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Evaluation of infertile women: Mini-review

Mohannad Abu Faza¹, Ibrahim A Abdelazim^{1,2✉}, Hossam S Osman¹, Dareen A Alsharif⁴

¹Department of Obstetrics and Gynecology, Ahmadi Hospital, Kuwait

²Department of Obstetrics and Gynecology, Ain Shams University, Egypt

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ABSTRACT

Evaluation of infertility indicated for women failed to conceive after one year of unprotected intercourse and for women over 35 years failed to conceive after 6 mo of unprotected intercourse, because the fertility decline as women approach 40 years. Evaluation of infertile couple should begin with semen analysis of male partner. If the semen analysis is within normal range, evaluation then move on to female partner. Evaluation of the infertile woman should be carried in cost-effective manner to identify the causes of infertility using the least invasive methods. Methods of evaluation of infertile women include: 1) history and physical examination; 2) evaluation of the male partner; 3) documentation of ovulation; 4) evaluation of the ovarian reserve; 5) evaluation of cervical causes of infertility; 6) evaluation of uterine causes of infertility; 7) documentation of the tubal patency; and 8) exclusion of peritoneal causes of infertility. Evaluation of infertile couple should include evaluation of both partners. Semen analysis for the male partner, followed by documentation of ovulation and evaluation of genital tract patency. PCT is not used as routine evaluation of infertile women. Laparoscopy is not used as routine evaluation of infertile women unless there is suspected peritoneal factors of infertility or endometriosis or tubal occlusion. Ovarian reserve should only be done for infertile women with diminished response to external gonadotropins (not routine).

1. Introduction

Evaluation of infertility indicated for women failed to conceive after one year of unprotected intercourse and for women over 35 years failed to conceive after 6 mo of unprotected intercourse, because the fertility decline as women approach 40 years[1,2].

Evaluation of infertile couple should begin with semen analysis of male partner. If the semen analysis of the male partner is within normal range, evaluation of the female partner should start.

The evaluation of the infertile woman should be carried in cost-effective manner to identify the causes of infertility using the least invasive methods.

2. Methods of evaluation of infertile women

Methods of evaluation of infertile women include; 1) history and physical examination; 2) evaluation of the male partner; 3) documentation of ovulation; 4) evaluation of the ovarian reserve; 5) evaluation of cervical causes of infertility; 6) evaluation of uterine causes of infertility; 7) documentation of the tubal patency; and 8) exclusion of peritoneal causes of infertility[1,2].

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✉Corresponding author: Ibrahim A Abdelazim, Obstetrics and Gynecology, Ain Shams University, Egypt and Consultant at Ahmadi Hospital, Kuwait Oil Company (KOC), Kuwait.

Tel: (+965)–66551300.

E-mail: dr.ibrahimanwar@gmail.com

ORCID: <http://orcid.org/0000-0002-7241-2835>

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2.1. Thorough history includes

Infertility duration and previous treatment of infertility, menstrual history (menarche, length of the menstrual cycle, dysmenorrhea), obstetrics history and pregnancy outcome, history of contraception, sexual history (frequency, sexual dysfunction and/or dyspareunia), past surgical history, previous pelvic inflammatory disease or sexually transmitted disease, endocrine disorders (thyroid disease, galactorrhea, hirsutism), previous cervical cytology, drug allergy, family history of congenital malformations and/or infertility problem, smoking, use of alcohol or exposure to environmental toxins[1,2].

2.2. Physical examination

Physical examination includes blood pressure, pulse rate, body mass index (BMI), weight, thyroid and breast examinations, hair distribution, vaginal and pelvic examination (vaginal, cervical, uterine, adnexal pathology or masses and pouch of Douglas).

Subsequent evaluation of the infertile woman should be carried in cost-effective manner to identify the causes of infertility using the least invasive methods[2,3].

2.3. Documentation of ovulation

Ovulatory disorders identified as possible cause of infertility in 40% of infertile women[3], and commonly associated with menstrual disturbances. Commonest ovulatory disorders associated with infertility include polycystic ovarian disease (PCOD), excess weight gain or excess weight loss, vigorous exercise, thyroid problems and hyperprolactinemia. Methods for documentation of ovulation state as follow.

2.3.1. Basal body temperature (BBT)

In ovulatory women, the menstrual cycle is regular, which occurs every 21-35 d with constant premenstrual symptoms[4]. BBT provides a simple method for evaluation of ovulation. Ovulatory cycles associated with biphasic BBT recordings, and an-ovulatory cycles associated with monophasic BBT pattern[5]. BBT assay is not the best method for documentation of ovulation in most of women.

2.3.2. Serum progesterone assay

Serum progesterone was considered a reliable indicator of ovulation and luteal function. Serum progesterone assay should be done 1 wk before the beginning of the menses rather than day-21 assay. Serum progesterone more than 3 ng/mL is a reliable indicator of ovulation[6]. Serum progesterone more than 10 ng/mL is a reliable indicator of proper luteal function[7].

2.3.3. Luteinizing Hormone (LH) assay in urine

Commercial 'ovulation detection kits' was used to identify the LH surge occurring 1 or 2 d before the ovulation. Urinary LH is an accurate, easy and a reliable method to identify the best ovulation and fertility time[8,9].

2.3.4. Endometrial biopsy and dating

Detection of secretory endometrium, resulting from the post-ovulatory progesterone effect and endometrial dating to diagnose luteal phase defect was the gold standard method to diagnose ovulation and/or luteal phase defect. However, this method can't differentiate between fertile and infertile female and should be considered for diagnosis of pathological endometrial lesions as endometrial neoplasia and/or chronic endometritis[10,11].

2.3.5. Trans-vaginal ultrasound (TVS)

Trans-vaginal ultrasound was used to detect the growth of the ovarian follicles and evidence of ovulation through, collapse of the mature follicles, loss of the follicular margins, and appearance of post-ovulatory clear fluid in the pouch of Douglas[12].

2.3.6. Endocrine assessment

Thyroid-stimulating hormone and prolactin levels assay indicated in infertile women, because the thyroid problems and hyperprolactinaemia are the commonest endocrine disorders associated with ovulatory dysfunction and subsequent infertility.

2.4. Evaluation of the ovarian reserve

Ovarian reserve describes the reproductive ability of the woman through identification of the number and quality of the oocytes available[13]. Decreased ovarian reserve (DOR) means women whose response to ovarian stimulation reduced compared to women of the same age. Ovarian reserve can be detected by cycle-day 3 Follicle Stimulating Hormone (FSH) and estradiol levels, clomiphene citrate challenge test, antral follicle count (AFC), and anti-mullerian hormone (AMH).

These above mentioned tests may provide prognostic information about women at increased risk of DOR, such as women who; 1) over age 35; 2) family history of premature ovarian failure; 3) past history of ovarian surgery or radiation; 4) unexplained infertility[13]. Ovarian reserve helps to detect the ovarian response to exogenous gonadotropins stimulation during *in-vitro*-fertilization (IVF) treatment[14].

Cycle-day 3 Serum FSH and estradiol: Cycle-day 2-4 FSH commonly used to measure the ovarian reserve. FSH more than 10-20 mIU/mL is associated with DOR[15]. Serum estradiol is not used

alone for assessment of the ovarian reserve and its measurement should be combined with measurement of the serum FSH[16].

Normal serum FSH with elevated estradiol more than 60 pg/mL in follicular phase associated with DOR and increased rate of IVF cycle cancellation[17,18].

Clomiphene Citrate Challenge: The clomiphene citrate challenge test means assessment of the FSH on day 3 and day 10 of the menstrual cycle after 100 mg clomiphene citrate daily from day 5 to day 9 of the menstrual cycle. High serum FSH after clomid stimulation suggest DOR[19].

AFC: AFC assessment by TVS should be done in early follicular phase. Antral follicles means detection of the follicles measuring 2-10 mm in diameter in the ovaries. Data are expressed as mean±SD. AFC of (5.2±2.1) is associated with DOR[20,21]. AFC increased in women with PCOD and decreased in women receiving combined contraceptive pills[22-25].

Serum AMH Level: AMH secreted by follicular granulosa cells, gonadotropin-independent and therefore can be measured in any day of the cycle[26-31]. AMH decreased with external use of contraceptive pills or gonadotrophic releasing hormones (GnRH), and hypogonadotropic hypogonadism[32-35]. AMH less than 1 ng/mL usually associated with DOR and poor IVF outcome[32-35]. AMH increased in women with PCOD[36-40].

2.5. Evaluation of cervical causes of infertility

Evaluation of the cervical causes of infertility using post-coital test (PCT) which means microscopic examination of the cervical mucus specimen taken before the ovulation for the appearance of the motile sperms is not recommended for routine assessment of infertile women, because of the subjective nature of the PCT[41,42].

2.6. Evaluation of uterine causes of infertility

Methods used for assessment of the uterine causes of infertility include TVS, three-dimensional ultrasound and MRI, with the purpose to diagnose uterine leiomyomas, congenital uterine anomalies and pathological ovarian lesions.

Hysterosalpingography (HSG) used in infertile women for diagnosis of uterine anomalies, endometrial polyps and sub-mucous myomas with high positive predictive value (PPV)[43].

Sonohysterography or saline infusion sonography (SIS) means infusion of saline through the cervical canal during the trans-vaginal ultrasound. Sonohysterography or SIS used in infertile women for diagnosis of uterine anomalies, endometrial polyps and sub-mucous myomas with more than 90% PPV[44-47]. Hysteroscopy is the gold standard for evaluation of the uterine cavity and for diagnosis of the

intrauterine pathology[47].

2.7. Documentation of the tubal patency

Methods used to document tubal patency include HSG that is the standard method used for evaluation of the tubal patency. HSG can diagnose tubal occlusion, salpingitis isthmica nodosa, fimbrial phimosis or peritubal adhesions. The positive predictive value (PPV) and negative predictive value (NPV) of HSG are 38% and 94% respectively[48,49]. SIS can also be used to document the tubal patency. Diagnostic Laparoscopy with dye test used for the diagnosis of tubal occlusion and peritubal adhesions, which is not diagnosed by HSG[50]. Chlamydia trachomatis antibodies detected in infertile women with tubal pathology with high negative value 80%-90%[51,52].

2.8. Evaluation of peritoneal causes of infertility

Peritoneal factors of infertility such as endometriosis and pelvic adhesions should be expected in women with unexpected infertility[53]. Laparoscopy is the most specific method used for the diagnosis of peritoneal factors of infertility. Laparoscopy indicated in infertile women with abnormal HSG or abnormal ultrasound findings or risk factors of peritoneal diseases and not recommended as routine evaluation of infertility women[54,55].

3. Conclusion

Evaluation of infertility indicated for women failed to conceive after one year of unprotected intercourse and for women over 35 years failed to conceive after 6 mo of unprotected intercourse. Evaluation of infertile couple should include evaluation of both partners. Semen analysis for the male partner is followed by documentation of ovulation and evaluation of genital tract patency. PCT was not used as a routine evaluation of infertile women. Laparoscopy was not used as a routine evaluation of infertile women unless there is suspected peritoneal factors of infertility, endometriosis or tubal occlusion. Ovarian reserve should only be done for infertile women with diminished response to external gonadotropins (not routine).

Conflict of interest statement

The authors declare that they have no conflict of interest.

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