Intrauterin insemination

- iui has performed from 200 years ago . iui use to reduse the effect of factor that may impede the progress of spermatozoa.

Main indication for iui:

1-Anatomical(hypospadias)

Neurological(spinal-cord injery)

Retrograde ejaculation.(multiple sclerosis)

Psychological(impotence)

- Cervical factor
  - Cervical mucushostility
  - Poor cervical mucus

Mild male subfertility

Hypospermia

Oligospermia

Asthenozoospermia

Teratozoospermia

oligoasthenoteratozoospermia

- Immunological
  - Male anti sperm antibodies
  - Female antisperm antibodies
- Unexplained infertility
- Endometriosis

Minimal

mild

- Ovulatory dysfunction

- Hiv positive male partner and hiv negative female partner.
- Combined infertility factors.

Methods of intrauterine insemination

- Ovarian stimulation.
- Monitoring of follicular growth and endometrial development.
- Timing of insemination.
- Semen preparation.
- Iui with prepared sperm.

Ovarian stimulation

Many ovarian stimulation protocols have been devised for use with iui.

Clomiphen citrate alone.

Combination clomiphene and gonadotropins and HCG.

Gonadotropins alone.

Aromatas inhibitor regimes.

- Fsh in a dose of 75 iu of recombinant human (r-fsh)from day 3 of menstruation .when the mean diameter of the folliclr is >18mm,HCG 5000-1000 is administered.

Clomiphene Treatment Regimens

- Clomiphene is administered orally, typically beginning on the 3 – 5 day after the onset of a spontaneous or progestin-induced menses.
- In women with amenorrhea, treatment can begin immediately, without inducing endometrial shedding, if pregnancy has been excluded.
- The dose of clomiphene required to induce ovulation correlates with body weight .
- Treatment usually starts with a single 50-mg tablet daily for a 5-day interval and, if necessary, increases by 50 mg increments in subsequent cycles until ovulation is achieved.
- Clomiphen resistant patients are identified after a course of three cycles and shifted to injectable gonadotropins.

Side effect of clomifen

- Increased risk for a multiple pregnancy (7-10%) .
- There is no evidence that increases the overall risk of birth defects , developmental delay or learning disability in children conceived during clomiphene treatment.
- Mild symptoms of OHSS (transient abdominal discomfort, mild nausea, vomiting, diarrhea, and abdominal distention) are not uncommon but require only expectant management.
- No causal relationship between ovulation-inducing drugs and ovarian, breast, or endometrial cancer has been established

Aromataz inhibitor treatment regimes

- Letrozole (2.5-7.5 mg daily) and anastrozole (1 mg daily) administered for a 5-day interval.
- Letrozole is administered orally, typically beginning on the 3 – 5 day after the onset of a spontaneous or progestin-induced menses.
- Ovulation and conception rates and pregnancy outcomes are similar when treatment starts anywhere between cycle days 3 and 5.
- In women with amenorrhea, treatment can begin immediately, without inducing endometrial shedding; however, pregnancy must be excluded

- In sum, the available data suggest that letrozole is more effective than clomiphene as a first-line treatment for ovulation induction in anovulatory women with PCOS, without a significant increase in complications or side effects.

Side effect of aromatase inhibitor

- The major risk of ovulation induction is the occurrence of a multiple pregnancy.
- There is no evidence suggesting letrozole is any more teratogenic than clomiphene.
- The incidence of congenital malformations in newborns of women who conceived after treatment with letrozole or clomiphene found no difference.(the same as pregnancies without treatment) .
- The risk of clinically significant OHSS is very low with letrozole

- Letrozole is generally well tolerated, and the most common side effects of letrozole are headaches and cramps.
- Women on letrozole report more fatigue and dizziness than women on clomiphene.
- Hot flushes are ↓ common with letrozole

- Anovulatory PCOS patients who fail to ovulate or conceive with oral agents may be considered for ovulation induction with exogenous gonadotropin injections .
- Typical protocols monitor at baseline, 4 - 5 days after treatment initiation, and every 1 - 3 days until follicular maturation.
- Expected follicle growth is 1 - 2 mm daily after achieving 10 mm diameter .
- Given the goal of promoting growth of a single mature follicle, low initial gonadotropin doses of 37.5 – 75 IU / day are generally recommended, with increases in doses by 50% of the previous dose after 7 days if no follicle >10 mm is observed .

We prefer gonadotropins in this case:

- longer durations of unexplained infertility (>3 years)
- couples who fail to conceive with clomiphene + IUI
- clomiphene treatment fails to stimulate multiple follicular development
- when IVF is not a viable option

Monitoring of follicular growth and endometrial development

- A baseline ultrasound scan should be performed on day 2 or 3 of menstruation,

  In order to exclude the presence of ovarian cysts or endometrial pathology Such as endometrial polyps.

From day 7 or 8 of stimulation ,serial ultrasound scanning are performed and the results charted.

Timing of insemination

- There are several methods for timing ovulation in natural or stimulated cycles , including simple methods such as BBT , or use dipstick for detect lh surge.
- In a stimulated cycle , if HCG is administered when the average diameter of the leading is 20 mm , rupture of the follicle may be expected 34-46h lAter , with a mean time interval of 38h.
- A combination of LH testing and US can be used ,with LH kits starting when the largest US measured follicle reaches 14 mm in diameter.

- If the number of mature follicles exceeds four or the total number of follicles over 12 mm in diameter exceeds eight , hcg administration should be withheld and the couple advised to abstain from intercourse.
- Many clinician will perform two insemination at 24 and 48 h from the timing of hcg administration.
- The fertility guidelines in uk advocate single rather than double intrauterine insemination.

- If a dominant follicle develops, but there is no spontaneous LH surge, hCG can be used to induce final follicular maturation , with ovulation occurring approximately 40 hours following administration .

HCG

- HCG is recommended for gonadotropin cycles and is used when 1 - 2 follicles are 16 to 18 mm diameter and the E2 level per dominant follicle is 150 to 300 pg/mL .
- Ovulation is expected 24 - 48 hours after the hCG trigger.
- Intercourse should be recommended within 24 - 48 hours of ovulation triggering or IUI 24 - 36 hours after triggering .
- Testing for pregnancy is performed within 15 - 16 days after ovulation triggering and the cycle reviewed if pregnancy testing is negative.
- Gonadotropin dosage in future cycles should be altered if the prior response was inadequate or excessive.

Semen parameter and prognose

- Best results are achieved when the number of total motile sperms exceeds a approximately 10 million.
- Combining the yield from two ejaculates obtained approximately 4 hours apart may increase the numbers of sperms available from oligospermic men.
- **Success rates with IUI are highest when 14% or more of normal morphology, intermediate with values between 4% and 14%, and generally quite poor when fewer than 4% of sperms are normal.**

Sperm preparation and insemination procedure

- Fresh semen is usually produced by masturbation .
- The ideal sperm preparation technique is achieve the largest number of morphological normal motile spermatozoa in a small volume of physiological culture medium free from seminal plasma , leukocytes and bacteria.
- Most conceptions occur when the concentration of inseminated motile sperm is more than 1 million/ml.

- Washing sperm the greatest numbers of sperms, but the final specimen also contains dead and abnormal sperms and other cellular debris.
- Swim-up cleaner specimen, devoid of dead sperms and other cellular debris, but also yields significantly lower numbers of sperms
- Density gradient centrifugation select a population of sperms with normal morphology
- The best choice among them may vary with the quality of the semen sample

- IUI is usually performed with fresh sperm (morning after 2 - 3 days of sexual abstinence)
- The LH surge can be detected in serum 36 hours before ovulation and in urine 24 hours before ovulation.
- The oocyte can be fertilized up to 24 hours after ovulation; sperm are most capable of fertilization up to 48 hours after entering the female genital tract.
- ***We perform a single IUI the day after a urinary LH surge .***

Description of iui procedure

- The vulve is cleaned with normal salin.the cervix is exposed by inserting a bivalve speculum and the cervix is in turn cleansed with normal saline.
- The catheter is inserted through the cervix os and into the uterus to a depth of approximately 6-7cm so that the tip of the catheter rests just short of the fundus.
- Touching the fundus would result in cramping or bleeding ,both toxic to embryo development.

- In difficult inseminations ,rigid stylets , tenaculum or abdominal ultrasound guidance should be considered.
- The catheter is withdrawn after slow injection of the sperm over 60-80 s.

Post procedure care

- Patients lie supine for 10 min , after which they can resume their normal activities.
- They are then instructed to do a serum beta- hcg evaluation 14 days from the insemination.

Iui versus timed intercourse

- Most of current available data show that iui is more effective than timed intercourse (TI) either in couples with unexplained infertility or with male subfertility.

Number of cycles

- If pregnancy is not achieved by the fourth to six cycle ,the couple should then be offered IVF.

Risk and complication of IUI

- Early complications:

Bleeding or spotting

Infection

Pain

Sensitization/anaphylaxis

Vasovagal response

Identification errors

- Late complications:

Ovarian stimulation , ohss , multiple births.

Out comes IUI

- The overall success rate of IUI varies widely between international studies , with a mean pregnancy rate per iui cycle around 9%,ranging from as low as 5% to as high as 70%.