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Abstract

Impact of haemostatic sealant versus electrocoagulation on ovarian reserve after laparoscopic ovarian cystectomy of ovarian endometriomas: a randomised controlled trial.

JPW Chung ,TSM Law ,CHS Chung ,JSM Mak ,DS Sahota ,TC Li

BJM, 30 April 2019

Objective: To evaluate the effect of haemostatic sealant compared with bipolar coagulation on ovarian reserve after laparoscopic cystectomy for ovarian endometriomas. **Design**: Patient blinded, randomised controlled trial.Setting:University affiliated tertiary hospital. **Population**: Women aged 18–40 years with 3–8 cm unilateral or bilateral endometriomas**. Methods**: Ninety four patients were randomised to receive haemostasis by the application of haemostatic sealant (*n* = 47) or standard care of electrocoagulation (*n* = 47). **Main outcome measures**: Primary outcome was the effect on the antral follicular count 3 months after the operation as it captures the effect on the ovary subjected to treatment. Secondary outcomes included the change in anti Mullerian hormone, follicular stimulating hormone and peri operative outcomes including haemostasis, pain, and satisfaction scores. **Results**: A total of 94 patients aged 32.36 ± 4.92 years underwent laparoscopic cystectomy for ovarian endometriomas. The average diameter of the endometrioma was 4.21 ± 1.38 cm. The increase in antral follicle count of the affected ovaries at 3 months in the intervention group (+2.36 ± 0.37) was significantly (*P* = 0.013) higher than that in the control group (+1.08 ± 0.36). Repeated measures analysis of variance revealed significant effect with time (*P* < 0.001) and of interaction of group × time (*P* = 0.029) for affected ovary antral follicle count. No significant difference was noted between the two groups with regard to follicular stimulating hormone, anti Mullerian hormone, and other secondary outcomes.

Conclusions: Applying haemostatic sealant after laparoscopic cystectomy of ovarian endometriomas produced a greater increase in antral follicle count 3 months after surgery compared with the control group.

Cervical mucus removal prior to intrauterine insemination: a randomized trial

MA Maher ,TM Sayyed, N Elkhouly

BMJ, 27 October 2017

Objective: To detect if removing the cervical mucus before performing intrauterine insemination (IUI) could improve pregnancy outcomes in patients with unexplained infertility. **Design**: Prospective randomized study. **Setting**: An Egyptian University Hospital. **Population**: Seven hundred and fourteen couples with unexplained infertility who underwent intrauterine insemination (IUI) with or without cervical mucus removal. **Methods:** Using computer generated numbers, patients were randomly allocated to cervical mucus removal (removed from both internal and external os) or non mucus removal groups. Only participants were blinded as to group assignment. **Main outcome measures:** The clinical pregnancy rate. **Results:** Of 714 IUI patients between November 2014 and March 2017, 361 were in the mucus removal group, and 353 in the non mucus removal group. Difficult catheterization was encountered in 17 cases out of 666 (2.6%) 12 in the cervical mucus removal group and five in the non mucus removal group). A total of 666 IUI cycles were completed while 48 were either cancelled or lost in their follow up. The clinical pregnancy rate was significantly higher in the mucus removal group [31.0% (*n* = 112)] than in the non mucus removal group [21.8% (*n* = 77); *P* = 0.005]. Ovarian hyperstimulation developed in 33 (4.6%) cases: 18 cervical mucus removal and 15 non mucus removal. All except one were mild and managed with outpatient care. **Conclusions:** Cervical mucus removal before IUI could improve pregnancy outcomes in women with unexplained infertility.

Aromatase inhibitors (letrozole) for subfertile women with polycystic ovary syndrome.

Franik S[1], Eltrop SM, Kremer JA, Kiesel L, Farquhar C.

Cochrane Database Syst Rev. 2018 May 24;5

Objectives: To evaluate the effectiveness and safety of aromatase inhibitors for subfertile women with anovulatory PCOS for ovulation induction followed by timed intercourse or intrauterine insemination (IUI).

Results: This is a substantive update of a previous review. We identified 16 additional studies for the 2018 update. We include 42 RCTs (7935 women). The aromatase inhibitor letrozole was used in all studies. Letrozole compared to clomiphene citrate (CC) with or without adjuncts followed by timed intercourse. Live birth rates were higher with letrozole (with or without adjuncts) compared to clomiphene citrate (with our without adjuncts) followed by timed intercourse (OR 1.68, 95% CI 1.42 to 1.99; 2954 participants; 13 studies; I^2 = 0%; number needed to treat for an additional beneficial outcome (NNTB) = 10; moderate-quality evidence). There is high-quality evidence that OHSS rates are similar with letrozole or clomiphene citrate (0.5% in both arms: risk difference (RD) -0.00, 95% CI -0.01 to 0.00; 2536 participants; 12 studies; I^2 = 0%; high-quality evidence).

There is evidence for a higher pregnancy rate in favour of letrozole (OR 1.56, 95% CI 1.37 to 1.78; 4629 participants; 25 studies; I^2 = 1%; NNTB = 10; moderate-quality evidence). There is little or no difference between treatment groups in the rate of miscarriage by pregnancy (20% with CC versus 19% with letrozole; OR 0.94, 95% CI 0.70 to 1.26; 1210 participants; 18 studies; I^2 = 0%; high-quality evidence) and multiple pregnancy rate (1.7% with CC versus 1.3% with letrozole; OR 0.69, 95% CI 0.41 to 1.16; 3579 participants; 17 studies; I^2 = 0%; high-quality evidence). However, a funnel plot showed mild asymmetry, indicating that some studies in favour of clomiphene might be missing.Letrozole compared to laparoscopic ovarian drillingThere is low-quality evidence that live birth rates are similar with letrozole or laparoscopic ovarian drilling (OR 1.38, 95% CI 0.95 to 2.02; 548 participants; 3 studies; I^2 = 23%; low-quality evidence). There is insufficient evidence for a difference in OHSS rates (RD 0.00, 95% CI -0.01 to 0.01; 260 participants; 1 study; low-quality evidence). There is low-quality evidence that pregnancy rates are similar (OR 1.28, 95% CI 0.94 to 1.74; 774 participants; 5 studies; I^2 = 0%; moderate-quality evidence). There is insufficient evidence for a difference in miscarriage rate by pregnancy (OR 0.66, 95% CI 0.30 to 1.43; 240 participants; 5 studies; I^2 = 0%; moderate-quality evidence), or multiple pregnancies (OR 3.00, 95% CI 0.12 to 74.90; 548 participants; 3 studies; I^2 = 0%; low-quality evidence).Additional comparisons were made for Letrozole versus placebo, Selective oestrogen receptor modulators (SERMS) followed by intrauterine insemination (IUI), follicle stimulating hormone (FSH), Anastrozole, as well as dosage and administration protocols. There is insufficient evidence for a difference in either group of treatment due to a limited number of studies. Hence more research is necessary.

Conclusions: Letrozole appears to improve live birth and pregnancy rates in subfertile women with anovulatory polycystic ovary syndrome, compared to clomiphene citrate. There is high-quality evidence that OHSS rates are similar with letrozole or clomiphene citrate. There is high-quality evidence of no difference in miscarriage rates or multiple pregnancy rates. There is low-quality evidence of no difference in live birth and pregnancy rates between letrozole and laparoscopic ovarian drilling, although there were few relevant studies. For the 2018 update, we added good-quality trials, upgrading the quality of the evidence.

Risk of ovarian cancer in women treated with ovarian stimulating drugs for infertility.

Rizzuto I[1], Behrens RF, Smith LA.

Cochrane Database Syst Rev. 2019 Jun 18

Objectives: To evaluate the risk of invasive ovarian cancer and borderline ovarian tumours in women treated with ovulation inducing drugs for subfertility.

Main Results: We included 13 case-control and 24 cohort studies (an additional nine new cohort and two case-control studies), which included a total of 4,684,724 women. Two cohort studies reported an increased incidence of invasive ovarian cancer in exposed subfertile women compared with unexposed women. One reported a standardized incidence ratio (SIR) of 1.19 (95% confidence interval (CI) 0.54 to 2.25) based on 17 cancer cases. The other cohort study reported a hazard ratio (HR) of 1.93 (95% CI 1.18 to 3.18), and this risk was increased in women remaining nulligravid after using clomiphene citrate (HR 2.49, 95% CI 1.30 to 4.78) versus multiparous women (HR 1.52, 95% CI 0.67 to 3.42) (very low-certainty evidence). The slight increase in ovarian cancer risk among women having between one and three cycles of in vitro fertilisation (IVF) was reported, but this was not statistically significant (P = 0.18). There was no increase in risk of invasive ovarian cancer after use of infertility drugs in women with the BRACA mutation according to one cohort and one

case-control study. The certainty of evidence as assessed using GRADE was very low. For borderline ovarian tumours, one cohort study reported increased risk in exposed women with an SIR of 3.61 (95% CI 1.45 to 7.44), and this risk was greater after treatment with clomiphene citrate (SIR 7.47, 95% CI 1.54 to 21.83) based on 12 cases. In another cohort study, the risk of a borderline ovarian tumour was increased, with an HR of 4.23 (95% CI 1.25 to 14.33), for subfertile women treated with IVF compared with a non-IVF-treated group with more than one year of follow-up. A large cohort reported increased risk of borderline ovarian tumours, with HR of 2.46 (95% CI 1.20 to 5.04), and this was based on 17 cases. A significant increase in serous borderline ovarian tumours was reported in one cohort study after the use of progesterone for more than four cycles (risk ratio (RR) 2.63, 95% CI 1.04 to 6.64). A case-control study reported increased risk after clomiphene citrate was taken, with an SIR of 2.5 (95% CI 1.3 to 4.5) based on 11 cases, and another reported an increase especially after human menopausal gonadotrophin was taken (odds ratio (OR) 9.38, 95% CI 1.66 to 52.08). Another study estimated an increased risk of borderline ovarian tumour, but this estimation was based on four cases with no control reporting use of fertility drugs. The certainty of evidence as assessed using GRADE was very low. However, although some studies suggested a slight increase in risks of ovarian cancer and borderline ovarian tumour, none provided moderate- or high-certainty evidence, as summarized in the GRADE tables.

Conclusions: Since the last version of this review, only a few new relevant studies have provided additional findings with supporting evidence to suggest that infertility drugs may increase the risk of ovarian cancer slightly in subfertile women treated with infertility drugs when compared to the general population or to subfertile women not treated. The risk is slightly higher in nulliparous than in multiparous women treated with infertility drugs, and for borderline ovarian tumours. However, few studies have been conducted, the number of cancers is very small, and information on the dose or type of fertility drugs used is insufficient.

Correlation of fetal blood vessel Doppler measurements with fetal anemia among Rhesus isoimmunized pregnancies after two intrauterine transfusions

Sarita Kumari, Dipika Deka ,Vatsla Dadhwal, Vanamail Perumal

IJOG, 20 April 2019

Objective: To assess the correlation between fetal blood vessel Doppler measurements and fetal anemia among Rhesus isoimmunized pregnancies after two intrauterine transfusions as a potential guide to therapy.

Methods: A prospective observational study was conducted among 30 women who attended a single hospital in India between April 2, 2015 and October 30, 2016. The participants underwent a third intrauterine transfusion based on a middle cerebral artery (MCA) peak systolic velocity (PSV) of greater than 1.50 multiples of the median (MoM). Cordocentesis was performed before the third intrauterine transfusion and hematocrit values correlated with the blood vessel Doppler measurements.

Results: The MCA PSV MoM and fetal hematocrit MoM had a correlation coefficient of “0.43 (95% confidence interval “0.68 to 0.08; *P*=0.017). The sensitivity, specificity, positive predictive value, and negative predictive value were 68%, 57%, 83%, and 33%, respectively. The descending aorta PSV ´ and fetal hematocrit ´ had a correlation coefficient of “0.54 (95% confidence interval “0.75 to “0.23; *P*=0.001). An area under the curve of 0.80 (standard error 0.085; *P*=0.017) had 87% sensitivity and 57% specificity for diagnosing fetal anemia.

Conclusion: The descending aorta PSV could offer a useful diagnostic adjunct to MCA PSV after two intrauterine transfusions.

Effects of betamethasone on fetoplacental and maternal hemodynamics in preterm pregnancies†

Cihan Inan ,N. Cenk Sayin ,Zehra N. Dolgun ,Selen G. Erzincan ,Isil Uzun ,Havva Sutcu ,Necdet Sut ,Fusun G. Varol

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Objective: To evaluate the possible effects of prenatal steroid administration on Doppler

parameters of the umbilical artery, uterine artery, middle cerebral artery, and ductus venosus, the cerebroplacental ratio, and the amniotic fluid index in preterm fetuses.

Methods: The present prospective observational study was performed at the Perinatology Department of Trakya University, Edirne, Turkey, between June 1, 2015, and September 1, 2016. It included patients with healthy singleton pregnancies who had received betamethasone at 24–34 weeks of pregnancy. Doppler parameters were measured before (0 hours) and 24, 48, and 72 hours after the administration of betamethasone (two intramuscular doses of 12 mg each, administered 24 hours apart).

Results: There were 68 patients included. Pairwise comparisons demonstrated that, at 72 hours after betamethasone administration, the umbilical artery resistance index (P=0.038), the middle cerebral artery systolic/diastolic velocity ratio (P=0.007), and the amniotic fluid index (P=0.017) were reduced, whereas the end diastolic velocity of the middle cerebral artery was increased (P=0.012), compared with baseline values.

Conclusion: Betamethasone had favorable effects on fetal cerebral circulation, with increased end diastolic velocity in the middle cerebral artery; this could represent a positive effect on cerebral blood circulation and decreased flow resistance in the umbilical artery.