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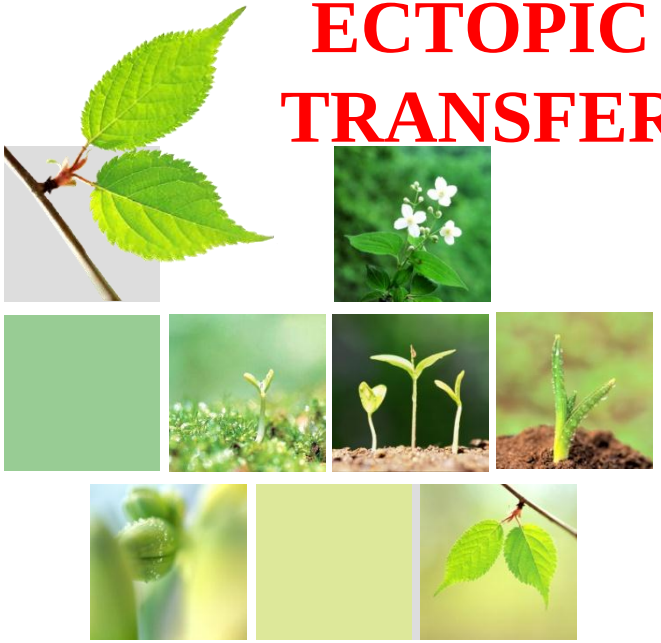

ECTOPIC PREGNANCY AFTER EMBRYOS TRANSFER OF IN VITRO FERTILIZATION: HOW SHOULD RECOGNIZE?

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1. INTRODUCE

➢ **Ectopic pregnancy (EP)** make threats against of life- woman, this tendency increased along with the rise of cycles implementing assisted reproduction.

➢ **Rate:** EP after embryos transfer flunctuates in each study

+ **Tel Avis (1993):** 2-12% >< 1%

+ **D.A. Keegan (2005):** The infertility and assisted reproductive group increase double with the risk of ectopic pregnancy

+ **Mohammed Malak (2011):** 4,9%

+ **L.Y. Cheng (2015):** 2,1-8,6% >< 2%

1. INTRODUCE

- What do the risk factors increase the incidence of ectopic pregnancy in group of patients in vitro fertilization?

- What is the method of ectopic pregnancy treatment to limited the influences the chance having pregnancy of a subsequent assisted reproductive cycle ?

2. THE RISK FACTORS OF EP

2.1. The tubal factor infertility

- **Dubuisson JB (1991):** 11,1% >< Endometriose: 2,1% >< unexplained infertility : 3,4%

- **Zouves C (1991):** 12% >< non tubal factor: 2,6%

2. THE RISK FACTOR OF EP

2.1. The tubal factor infertility

Tel Avis (1993): 860 women -> 2156 IVF treatment cycles -> 1430 embryo tranfers

7 EP: **6 of EP with tubal infertility**+ only one for nontubal indication >< 324 cases of intra uterine pregnancy

Mock ET: it has recently been found that as little as 40 u1of radioopaque fluid injected was associated with flux of dye into the fallopian tubes in as many as 38.2%

+ **With normal tubal:** embryos return to the uterine capacity

+ **With unnormal tubal:** ectopic implantation

2. THE RISK FACTORS OF EP

2.2. ET techniques

- **Yovich JL (1985):** a fixed-length transfer site (55 mm from the external os) achieves pregnancy rates equal to that of the transfer catheter touching the uterine fundus, with a reduced rate of EP

- **Cohen J (1986), Steptoe PC (1976):**transfer technique, including patient's position, type of catheter, and volume injected, have no effect on EP rate

- **Tel Avis (1993):** transfer embryos in 10 to 20ul of fluid using the Wallace catheter.
- **Dubuisson JB (1991), Zouves (1991):** 10-20ul -> 2,1%

  >< 20-50ul -> 8,6 và 9,4%

2. THE RISK FACTORS OF EP

2.2. ET techniques

Cheng LY (2015): 1999-2013, The incidence was significantly higher in 2011 than in the previous years: **ET with full bladder distention.**

- **Full bladder distension:**

+ straighten the uterocervical angle

+ straighten the utore-fallopian angle -> the uterus and the fallopian tubes lie nearly on the same plane.

- **The relationship between ectopic pregnancy and bladder distention requires further investigation.**

2. THE RISK FACTORS OF EP

2.3. Level of estrogen

The controversial

- **Pyrgiotis E (1994), Marcus SF (1995), Zhu L (2012), Sadik Sahin (2014):** not found correlation

- **Fernendez H (1991), Wu Z (2012), Wang J (2013):** increased risk of EP

2. THE RISK FACTORS OF EP

2.3. Level of estrogen

Zhu L (2012):

- **COH:** proportin of uterine waves were higher + proportion of fundocervical waves were lower >< natural cycles

- **Physiologic levels of estrogen :** correlative positively with uterine peristaltic wave frequency. However, **supraphysiologic levels of estrogen** were not shown to contribute significantly to changes in uterine peristaltic wave frequencies

2. THE RISK FACTORS OF EP

2.4. GnRHa triggered

- **Sadik Sahin (2014):** GnRHa triggered group -> MII oocytes, fertilized oocytes, quality embryos > hCG triggered group **(p<0,001)**
- **Tuy nhiên**, GnRHa triggered: the clinical pregnancy, implantation rates: 24,7%, 22% < 38,6%, 31,1%: hCG triggered
- EP rate, **p<0,05**
  - + GnRHa triggered group: 5,3%
  - + hCG triggered group : 1,4%

The corpus luteum function and endometrial receptivity are adversely affected due to the relatively low levels of LH in cycles triggered with GnRHa

2. THE RISK FACTORS OF EP

2.4. GnRHa triggered

- **Imbar T (2012):** 70 bn -> GnRHa triggered + intensive luteal support (50mg of progesterone intramuscularly+ 6mg of estradiol hemihydrate until 10th week of gestation) -> 1 EP

- **Humaidan P (2010):** 1500IU hCG administered at oocyte retieval for GnRHa triggered cycles -> **the pregnancy rates are comparable** to the hCG triggered cycles

2. THE RISK FACTORS OF EP

2.4. GnRHa triggered

- **Humaidan P (2012): similar endometrial gene expression** patterns in oocyte donors receiving hCG triggering and GnRHa triggering with 1500IU hCG for luteal support.

To improved endometrial receptivity and implantation conditions in GnRHa triggered cycles employing luteal support with low-dose hCG, ectopic pregnancy rates may be lower in such cycles.

2. THE RISK FACTORS OF EP

2.5. Frozen ET or fresh ET

- **At the annual meeting of the ASRM (10/2013), Keefe:** EP was higher after frozen ET 31,6% >< 1,8% ET **(RR 17,2; 95% Cl; 6,8-4,3, p<0,0001).**
- **Shapiro BS (2011):**

+ The clinical pregnancy rate was higher following frozen-thawed than fresh ET.

+ the EP rate was lower after frozen-thawed ET than fresh ET

May be due to the negative effect of ovarian stimulation on endometrial receptivity in the latter

2. THE RISK FACTORS OF EP

2.5. Frozen EP or fresh EP

- **A. A. Al Shaikh (2005):** 109 frozen ET cycles: 2,75% EP, 1098 fresh ET cycles: 3,46% TNTC, **p>0,05**

- **Cheng LY (2015):** no significant difference in EP rate between fresh ET and frozen-thawed ET

- **There is no different in the rate of EP after fresh versus FET. The option of embryo cryopreservation and subsequent transfer is an important part of a stratery to reduce the incidence of multiple pregnancies and OHSS after IVF**

2. THE RISK FACTORS OF EP

2.6. Day 3 versus day 5 embryo transfers in fresh IVF cycles

Theoretically, blastocyst ET is more similar to the natural cycle -> a higher implantation potential + a decrease the rate of EP >< cleavage-stage ET

- **Keegan DA (2007), Rosman ER (2009):** the EP rate was found to be significantly higher after blastocyst ET

- **Jun SH (2003), Smith LP (2013):** the rate of EP was not reduced after blastocyst ET compared with cleavage-stage ET

2. THE RISK FACTORS OF EP

2.6. Day 3 versus day 5 embryo transfers in fresh IVF cycles

- **Kathiresan (2013):** ngày 3: 2,8% EP

  ngày 5: 4,7% EP **(p>0,05)**

- There was no difference in EP rate following D3 or D5 ETs. The decision to tranfers D3 or D5 embryos should be made on an individual case-by-cáe basis, independent of EP risk

3.THE EFFECTS OF TREATMENT OF EP


- MTX affect rapidly proliferating cells such as trophoblasts + the proliferating germinal cells in the ovary -> reduced ovarian reserve after MTX treatment

- **Chan (2003):** Salpingectomy can also affect the ovarian function by impairing the ovarian blood supply and reducing antral follicle count

3.THE EFFECTS OF TREATMENT OF EP


- **Amir W (2013):** 7 academic reproductive centres in Canada and Israel (2005-2012), 36 patients with MTX, 22 others by laparoscopic salpingectomy

+ Baseline serum FSH concentration as an index of ovarian reserve by prior MTX and surgical treatment for EP

+ AFC was lower in both groups after treatment, p>0,05

+ Ovarian reserve during the IVF cycle were compared before and after treatment, there were no significant differences in both groups

3.THE EFFECTS OF TREATMENT OF EP


- **Ovrieto (2007):** MTX treatment of EP did not influence the subsequent ovarian response to IVF treatment

- **Oriol (2008):** MTX did not influence serum anti-Mullerian hormone concentration in subsequent cycles

- **On the other hand, McLaren (2009):** MTX -> a time-limited: an IVF cycle occurred within 180 days of MTX exposure-> a significant decline in retrieved oocytes -> **The interval between the MTX and the next IVF cycle was 7,4 ± 0,6 months**

3.THE EFFECTS OF TREATMENT OF EP

- **Shulman (2002), Almog (2011), Xi (2012):** salpingectomy did not influence the ovarian response during ovarian stimulation

- **Orvieto (2011): a significant decrease in the ipsilateral ovarian response following salpingectomy, as reflected by the quantity of developing follicles during ovarian stimulation for IVF**

- **It is important to excise the hydrosalpinx close to the tube to avoid compromising the blood supply to the ovary**

3.THE EFFECTS OF TREATMENT OF EP

- **Singer T (2011):** to evaluate AMH before and after EP treatment with MTX and laparoscopic salpingectomy

+ MTX: AMH before 2,32±1,94ng/mL ><AMH after 2,04±1,56ng/mL

+**Surgery:** AMH before 2,49±1.44ng/mL><AMH after 2,19±1,7ng/mL

Time interval between serum AMH levels in the MTX group was longer by 6 weeks due to the time required to achieve negative serum BhCG.

3.THE EFFECTS OF TREATMENT OF EP


Single-dose MTX is a safe first line treatment for EP and does not seem to decrease AMH serum levels or affect the reproductive outcome in women undergoing subsequent IVF treatment

4. CONCLUDE

- **The tubal factor is the obvious causes which causes EP after IVF**

- **ET technique, level of estrogen, GnRHa triggered, fresh ET or frozen ET, day 3 or day 5 ET: controversial**

- **Prior MTX treatment or laparosocopic salpingectomy does not affect ovarian response and ovarian reserve in the subsequent IVF cycle**

TRUNG TÂM NỘI TIẾT SINH SẢN VÀ VÔ SINH

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