Cervical cerclage versus weekly progesterone injection in prevention of preterm labor

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Abstract

Objective: Prematurity is the leading cause of neonatal death and handicap. Although all births before 37 weeks of gestation are defined as preterm, most damage and death occurs in infants delivered before 34 weeks. Improvements in neonatal care have led to higher rates of survival among very premature infants, but a major effect on the associated mortality and morbidity will be achieved by better Identification of women at high risk for preterm delivery and by development of an effective intervention to prevent this complication. The aim of this study is to compare the effect of weekly progesterone injection and cervical cerclage on the outcomes of pregnancy in patients with history of preterm labor.

Materials & Methods: The study comprised of 80 patients involved in the study then, 20 patients were excluded from the study due to different causes. Patients were randomly allocated to two groups. Randomization was done by sealed envelopes. **Group A:** (30 patients); in this group we had given them 17 OH progesterone (cidulot depot 250 mg) IM weekly starting from 16-20 Weeks till 36 weeks gestation. **Group B:** (30 patients); in this group we had done cervical cerclage operation at 14 weeks. First we assessed the effect of cidulot depot on the gestational age in comparison to the gestational age at previous preterm deliveries in group A. Secondly we assessed the effect of cervical cerclage on the gestational age in comparison to the gestational age at previous preterm deliveries in group B. The primary outcome was the gestational age at time of delivery documented by the LMP and abdominal US. The secondary outcomes were the need to the tocolytic therapy, estimated fetal weight at the time of delivery, the neonatal outcome regarding admission to the incubator or the need to ICU admission and neonatal mortality.

Results: of the study were analyzed, matched and compared.

Conclusion: We concluded that the prophylactic administration of progesterone beginning in mid-gestation to women who previously had a preterm birth has been shown to reduce the rate of recurrence. Also use of prophylactic cervical cerclage reduces preterm labor but the preference of which method remains an area of discussion.

Key Words: Preterm labor, 17-OH progesterone, cervical cerclage.

Introduction

Preterm birth, defined as childbirth occurring at less than 37 weeks. Preterm labor is a major determinant of neonatal mortality and morbidity and has long term adverse consequences on health (1). Preterm birth rates have been reported to range from 5% to 7% of live births in some developed countries, but are estimated to be substantially higher in developing countries (2).

These figures appear to be on the rise. Events leading to preterm birth are still not completely understood, although the etiology is thought to be multifactorial. It is, however, unclear whether preterm birth results from the interaction of several pathways or the independent effect of each pathway. Causal factors linked to preterm birth include medical conditions of the mother or fetus, genetic influences, environmental exposure, infertility

treatments, behavioral and socioeconomic factors and iatrogenic prematurity (3).

Children who are born prematurely have higher rates of cerebral palsy, sensory deficits, learning disabilities and respiratory illnesses compared with children born at term. The morbidity associated with preterm birth often extend to later life, resulting in enormous physical, psychological and economic cost (4). Although progesterone is known to have many actions beneficial to the maintenance of pregnancy, the exact mode of action of 17 alpha hydroxyprogesteronecaproate therapy in preventing preterm labor is not known (5). Intervention with weekly progesterone injections (250 mg 17 alpha hydroxyprogesteronecaproate (17OHPC) from 16–20 weeks up to 36 weeks of gestation had been chosen as it has been proven that this prophylactic administration of 17OHPC injections is effective in reducing the preterm birth rate in singleton pregnancies at high risk for spontaneous preterm delivery but, there are no data on the effectiveness of progesterone in the prevention of preterm birth in multiple pregnancy.(6).

In four trials that compared elective cerclage versus no cerclage or bed rest, no overall reduction in total pregnancy loss and early pregnancy loss (less than 24 weeks' gestation) was observed in the women who underwent cerclage [relative risk (RR) 0.86; 95% confidence interval (CI) 0.59–1.25]. There were also no overall significant differences between preterm delivery rates (RR 0.88; 95% CI 0.76–1.03). The largest among the four trials was coordinated by MRC/RCOG and this trial yielded a small reduction in births under 33 weeks of gestation (RR 0.75; 95% CI 0.58–0.98) (7).

The aim of this study is to compare the effect of cervical cerclage and weekly progesterone injection on outcome of pregnancy in patients with past history of preterm labor.

Subjects and methods

The patients were selected from the outpatient clinics in Fayoum, kaser Al- Alini and AL-Azhar university hospitals. 60 patients were involved in this study and the study started in Jun 2011 for a period of two years.

Inclusion criteria:

- Age of patients between 20-40years.
- Single living fetus at least
- The patient has history of preterm labour (preterm labour between 28 weeks and 34 weeks) once or more.
- Intact membrane.
- Time of inclusion at 12 weeks gestational age .
- Non smokers or Alcoholic women .
- Average BMI 20-25.
- Women are getting pregnant spontaneously or by induction of ovulation but not by ART.
- Women not known to have uterine anomalies documented by previously done HSG.
- No history of Scarred uterus (previous CS or myomectomy).
- Not known diabetic patient or hypertensive.
- No history of ablative or excision procedures of the cervix.

Exclusion criteria:

- Cervical length less than 2.5cm during antenatal period.
- Congenital anomalies in the fetus discovered during the follow up.
- Myoma with pregnancy.
- Polyhydramnios.
- Rupture of membranes during follow up
- Placenta previa diagnosed during the follow up.
- Accidental hemorrhage happens during the follow up.
- IUFD.
- Medical disorders predisposing to preterm delivery.

All the patients will be submitted to the following steps:

- Informed consent was taken from each patient.
- Full history.
- General, abdominal examination and obstetric ultrasound for checking the number of the fetuses, viability, gestational age and placental location.
- Routine antenatal investigations.
- Single course dexamethasone 12 mg IM every 12 hours for 48hs for improvement of fetal lung maturity given at gestational age 32 weeks.
- Documentation of receiving tocolytic drugs or not and time of delivery.

First, we selected 80 patients involved in the study then, 20 patients were excluded from the study due to different causes. Patients were randomly allocated to two groups. Randomization was done by sealed envelopes.

Group A: (30 patients); in this group we had given them 17 OH progesterone (cidulot depot 250 mg) IM weekly starting from 16-20 Weeks till 36 weeks gestation. **Group B:** (30 patients); in this group we had done cervical cerclage operation at 14 weeks.
First we assessed the effect of cidulot depot on the gestational age in comparison to the gestational age at previous preterm deliveries in group A. Secondly we assessed the effect of cervical cerclage on the gestational age in comparison to the gestational age at previous preterm deliveries in group B.
then, we compared between the 2 groups regarding:
The primary outcome was the gestational age at time of delivery documented by the LMP and abdominal US. The secondary outcomes were the need to the tocolytic therapy, estimated fetal weight at the time of delivery, the neonatal outcome regarding admission to the incubator or the need to ICU admission and neonatal mortality.

Statistical analysis:

Results were expressed as means ±standard deviation of the means (SD) or number (%).Comparison between different parameters in the two studied groups was performed using unpaired T test. Comparison between categorical data was performed using Chi square test. The data were considered significant if P value was equal to or less than 0.05and highly significant if P value<0.01. Statistical analysis was performed with the aid of the SPSS computer program.

Results

Table (1)
Mean age in the two studied groups.

	Cidulotdepot group(n=30)	Cerclage group (n=30)	P value
Age (yrs.)	27.43±4.00	27.77±3.48	0.732(NS)

Table (2)
Gravidity and parity in the two studied groups.

	Cidulot depot group (n=30)	Cerclage group (n=30)	P value
G2P1	14 (46.67%)	11 (36.67%)	0.272 (NS)
G3P1	0 (0%)	2 (6.66%)	
G3P1A1	2 (6.67%)	5 (16.67%)	
G3P2	9 (30%)	7 (23.33%)	
G4P1A2	1 (3.33%)	0 (0%)	
G4P2A1	2 (6.67%)	2 (6.67%)	
G4P3	2 (6.67%)	0 (0%)	
G5P2A2	0 (0%)	1 (3.33%)	
G5P3A1	0 (0%)	2 (6.67%)	

Table (3)
GA in previous delivery in comparison to GA at current delivery (weeks) in group A (Cidulot depot group).

	Previous delivery	Current delivery	P value
< 34	30 (100%)	6 (20%)	0.001**
≥ 34	0 (0%)	24 (80%)	

Table (4)
GA in previous delivery in comparison to GA at current delivery (weeks) after cerclage in group B (Cerclage group).

	Previous delivery	Current delivery	P value
< 34	30 (100%)	10 (33.3%)	0.001**
≥ 34	0 (0%)	20 (66.7%)	

Table (5)
Mean gestational age in the two studied groups.

	Cidulot depot group (n=30)	Cerclage group (n=30)	P value
Gestational age (wks.)	36.33 ± 2.51	34.60 ± 2.55	0.010**
< 37 wks.	11 (36.67%)	20 (66.67%)	P= 0.020* RR= 0.5500 95% CI= 0.3224 -0.9382
≥ 37wks	19 (63.33%)	10 (33.33%)	

RR= Relative risk CI= confidence interval*p< 0.05= significant.**p< 0.01= highly significant

Table (6)
Need for Tocolysis between the two studied groups.

	Cidulot depot group (n=30)	Cerclage group (n=30)	P value
Positive	7 (23.33%)	25 (83.33%)	P= 0.001** RR= 0.2800 CI= 0.1436 - 0.5461
Negative	23 (76.67%)	5 (16.67%)	

Table (7)
Fetal birth weight in the two studied groups.

	Cidulot depot group (n=30)	Cerclage group (n=30)	P value
FBW (kg.)	2.58 ± 0.66	2.26 ± 0.64	0.065 (NS)
< 2.5 kg	8 (26.67%)	14 (46.67%)	0.108 (NS) RR = 0.5714 95 % CI= 0.2821 - 1.1577
≥ 2.5 kg	22 (73.33%)	16 (53.33%)	

Table (8)
Need for NICU admission in the two studied groups

	Cidulot depot group (n=30)	Cerclage group (n=30)	P value
Positive	8 (26.67%)	13 (43.33%)	0.176 (NS) RR= 0.6154 95% CI= 0.2993 - 1.2653
Negative	22 (73.33%)	17 (56.67%)	

Table (9)
Neonatal deaths in the two studied groups.

	Cidulot depot group (n=30)	Cerclage group (n=30)	P value
Positive	5 (16.7%)	11 (36.7%)	0.080 (NS) RR= 0.4545 95% CI= 0.1797 - 1.1499
Negative	25 (83.3%)	19 (63.3%)	

Discussion

Preterm labor defined as childbirth occurring at less than 37 weeks is estimated to annually affect approximately 12.9 million births or 9.7% of all births worldwide. Although the prognosis of preterm infants has significantly improved through recent developments in neonatal medicine, complications and aftereffects influencing preterm infants are still a major concern not only for medical management but also for the medical cost of neonatal care(8) Prematurity is the leading cause of neonatal death and handicap. Although all births before 37 weeks of gestation are defined as preterm, most damage and deaths occurs in infants delivered before 34 weeks. Progesterone has an important role in maintaining quiescence acting to reduce calcium influx to smooth muscles through suppression of calcium-calmodulin-myosin light chain kinase system. In four trials that compared elective cerclage versus no cerclage or bed rest, no overall reduction in total pregnancy loss was observed in women who underwent cerclage (7).

In study done by Groom et al 2004 comparison between elective cerclage in the first trimester and the control group but in this control group cerclage done only if short cervix proved by serial vaginal ultrasound done in the second trimester. this is done to be matched with the ethics of research (9). So the results showed no difference between both groups regarding the gestational age at time of delivery and cerclage is indicated to the ultrasound finding of short cervix .In present study cerclage is done based on history indication and not on ultrasound indication and done at 13- 14 weeks and is found to improve the gestational age at time of delivery.

Alfirevic et al., 2004 (10) selected the high-risk group for early preterm delivery depending on the transvaginal sonographic measurement of cervical length. They undertook a multicenter randomized controlled trial to investigate whether, in women with a short cervix identified by routine transvaginal scanning at 22-24 weeks' gestation, the insertion of a Shirodkar suture reduces early preterm delivery. Cervical length was measured in 547pregnant women. One hundred and twenty three women were excluded. The cervix was 15 mm or less in 470, and 253 (54%) of these women participated in the study and were randomized to cervical cerclage (127) or to expectant management (126) no cerclage. Primary outcome was the frequency of delivery before 33 completed weeks of pregnancy. The results were the proportion of preterm delivery before 33 weeks was similar in both groups, 22% (28 of 127) in the cerclage group versus 26% (33 of 126) in the control group (relative risk=0.84, 95% CI 0.54-1.31, p=0.44), with no significant differences in perinatal or maternal morbidity or mortality. They concluded that the insertion of a Shirodkar suture in women with a short cervix does not substantially reduce the risk of early preterm delivery. In this study we see that the cerclage has no significant benefit even in cases with short cervix.(Alfirevic et al.,2004) .This is in contrast to present study, cerclage improved the gestational age depending on history of preterm labour.

Berghella et al 2005 (11) carried out A meta-analysis of trials of women with singleton gestations and second-trimester transvaginal sonographic CL < 25 mm randomized to cerclage or no cerclage. The degree of CL shortening was correlated to the efficacy of cerclage in preventing preterm birth. There was a significant reduction in preterm birth < 35 weeks in the cerclage compared with no cerclage groups in 208 singleton gestations with both a previous preterm birth and CL < 25 mm (relative risk, 0.61; 95% CI, 0.40-0.92). In these women, preterm birth < 37 weeks was significantly reduced with cerclage for CL more than15 mm and < 25 mm. None of the analyses for 344 women without a previous preterm birth was significant. They concluded that cerclage, when performed in women with a singleton gestation, previous preterm birth and cervical length < 25 mm, seems to have a similar effect regardless of the degree of cervical shortening, including CL 16-24 mm. In this study the comparison between 2 groups, both having short cervix, one group undergo cerclage and the other group no cerclage and the study shows that the cerclage improves the pregnancy outcome regardless the degree of cervical shortening.This study goes in favor with our study, where cerclage improves the gestational outcome of patients with history of preterm labour.

Meis et al 2003 (6) conducted a double-blind, placebo-controlled trial involving pregnant women with a documented history of spontaneous preterm delivery. Women were enrolled at 19 clinical centers at 16 to 20

weeks of gestation and randomly assigned by a central data center, in a 2:1 ratio, to receive either weekly injections of 250 mg of 17P or weekly injections of an inert oil placebo; injections were continued until delivery or to 36 weeks of gestation. The primary outcome was preterm delivery before 37 weeks of gestation. Analysis was performed according to the intention-to-treat principle. Base-line characteristics of the 310 women in the progesterone group and the 153 women in the placebo group were similar. Treatment with 17P significantly reduced the risk of delivery at less than 37 weeks of gestation (incidence, 36.3 percent in the progesterone group vs. 54.9 percent in the placebo group; relative risk, 0.66 [95 percent confidence interval, 0.54 to 0.81]), delivery at less than 35 weeks of gestation (incidence, 20.6 percent vs. 30.7 percent; relative risk, 0.67 [95 percent confidence interval, 0.48 to 0.93]), and delivery at less than 32 weeks of gestation (11.4 percent vs. 19.6 percent; relative risk, 0.58 [95 percent confidence interval, 0.37 to 0.91]). Infants of women treated with17 P had significantly lower rates of necrotizing enterocolitis, intraventricular hemorrhage, and need for supplemental oxygen.

Meis et al 2003 (6) concluded that weekly injections of 17P resulted in a substantial reduction in the rate of recurrent preterm delivery among women who were at particularly high risk for preterm delivery and reduced the likelihood of several complications in their infants. So there is difference between our study and Meis et al 2003, as the second group in our study did not take placebo but undergo cervical cerclage. Our study Support the results of Meis t al 2003 regarding that 17 OH progesterone reduce the rate of preterm labor and decrease the infant morbidity and mortality and when 17OH progesterone compared to cerclage ,progesterone was better regarding the gestational age with (RR=0.5500 ,95% CI= 0.3224 -0.9382) and less need for tocolysis with RR= 0.2800, CI= 0.1436 - 0.5461). Moustafa Ibrahim 2009 has compared between 2 groups. Both have history of spontaneous preterm labor .One group received cidulot depot 250 mg (17 hydroxy progesterone) once weekly and the other group received placebo (12).

According to Moustafa Ibrahim 2009 (11), the mean age in progesterone group was 25.32±4.15 vs. 25.60±3.85years in placebo group with no significant difference (P>0.05) between both groups. Gravidity in progesterone group was 3.96±1.06 vs. 4.08±0.997 in placebo group with no significant difference (P>0.05). The mean gestational age was 37.47±1.559 in progesterone group vs. 34.71±2.49 in placebo group (P<0.05). In the progesterone group 8 of 25 women delivered before completion of 37 weeks of gestation (32%) and 17 women delivered full term (68%). In placebo group 13 of 25 women delivered before completion of 37weeks of gestation (52%) and 12 women delivered full term (48%).

Fetal birth weight (FBwt) in progesterone group was 2988.00±477.031 vs. 2702.00±501.140 in placebo group with significant difference (P>0.05) while an increase in the rate of fetal birth weight over 2500g that occurred in progesterone group was 20 (80%) vs. 15 (60%) in placebo group. Three of neonates in progesterone group needed NICU for different causes and represented 12% vs. 9 and represented 36% in placebo group. Also 1 neonatal death occurred in progesterone group and represented 4% vs. 4 and represented 16% in placebo group with significant difference (P<0.05) between two groups. The results of Moustafa study demonstrated the positive effect of injectable progesterone on the incidence of preterm labor. Delivery at <37 gestational weeks was reduced by 20% compared with the placebo group. Similar reductions were seen in delivery less than 34weeks. Additionally, he had demonstrated that patient compliance with the use of the inexpensive injectable progesterone is not of concern (12).

The results of our study support Moustafa Ibrahim study 2009 as the progesterone improve the gestational age in group A with the mean gestational age in our study is 36.33 ± 2.51and higher in Mostafa Ibrahim study in the same group 37.47±1.559. Regarding the fetal weight the mean Fetal birth weight (FBwt) in progesterone group was 2988.00±477.031 and the mean FBW in our study in group A(injectable progesterone) 2.58 ± 0.66 and the rate of fetal birth weight over 2500g that occurred in progesterone group according to Mostafa Ibrahim study 2009 was 20 (80%) and according to our study 22 (73.33%)(12).

Condo et al 2013 (13) had done a retrospective indirect comparison between progesterone and cervical cerclage in prevention of preterm labor as no randomized controlled trial has compared vaginal progesterone and cervical cerclage directly for the prevention of preterm birth in women with a sonographic short cervix in the mid trimester, singleton gestation, and previous spontaneous preterm birth. Condo et al 2013 performed an indirect comparison of vaginal progesterone versus cerclage using placebo/no cerclage as the common comparator .They taken four studies that evaluated vaginal progesterone versus placebo (158 patients) and 5 studies that evaluated cerclage versus no cerclage (504 patients) were included in women with a sonographic short cervix in the mid trimester, singleton gestation, and previous spontaneous preterm birth. Both interventions were associated with a statistically significant reduction in the risk of preterm birth at <32 weeks of gestation and composite perinatal morbidity and mortality compared with placebo/no cerclage. Adjusted indirect meta analyses did not show statistically significant differences between vaginal progesterone and cerclage in the reduction of preterm birth or adverse perinatal outcomes. Based on state-of-the-art

methods for indirect comparisons, either vaginal progesterone or cerclage are equally efficacious in the prevention of preterm birth in women with a sonographic short cervix in the mid trimester, singleton gestation, and previous preterm birth. Selection of the optimal treatment needs to consider adverse events, cost and patient/clinician preferences (13).This study goes in contrast to our study as our study is direct comparison between cerclage and progesterone and our study shows that progesterone is better than cerclage regarding the gestational age and less need for tocolysis

17 OH progesterone 250 mg weekly IM injection starting at 16- 20 weeks gestational age and prophylactic cervical cerclage operation reduce the recurrence of preterm labor. 17 OH progesterone 250 mg weekly IM injection more superior as this method was associated with longer gestational age at time of delivery, less need to tocolysis and patient's compliance is good. Moreover more complications associated with cerclage regarding need to tocolysis.

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NEWS AND VIEWS

Compiled and abstracted by prof. Ahmed Badawy, MD FRCOG PhD

- **Do clothes make the doctor? U-M researchers report on patient perceptions of physicians based on attire**

University of Michigan Health System, 02/11/2015

Age, culture & type of care matter – and new survey will look at impact further. What should doctors wear? And how does something as simple as their choice of a suit, scrubs or slacks influence how patients view them? A new analysis takes a comprehensive look – and finds that the answer isn't as simple as you might think. It also finds that doctors don't seem to be getting a lot of guidance on how to dress – despite the influence their attire can have on patients' perceptions. In general, the study finds, people prefer their physicians dress on the formal side – and definitely not in casual wear. Doctors of either gender in suits, or a white coat, are more likely to inspire trust and confidence. But fashion takes a back seat when it comes to emergency, surgical or critical care, where data show clothes don't matter as much – and patients may even prefer to see doctors in scrubs. In general, Europeans and Asians of any age, and Americans over age 50, trusted a formally dressed doctor more, while Americans in Generation X and Y tended to accept less–dressy physicians more willingly. The findings were compiled by a University of Michigan Health System team, from a comprehensive international review of studies on physician attire, and other sources. In all, the data they reviewed came from 30 studies involving 11,533 adult patients in 14 countries. Their review has been published in British Medical Journal Open.

- **1.Metformin use in patients undergoing in vitro fertilization treatment: Results of a worldwide web-based survey**

Journal of Assisted Reproduction and Genetics, 02/24/2015 by Christianson MS, et al.

In this study, authors wanted to identify trends regarding therapeutic approaches to metformin administration in patients undergoing in vitro fertilization (IVF) treatment worldwide. While metformin is used worldwide as an adjunct to standard IVF protocols, there is much variation in its use and the majority of centers report lack of evidence supporting its use.

- A retrospective evaluation utilizing the results of a web–based survey, IVFWorldwide (www.IVF–worldwide.com/), was performed.
- Responses from 101 centers performing a total of 50,800 annual IVF cycles were performed.
- Of these cycles, 10.4 % (n = 5,260) reported metformin use during IVF cycles.
- Indications for metformin use in IVF cycles included polycystic ovary syndrome (PCOS) patients who were habitual abortions (67 %), had prior poor egg quality (61 %), had high serum insulin levels (56 %).
- Less reported was PCOS with obesity/anvoulation (29 %), PCOS with multiple manifestations (23 %) and glucose intolerance and insulin resistance (23 %).
- Over half of cycles (54 %) treated patients with metformin up to 3 months prior to starting IVF.
- A majority (82 %) of IVF cycles utilized 1500–2000 mg/day of metformin.
- A nearly equal percentage of centers continued metformin up to a positive β–HCG test (35 %) or to 12 weeks gestation (33 %).
- 70 % of IVF cycles reported increased pregnancy rates and decreased miscarriage rates due to the use of metformin.
- 75 % reported the data in the literature is not sufficient for reaching a definitive conclusion concerning metformin treatment in patients undergoing IVF.

- **Assisted reproductive technology and somatic morbidity in childhood: A systematic review**

Fertility and Sterility, 02/06/2015 by Kettner LO, et al.

The authors want to assess whether children conceived by assisted reproductive technology are at increased risk of somatic morbidity in childhood compared with spontaneously conceived children. Children conceived by assisted reproductive technology may be at increased risk of somatic morbidity in childhood compared with spontaneously conceived children, although some inconsistency exists between study results.

- **1.Impact of metformin on Anti-Mullerian Hormone in women with PCOS: A secondary analysis of a randomized controlled trial.**

Acta Obstetricia et Gynecologica Scandinavica, 02/26/2015 by Madsen HN, et al.

- Comparing individual metformin/placebo AMH values, a small absolute decrease of 9.3 pmol/l (p=0.03) was observed in obese women after six months relative to baseline, suggesting a trend toeards decreasing values after metformin treatment, mainly in obese women.
- Conclusions on the effect of metformin on circulating anti–Mullerian hormone (AMH) levels in women with polycystic ovary syndrome (PCOS) are ambiguous.

- Authors performed a secondary analysis of a randomized, double–blind, placebo–controlled cross–over trial.
- Fifty–six women with hyperandrogenemic PCOS were included.
- Each woman served as her own control receiving a daily dose of either 1700 mg metformin or placebo for six months. After a three months wash–out period they received the opposite treatment. The decrease in AMH from a median of 49.5 to 46.9 pmol/l after six months on metformin was overall not significant (p=0.81), nor were changes in obese women (49.5 to 38.2 pmol/l; p=0.53).

- **1.Luteal phase supplementation after gonadotropin-releasing hormone agonist trigger in fresh embryo transfer: the American versus European approaches**

Fertility Sterility, February 11, 2015 by Peter Humaidan

The challenges in attaining an adequate luteal phase after GnRH agonist (GnRHa) trigger to induce final oocyte maturation have resulted in different approaches focused on rescuing the luteal phase insufficiency so that a fresh transfer can be carried out without jeopardizing IVF outcomes. Over the years, two different concepts have emerged: intensive luteal support with aggressive exogenous administration of E2 and P; and low-dose hCG rescue in the form of a small dose of hCG either on the day of oocyte retrieva or on the day of GnRHa trigger (the so called "dual trigger"). Both approaches have been shown to be effective in achieving pregnancy rates similar to those obtained after conventional hCG trigger and resulting in a very low risk of ovarian hyperstimulation syndrome (OHSS). Although the idea of freezing all embryos after GnRHa trigger and transferring them in a subsequent frozen-thawed cycle has been gaining momentum, a fresh transfer leading to the live birth of a healthy child is currently considered to be the goal of IVF treatment.

- **1.Risk of uterine perforation with levonorgestrel-releasing and copper intrauterine devices in the European active surveillance study on intrauterine devices**

Contraception, 01/30/2015 by Heinemann K, et al.

In this study, authors want to identify and compare the incidence of uterine perforation and other medically adverse events associated with levonorgestrel–releasing IUDs (LNG–IUSs, releasing 20 mcg LNG daily) and copper IUDs under routine conditions of use in a study population representative of typical users. Uterine perforation incidence in this study was low, with a benign clinical course thereafter. The LNG–IUS and copper IUDs did not have clinically important differences in perforation rates.

- **1.Age at menopause in women with type 1 diabetes mellitus: The OVADIA study**

Human Reproduction, 01/26/2015 by Yarde F, et al.

In this study, authors want to explore the type 1 diabetes a determinant of advanced ovarian ageing, resulting in an early age at natural menopause. No clear evidence was provided that type 1 diabetes is a determinant of accelerated ovarian ageing resulting in an early menopause.

A cross–sectional study was performed in 140 post–menopausal women with, and 5426 post–menopausal women without, diabetes. Both women with and without diabetes had experienced natural menopause. Study participants filled out a standardized questionnaire including report of their age at last menstrual period. Differences in menopausal age were analysed using linear regression analyses, with adjustment for possible confounders.

Mean age at natural menopause was 49.8 ± 4.7 years in women with type 1 diabetes and 49.8 ± 4.1 in women without diabetes. Linear regression analyses showed that type 1 diabetes was not associated with an earlier menopause compared with the reference group without diabetes, after adjustment for age, smoking history and parity (difference in age at menopause between women with type 1 diabetes and reference group 0.34 years, 95% confidence interval –0.34, 1.01).

- **1.Impact of newly diagnosed endometrial polyps during controlled ovarian hyperstimulation on IVF outcomes**

Journal of Minimally Invasive Gynecology, 01/23/2015 by Elias RT, et al.

In this study, authors want to investigate the impact of newly diagnosed endometrial polyps during controlled ovarian hyperstimulation (COH) on the outcomes of fresh in vitro fertilization (IVF)–embryo transfer (ET) cycles. Newly diagnosed endometrial polyps during COH is associated with an increased biochemical pregnancy rate, but ultimately does not adversely impact clinical pregnancy or live birth rates after fresh IVF–ET.