative of ovulation.[6] Ovulation kits are useful to predict impending ovulation and transvaginal follicular tracking can assist in more precise estimation of impending ovulation.

The ovarian reserve is related to the size of the primordial follicle store within the ovary and this declines with age.[7] The rate of depletion of the ovarian follicle store hastens at around the age of 37 years. An estimate of ovarian reserve is especially useful before embarking on ovarian stimulation. This can be done by assessing the gonadotrophin FSH and LH levels on day 3 of the menstrual cycle. Elevated FSH levels would suggest a poor response to ovarian stimulation. This can also be done with a clomiphene challenge test.

Reports that direct measures of ovarian function, such as inhibins A and B, correlate inversely with age and FSH levels,[8] and that inhibin B levels are decreased in women with reduced ovarian reserve, require further evaluation.[9]

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Hence, the roles of inhibins A and B in predicting ovarian reserve are uncertain and, therefore, not recommended.

Tubal Patency

Tubal infertility accounts for 12% to 33% of female infertility. An ideal method of tubal assessment to predict pregnancy outcome has yet to be devised. Until recently, the assessment of tubal function is limited to its patency with hysterosalpingography (HSG) and hydrotubation at laparoscopy. The limitations are the length, tortuosity and small diameter of the fallopian tube.

HSG

A simple and non-invasive screening procedure for the assessment of patency and mucosal normality of the fallopian tube, HSG provides a very good outline of the uterine cavity. Peritubular adhesions can be suspected.

The diagnostic accuracy of HSG has been compared to that of laparoscopy and dye in a systematic review of 20 studies that distinguished tubal obstruction from peritubal adhesions. Meta-analysis based on these 3 studies gave pooled estimates of sensitivity and specificity for HSG, as a test for tubal obstruction, of 0.65 [95% confidence interval (CI), 0.50 to 0.78] and 0.83 (95% CI, 0.77 to 0.88), respectively. These estimates imply that when HSG suggests the presence of tubal obstruction in 8 out of 10 women, this will be confirmed by laparoscopy. Hence, HSG is a reasonably reliable indicator of tubal occlusion. However, when HSG suggests that the tubes are patent, 4 out of 10 women would at laparoscopy be found to have tubal occlusion. Thus, HSG may not be a reliable indicator of tubal patency.[10]

Sonohysterography

A variant of HSG, which employs real-time ultrasonography and either saline or ultrasound contrast medium, is increasingly being used as a screening tool for tubal patency. At the same time, Colour Doppler can be used. The advantage of this procedure is that it can be performed as an office procedure and the results made known immediately. This procedure is also well-tolerated by patients.

Evaluative studies of hysterosalpingo-contrast sonogaphy showed good statistical comparability and concordance with HSG and laparoscopy.[11]

Laparoscopy and Hydrotubation

Laparoscopy facilitates easy visualisation of the external appearance of the fallopian tubes. Instillation of dye through the cervix with a cannula intravaginally allows visualisatioin of tubal patency.

In the absence of dye flowing from the fimbrial end of the fallopian tube, the tube is deemed to be blocked. False positives have been attributed to tubal cornual spasm. Visible external peritubal adhesions can be due to previous pelvic infection, endometriosis or surgery. Some studies have suggested an inverse relationship between severity of periadnexal adhesions and pregnancy outcome; others have not. Several classifications for periadnexal adhesions have been devised, including that of the American Fertility Society (AFS).[12] There seemed to be a better correlation between periadnexal adhesions and pregnancy outcome when salpingostomy was included in the classification criteria. It was felt that the status of the tubal mucosa was the most powerful prognostic factor in predicting pregnancy outcome.[13]

Women who are thought to have other co-morbidities should be offered a laparoscopy and dye so that tubal and other pelvic pathologies can be assessed at the same time.

Fertiloscopy

Fertiloscopy is defined as the combination, in a single investigation, of transvaginal hydropelviscopy, dye test, optional salpingoscopy and hysteroscopy performed under local anaesthesia or neuroleptanalgesia.[14]

As this is a relatively new procedure and complications have been reported, this technique needs further prospective evaluation whilst taking into consideration the learning curve requirement.

Falloposcopy

The interior of the fallopian tube is the last frontier in the exploration of the anatomy of the pelvic organs in the field of reproductive surgery. Falloposcopy allows exploration of the cornua, isthmus and ampullary areas of the interior of the fallopian tubes. Besides ampullary assessment of the fallopian tube, cornua and isthmic abnormalities, such as intraluminal adhesion, debris and vascular damage, can be seen.[15]

Two commercial methods are available: the linear everting catheter system and co-axial guidewire system. Both systems use a very small-diameter, flexible telescope of 0.5 mm through a flexible and atraumatic catheter. Cannulation is considered a success when no resistance was met, while tuboplasty is considered successful when resistance was negotiated with the catheter.

Semen Quality

An essential investigation of the male partner is the semen analysis. Currently performed according to the World Health Organisation (WHO) criteria, it is a relatively sensitive test (89.6%) with poor specificity.[16] This can be improved with a repeat semen sample, which provides greater specificity in identifying semen abnormalities. A single analysis will falsely identify about 10% of men as abnormal; repeat testing reduces the rate to 2%.[17]

Interpretation of results should also take into consideration variations in the samples drawn from each individual. Should the semen analysis persistently prove suboptimal, other tests that ought to be considered include FSH and serum testosterone to help differentiate between obstructive and spermatogenic failure with FSH raised in the latter. If hypogonadism is suspected because of signs of hypo-androgenism, testosterone and prolactin will need to be measured in addition to FSH.

Microbiological assessment of semen would be necessary for men with symptoms of orchitis, epididymitis, prostatitis or the presence of excessive numbers of leukocytes in the semen. The presence of significant amounts of organisms in the ejaculate can cause poor sperm function. However, the presence of pus cells in the semen does not always indicate infection and may not always correlate well with impaired fertility.[18]

Conclusion

There are many investigations that can be performed for subfertility but the areas which correlate best with fecundability are semen analysis, tubal patency and ovulatiory function. Guidelines for the management and investigation of subfertile couples have been compiled by the Royal College of Obstetricians and Gynaecologists[19] and the National Institute for Clinical Excellence in the United Kingdom. These are evidence-based guidelines and are useful for patient care.

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QUESTIONS

1. Anovulation is a common cause of infertility.
   a) The incidence of anovulation in regularly menstruating women is 15%.
   b) Anovulation accounts for 21% of infertility.
   c) The presence of ovulation can be confirmed by serum progesterone on day 22.
   d) Inhibins A and B correlate inversely with age and FSH.
   e) The rate of depletion of the ovarian follicle store begins at age 45.

2. The following correlations are correct.
   a) Hypogonadotrophic hypogonadism = low gonadotrophins and low oestrogen.
   b) Polycystic ovarian syndrome = low gonadotrophins and low oestrogen.
   c) Premature ovarian failure = low gonadotrophins and high oestrogen.
   d) Thyroid dysfunction = low gonadotrophin and low oestrogen.
   e) Hypothalamic amenorrhoea = low gonadotrophin and low oestrogen.

3. Infertility.
   a) After a year of unprotected intercourse, about 84% of women will not be pregnant.
   b) The prevalence of infertility increases with increasing age.
   c) Elevated FSH levels on day 3 of the menstrual cycle suggest a good ovarian reserve.
   d) The most common cause of anovulation is PCOS.
   e) Nine-three per cent of women conceive after 3 years of unprotected intercourse.

4. The following can be used to assess tubal infertility.
   a) Laparoscopy and hydrotubation.
   b) Ultrasonography.
   c) Falloposcopy.
   d) Semen percoll swim-up test.
   e) Salpingoscopy.

5. Male infertility.
   a) A single semen sample provides adequate assessment as it only falsely identifies 2% as abnormal.
   b) Spermatogenic failure will be reflected with low gonadotrophins and low testosterone levels.
   c) Semen infections can affect sperm function.
   d) Hyperprolactinaemia can give rise to hypoandrogenism.
   e) Semen analysis is assessed according to WHO criteria.