

How can Infertility be managed in General Practice? – A review.

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Summary

About one in six couples are experiencing difficulties in conceiving a child. One in four couples may seek advice about infertility from their General Practitioner (GP) at some time in their life. The GP needs to make a decision about secondary care referral. The aim of the study is to understand the effective management of infertility in general practice. All GPs must do couple centered approach and be able to deal with initial presentations of infertility in terms of history taking, examination, routine investigations and timely referral to fertility specialist care. Many couples who face fertility problems end up with stress, anxiety and depression. GPs must provide ongoing support to couples even after referral and be able to provide adequate information in each stage of investigation and treatment as well as regarding available fertility management facilities.

Background

About one in six couples are experiencing difficulties in conceiving a child (RCOG, 1998) and seek help at some stage in their lives. Even though there is no increase in the prevalence of infertility, there seems to be a trend towards more patients seeking help with infertility problems (Gunnell and Ewings, 1994). According to them, one in four couples may seek advice about infertility from their GP. The GP needs to decide about the referral of infertility couples to secondary care. Even after the referral to specialists, the GPs are expected to provide continuous support for these couples. This places the primary care service at the heart of all issues related to infertility (Whitman-Elia, 2001).

The aim of the study is to understand the effective management of infertility in general practice.

Role of GP

Couple – centered management

Both partners should be involved in the management of infertility (RCOG, 1998). Both male and female partner of the couple should be assessed for infertility (Jenkins et al 2003).

Initial support

People who are concerned about delays in conception should be offered an initial assessment in general practice (NICE, 2004). Couples who seek earlier advice should be reassured about natural conception. About 50% of couples having regular unprotected intercourse in general population will have conceived within three months, two-thirds by six months and 90% by 12 months (Johnson and Everitt, 2000). The environment in which the initial assessment takes place should enable people to discuss sensitive issues like sexual abuse. Couples who have not conceived after one year of unprotected sexual intercourse should be offered further initial clinical investigations to both partners (NICE, 2004).

Initial assessment

GPs should have an idea about the commonest and main causes of infertility for assessing the couple for fertility problems. Collins et al 1995 reported that anovulation, tubal damage in female and abnormal semen analysis in male constitutes about 75% – 80% of all causes of infertility. The diagnosis of ‘unexplained infertility’ occurs in about 25% of both partners.

History

A detailed history taking is an essential part of initial assessment of infertility by the GP. In the female, ask about personal and life style history including age, occupation, exercise, stress in her life, previous anorexia nervosa, drug history, smoking and alcohol intake, frequency of sexual intercourse and the length of unprotected intercourse. Menstrual history should include regularity of cycle, amenorrhoea (absent periods) or oligomenorrhoea, any previous pregnancies with same or different partners, previous abdominal or pelvic surgery, previous sexually transmitted disease (STD) or pelvic inflammatory disease (PID), previous contraceptive history and previous tests like cervical smear and rubella status should be asked.

In male, ask for personal and life style details like female but with greater emphasis on factors that can increase intrascrotal temperature. Evidences show that a rise in testicular temperature may decrease sperm count and quality. Factors such as occupation (welder), sitting in a wheel chair or wearing tight underwear may be relevant to male infertility (RCOG, 1998). Soaking in a hot bath may affect intrascrotal temperature but not showers or saunas (Brindley et al 1982).

Elaborate drug history in male is important. Some medications may cause impotence or reduce libido or reduce sperm production. Most of the times, GPs know about the patients regular medication but it is important to get the drug history from the men themselves as part of infertility assessment. Drugs like sulfasalazine, nitrofurantoin, tetracyclines, phenothiazines, monoamine oxidase inhibitors, tricyclic anti-depressants, corticosteroids, anticancer drugs, cimetidine, allopurinol, ketoconazole, methyl dopa,

propranolol, guanethidine, reserpine, anabolic steroids(used for muscle building), cocaine and cannabis may have effect on fertility of male(Jenkins et al 2003).History about previous STD, urogenital infection or surgery, previous pregnancy with same or other partners should also be asked.

Clinical examination

In female, look for obesity (body mass index (BMI) > 29) or underweight, hirsutism and or acne may give clue to the diagnosis of polycystic ovary syndrome (PCOS, the commonest cause of anovulation). Look for galactorrhoea, if present suspect hyperprolactinemia (anovulation). Cervical smears to be done if not done already (NICE, 2004).Pelvic examination can help to find out vaginal infection, PID or endometriosis. Bimanual examination may reveal fibroid, ovarian cyst or endometriosis.

In male, assess the secondary sexual characteristics. Then do the genital examination to rule out small soft testes, lump in the testis, varicocele or an undescended testis. Varicocele is found out in about 25% of male partners who seek help for infertility (Hargreave and Mills, 1998). But the evidences are not clear about whether varicocele is a cause of male infertility which may be improved by surgery (Jenkins et al 2003).

Advice

Women

Women who are concerned about their fertility should be informed that female fertility declines with age. With regular unprotected sexual intercourse, 94% of fertile female aged 35 years and 77% of whom aged 38 years will conceive after three years of trying (NICE, 2004). Fertility falls steeply beyond 40 years of female's age.GP should encourage women who have BMI>29 to lose weight as they are likely to take longer to conceive. Moderate weight loss may restore ovulation and improve pregnancy rates (Health Education Authority, 1996). Women should be informed that participating in a group programme involving exercise and dietary advice leads to more pregnancies than weight loss advice alone(NICE,2004).

GPs should recommend women to limit their alcohol intake to one or two units once or twice per week so that the harm to the developing fetus can be reduced (Jensen et al 1998). Women who smoke should be advised to stop smoking as this improves her fertility and reduces the chances of miscarriage if she does conceive (RCOG, 1998). There is no consistent evidence of an association between consumption of caffeinated beverages (tea, coffee and colas) and fertility problems (NICE, 2004).

Genital tract infection with *Chlamydia trachomatis* is a major risk factor for subsequent tubal infertility (Winter and Ahmad, 1998). NICE guideline 2004 advices about offering screening for Chlamydia before undergoing uterine instrumentation. It is the duty of the GP to refer the women and their sexual partners for appropriate management and contact

tracing if the test result is positive for Chlamydia. Prophylactic antibiotic should be considered before uterine instrumentation if screening is deferred.

GPs should advise women presenting with infertility to take 0.4mg/ day of folic acid supplementation from before conception and up to 12 weeks of pregnancy to reduce the risk of neural tube defect and for women who had previous child with neural tube defect or who receive antiepileptic medication should take 5mg/ day of folic acid(NICE,2004).If the rubella status of a women is not known previously then the GP should check this.Seronegative women should have rubella vaccination and they should be advised not to become pregnant for atleast one month following vaccination(RCOG,1998).

Male

The effects of age on male fertility are still less clear (NICE, 2004). Men who have BMI> 29 should be informed that they are likely to have reduced fertility. Men should be advised about avoiding increased scrotal temperature like wearing loose underwear, not to take hot bath and to avoid hot occupational environments. They should be warned against recreational drugs usage so that good sperm quality can be maintained. Men should be informed by their GPs that alcohol intake within the Department of Health's recommendations of three to four units per day is unlikely to affect their fertility but excessive alcohol consumption is detrimental to semen quality(NICE,2004). Men should be given the advice about the association between smoking and reduced semen quality. Jenkins et al 2003 said that smoker's sperm concentration is on average 13-17% lower than non-smokers which is a concern for oligospermic men.

Couple

Couple should be informed that regular unprotected sexual intercourse every two to three days optimizes the chances of pregnancy rather than stressful ovulation timed sexual intercourse(NICE,2004). Women should be informed by GP that after discontinuation of long acting injectable progesterone contraceptives, it can take up to two years to achieve pregnancy (Wylie and Gebbie, 2002). GP should be alert and look for any psycho-sexual problems in couples who seek help for infertility. Even passive smoking is likely to affect the chances of conceiving in a woman, so the couple should be offered a referral to smoking cessation programme to support their efforts in stopping smoking (NICE, 2004).Couples should be informed that further research is needed regarding the effectiveness of complementary therapies for infertility as this has not been properly evaluated at present. GPs should explore and address the couple's fears and anxieties about the infertility and its management.

Information to couples

Souter et al 1998 had undertaken a postal study about patient satisfaction with initial infertility management and found out that 86% felt they had not been provided with enough help regarding emotional aspects of infertility, 47% felt there had been no clear

plan for the future and 23% reported that they were given little or no information about drug treatments in infertility and possible side effects.

GPs should be able to explain to the couple about each stage of infertility investigation and treatment. The information provided should be accessible to people who have additional needs such as physical, cognitive or sensory disabilities and people who are non-English as well. So verbal information should be supplemented with written or audio visual media(NICE,2004).It also insists that people should have the opportunity to make their own but informed decisions regarding their care and infertility management depending upon evidence based information.

Initial investigation in General Practice

The initial investigation of both male and female partners who are concerned about their fertility should be done in primary care which may help to decide about further management and need for referral to secondary care under fertility specialists.

Table 1 showing initial infertility investigations for both men and women in general practice (RCOG, 1998 and NICE, 2004).

Gender	Do's	Don'ts
Male	Semen analysis	1)Antisperm antibody 2)Sperm function test
Female	1)Midluteal serum progesterone 2)Serum gonadotrophins and ultrasound of ovaries(PCOS)	1)Basal body temperature 2) Serum prolactin, inhibin B, Thyroid function test. 3)Postcoital test 4)Endometrial biopsy 5)Ultrasound of endometrium

Semen analysis

Sperm samples are collected in a wide-mouthed sterile container and not in condom/ plastic bag. GPs should inform that it is best produced after two or three days of sexual abstinence. Sperm analysis should be carried out as soon as possible after production preferably within an hour (RCOG, 1998). It also recommends that GPs should send semen samples to the same laboratory used by the specialist infertility clinic to which the couple would be referred. The results of semen analysis should be compared to the World Health Organization (WHO, 1999) reference values.

Table 2 showing WHO reference values of Semen analysis

Volume:	2.0 ml or more
pH:	7.2 or more
Sperm concentration:	20 million/ml or more
Total sperm number:	40 million or more/ ejaculate
Motility:	50% or more motile(grade a and b) or 25% or more with progressive motility(grade a) within 60min of ejaculation
Morphology:	15% or more normal forms based on strict morphologic criteria
Vitality:	75% or more live
White blood cells:	< 1 million/ml

If the result of the first semen analysis is abnormal, GPs should offer repeat confirmatory test ideally to be done three months after the initial test to allow time for completed spermatogenesis. But in case of azoospermia(absence of sperm) or severe oligozoospermia(very few sperm number or more abnormal forms or more of reduced motility) the repeat test should be undertaken as soon as possible(NICE,2004).

Midluteal serum progesterone

Even though women with regular menstrual cycle are likely to be ovulating, if they are having more than one years infertility then GPs should offer them midluteal phase (day21 of a 28 day cycle) serum progesterone measurement to confirm ovulation. Timing in relation to menstrual cycle is very important for serum hormones measurement. In a women with prolonged periods, the measure of serum progesterone may be done later in the cycle(for example day 28 of a 35 day cycle) and repeated weekly thereafter until the next menstrual cycle starts(NICE,2004). Inference of this result is important to decide about ovulation.

Table 3 showing inference of midluteal serum progesterone (RCOG, 1998)

Level < or = 16nmol/lt	Repeat in another cycle and if consistently low, refer to specialist care.
Level > 16 and < 30 nmol/lt	Repeat in another cycle and if same or low, Indicates the need for controlled ovarian stimulation.
Level > 30 nmol/lt	indicates OVULATION

Other hormones measurement

Serum gonadotrophins (LH/ FSH) should be offered to women with irregular periods on day 2-5 of menstrual cycle to rule out PCOS but not routinely to all women seeking help.

Thyroid function test and serum prolactin are useful only in symptomatic women (NICE, 2004).

Referral to secondary care

Infertility should be defined as failure to conceive after regular unprotected sexual intercourse for two years in the absence of known reproductive pathology (NICE, 2004). The results of rubella status, assessment of ovulation for women and semen analysis for men should be known by GP before referral to secondary care. Women should be prescribed folic acid by GPs before referral. According to Jenkins et al 2003, referral letter by GP should include the following details. They are couple's personal details like age and contact details, reproductive histories about previous pregnancies, duration of trying to conceive and previous contraception, rubella immunity of woman, results of all previous investigations and finally any concerns about the welfare of any resulting child.

About 70% of couples attending fertility clinics who were referred for fertility treatment eventually achieve pregnancy although this may take a long time (Dowers and Yates, 1998). If the history, examinations and investigations are normal in both partners, GP can defer referral until the couple have been trying to conceive for at least 18 months (Jenkins et al 2003). There are some indications for early referral to secondary care (Hargreave and Mills, 1998).

Indications for early referral

In women

- Age > 35 years and trying to conceive for one year
- Amenorrhea or oligomenorrhoea
- Previous abdominal or pelvic surgery
- H/O PID / STD
- Abnormal pelvic examination/ investigation

In men

- Previous or current genital pathology
- Previous urogenital surgery
- H/O STD
- Significant Varicocele/ systemic illness
- Abnormal genital examination/ semen analysis

People who are known to have chronic viral infections such as hepatitis B, C or HIV and seeking help for their fertility should be referred to centers that have appropriate expertise and facilities to provide safe risk-reduction investigation and treatment (NICE, 2004). Even after referral to specialist fertility clinics for further infertility management, GPs should continue to offer ongoing support to the couple (RCOG, 1998).

Continuing support to couples

Stress can occur as a result of infertility problems itself along with infertility investigations and treatment. Therefore GPs should inform the couples that stress in the male and/ or female partner can affect the couple's relationship which can lead to reduce libido and frequency of sexual intercourse and can further aggravate the fertility problem (Bagshawe and Taylor, 2003). GPs should continue their support to the couples by providing contact details about fertility support group and counseling which may help to handle the psychological effects of fertility problems. Counseling should be offered before, during and after investigations and treatments, irrespective of the outcome of these procedures. NICE guideline 2004 recommends that counseling should be provided by someone who is not directly involved in the management of the couple's fertility problems.

GPs should be able to provide details of organizations (for example Human Fertilization and Embryology Authority, ISSUE, a National Fertility Association etc) to which the couples may apply for information about infertility, different types of treatment and relative advantages of different clinics and centers.

Ways to improve infertility care in General Practice

Considering the following factors may help to improve the infertility services in general practice.

Team work and Communication

A coordinated team work and good communication are crucial for delivering better infertility care. The disciplines necessary for providing team-based care to infertility problems include GP, practice nurse, non clinical staff, junior doctors, hospital consultants, and infertility specialist nurses, counselors specializing in infertility practice, pharmacist, clinical geneticist, genetic counselor and molecular biologist (Jenkins et al 2003). Morrison et al 2001 said that 'interventions are undermined if management in secondary care is not coordinated with that of primary care'. There are chances for hospitals to perform duplicated tests that had already been done in primary care and there was no evidence that subsequent hospital management was improved as a result of better investigations carried out before referral by GP.

The core requirement is good communication within the team and agreeing the roles and responsibilities in the team such as when nurses should refer to GPs or GPs refer to hospital specialists. This includes agreeing a local protocol derived from available National guideline for the management of infertile couple (RCOG, 1998).

Local guideline

The National guideline will not succeed without important activities for local implementation across the different levels of infertility care. There should be informal

discussion about infertility guidelines among GPs, nurses and the team from the local fertility treatment centre. Morrison et al 2001 suggested that the guidelines that aim to improve the referral process need to be disseminated and implemented. They also concluded that dissemination of infertility guidelines resulted in a modest increase in referrals having recommended investigations completed in general practice.

Audit and Evaluation

Improvement may be achieved by performing regular audits and acting on the findings to improve the quality of care for infertility couples in general practice.

Personal development plan (PDP)

Jenkins et al 2003 suggests that keeping a PDP by the GPs with a chosen topic relating to infertility in primary care and making action plans may help to improve the infertility service provided in general practice.

Conclusion

GPs who are using infertility guidelines are more likely to understand the process and undertake a more comprehensive work-up prior to referral, including seeing and examining both partners, initiating basic investigations and speeding up the referral process (Emslie et al 1993). Finally, the need for providing ongoing care and support throughout the investigation and treatment for infertility and dealing with the subsequent either positive or negative outcomes is an important role of GP in managing infertility couple.

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