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IUI – EVIDENCE-BASED UPDATES

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IVFMD

- IUI the most frequently performed treatment
- IUI is easy to perform, inexpensive and a minor burden to the couples
- There is still ongoing debate whether or not IUI is an effective treatment for various indications

DIAGNOSTIC WORK-UP BEFORE IUI

- Thorough history: duration of subfertility, menstrual cycle and risk assessment for presence of tubal pathology
- Semen analysis
- Gynecological examination and ultrasound
- Endocrine detection tests for ovulatory problems

DIAGNOSTIC WORK-UP BEFORE IUI

- Hysterosalpingography (HSG) and chlamydia antibody test (CAT)
  - HSG: Last test in the work-up for subfertility
    - Invasive procedure
    - Complications: infection or injury to the genital or internal organs
    - Indication: patients at high risk of bilateral tubal pathology

DIAGNOSTIC WORK-UP BEFORE IUI

- Antisperm antibodies (ASA)
  - Not routinely performed
  - Does not predict the chance of a spontaneous pregnancy
- Postcoital test
  - Used to be part o the diagnostic work-up for subfertility
  - RCT in isolated cervical factor subfertility: No significant benefit of IUI compared with no treatment (Steures, 2007)

INDICATIONS FOR IUI

- Cumulative pregnancy rate: 25-50% after 3-9 IUI cycles (Ben, 2014)
- Developed countries: IUI with or without MOH should be chosen before IVF
- Developing countries: IUI is applied for the right indications

INDICATIONS FOR IUI

- Cervical factor
  - IUI in natural cycles significantly increases the chance of conception (Steures, 2007)
- Male subfertility
  - IUI can be considered if postwash TMSC between $0.8*10^6$ to $5*10^6$ (Van Weert, 2004)
- Unexplained infertility
  - IUI + natural cycle: no significant beneficial effect (Verhulst, 2006)
  - IUI + ovarian stimulation: significantly improves live birth rates (Verhulst, 2006)

INDICATIONS FOR IUI

- Endometriosis
  - Mild endometriosis (American Fertility Society grade 1 and 2) should be treated as unexplained infertility
  - Moderate and severe endometriosis: no role of IUI (Ben, 2014)
- Sexual disorders
  - No need for IUI
  - Retrograde ejaculation: sperm preparation + IUI
- Ovarian dysfunction
  - MOH + IUI in case of ovarian dysfunction + male subfertility

FACTORS PREDICTING IUI OUTCOMES

- Female age
  - The proportion of infertile couples:
    - 20s: 4%
    - > 35: 10-20%
  - Ongoing pregnancy rate # 0% at the age of 41 (Ben, 2014)
  - Unexplained and mild male factor infertility: the effect of female age is more extensive

FACTORS PREDICTING IUI OUTCOMES

- Male age
  - Semen parameters start to decline after 35 years of age
  - Male fertility is maintained until very late, up to an age 94 years (Seymour, 1935)
  - Men with female partner > 35 years: paternal age ≥ 40 years → negative impact on IUI success (Brzechffa, 1997)

FACTORS PREDICTING IUI OUTCOMES

- Semen quality
  - Normal semen analysis: WHO 2010 criteria are met
    - Limited value in prediction of spontaneous pregnancy
    - No value in the prediction of a pregnancy after IUI

FACTORS PREDICTING IUI OUTCOMES

- Semen quality
  - TMSC (total motile sperm count) = volume * concentration * progressive motility
  - Diagnosis of male subfertility
    - TMSC > $3*10^6$: mild male subfertility
    - TMSC 1 – $3*10^6$: moderate male subfertility
    - TMSC < $1*10^6$: severe male subfertility
  - Approximate loss of motile spermatozoa of 70% with preparation
  - IUI can be considered if postwash TMSC between $0.8*10^6$ to $5*10^6$ (Van Weert, 2004)

FACTORS PREDICTING IUI OUTCOMES

- Sperm preparation techniques
  - Three techniques
    - Simple dilution and washing technique
      - Dilution of semen 5-10 times
      - Centrifugation twice
    - Swim-up
      - Select sperm by: their ability to swim out of seminal plasma
      - Morphological abnormal sperm will not be selected out
      - ROS are present in the semen
    - Density gradient centrifugation (DGC)
      - Select sperm by their density and gravity
      - Morphological normal sperm: density=1.12g/ml
      - Immature abnormal sperm: density=1.06-1.09g/ml

FACTORS PREDICTING IUI OUTCOMES

- Sperm preparation techniques (SPT): Wash and centrifugation, swim-up or DGC
  - DGC: superior to the swim-up and wash technique
    - Improvement of morphological normal sperm with grade A motility and normal DNA integrity
    - ROS and leukocyte concentration is highly reduced
  - Clinical outcome: there was no clear evidence of which SPT was superior (Boomsma, 2012)

FACTORS PREDICTING IUI OUTCOMES

- Number of cycles to perform
  - Advice on the optimum number of cycles to perform vary between 3-12 cycles
  - The largest chance of ongoing pregnancy is in the first three treatment cycles (Aboulghar, 2001; Bensdorp, 2009)
- Endometrial thickness
  - Endometrial thickness in stimulated IUI cycles is lower than in IVF
  - There is no correlation between endometrial thickness and pregnancy rate (Ben, 2014)

FACTORS PREDICTING IUI OUTCOMES

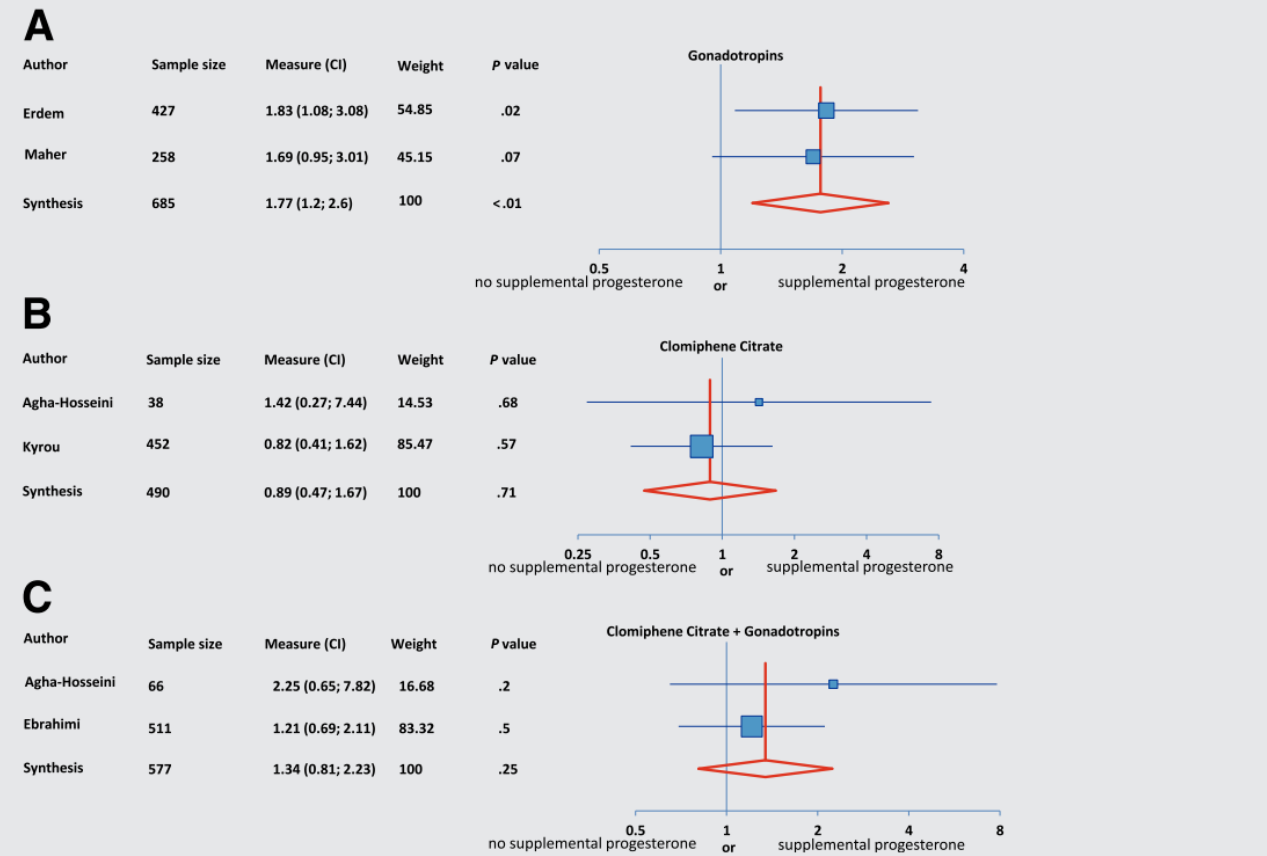
- Immobilization after IUI
  - Spermatozoa reach the fallopian tube as soon as 2 minutes after insemination (Hafez, 1979)
  - 10 to 15 minutes immobilization subsequent to IUI, with or without ovarian stimulation, significantly improves cumulative ongoing pregnancy rates and live birth rates (Saleh, 2000; Custer, 2009)

FACTORS PREDICTING IUI OUTCOMES

- Ovarian stimulation (OS)
  - IUI + OS: increasing the number of sperm and number of available oocytes
  - Goal of OS: 2-3 dominant follicles → maximize the probability of conception and thin unacceptable high percentages of multiple pregnancy rates
  - Gonadotropins are more effective than clomiphene citrate in IUI
  - IUI+OS in unexplained infertility, mild male subfertility, minimal to mild endometriosis: proven effective (Ben, 2014)

FACTORS PREDICTING IUI OUTCOMES

- Luteal phase support



Forrest plot of clinical pregnancy in subgroup analysis based on method of ovulation induction. (A) gonadotropins; (B) clomiphene citrate; (C) clomiphene citrate + gonadotropins. CI = confidence interval.

Hill. Progesterone luteal support for IUIs. Fertil Steril 2013.

CONCLUSIONS

- IUI is a simple, noninvasive, and affordable treatment for infertile couples
- Evidence-based update should be considered for treatment decision making in individual couple.

- THANK YOU!