

Ni-Chin Tsai 蔡妮瑾 (Y10)



The abnormal fertilization rate in IVF/ICSI in advanced reproductive age

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Background and Aims: Normal fertilization rate and/or abnormal fertilization (triploidy, 3PN) rate has been less discussed in advanced reproductive age. The etiology of 3PN/1PN was also less understood in poor responder in either conventional insemination (IVF) or intracytoplasmic sperm injection (ICSI). For investigating the mechanisms of abnormal fertilization, polar body conditions may be helpful.

Materials and methods: A retrospective cohort study was conducted at a teaching hospital reproductive center. All fresh IVF cycles performed from January 2018 to August 2018 were reviewed for possible inclusion. Inclusion criteria includes women aged 35 years or older, and autologous cycle with either IVF or ICSI. Excluding criteria included: the use of donor oocytes, or oocyte cryopreservation. All couples completed the standard infertility workup. All ICSI was due to male factor. Fertilization was confirmed 16 to 18 hours post-insemination. Normal fertilization, 1PN, and 3PN fertilization rate were reported according to insemination methods. Normal fertilization rate was defined as 2PN zygotes No./mature oocytes No.

Results: During this 8 months, total 429 fresh cycles were done. Of which, 73% of women was >35 y/o; 43% (184/429) was >=40 y/o. 22 cycles with no oocyte retrieved (22/429=5%). Total 251 cycles were included. 15 cycles with no oocyte retrieved. Finally, 236 cycles (IVF, n=193; ICSI, n=43) were included for fertilization evaluation. The mean age of the female patients was 40.5 ± 2.7 years. Baseline sperm characteristics were significantly poor in ICSI group (table 1). The mature oocytes rate, normal fertilization rate, total fertilization rate and 1PN rate were comparable among two groups. 3PN rate were significantly higher in IVF group (8% in IVF versus 1% in ICSI, p<0.05). Incorporating the polar body conditions in fertilization check, digyny was the major cause in IVF as well as in ICSI. As for 1PN zygote, only a small portion in IVF group would be considered as fertilization failure (2/31) (table 3).

Conclusions: The abnormal fertilization rate in this poor responder cohort was acceptable. Most of the trippronuclear zygotes (59/86=68.6%) were digynic due to failure in extrusion of the second polar body. Even ICSI couldn't circumvent these poor-quality oocytes.

Keywords: 3 pronuclei; trippronuclear zygotes; abnormal fertilization; polar body; advanced age; IVF; ICSI

Ting-Chi Huang 黃琹琦
(Y11)



A novel GnRH antagonist protocol by switching GnRH antagonist to medroxyprogesterone acetate when patients turn out to be at a high risk of ovarian hyperstimulation syndrome during ovarian stimulation

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BACKGROUND: To investigate whether switching GnRH antagonist (GnRHant) to medroxyprogesterone acetate (MPA) could effectively prevent premature LH surge in a GnRHant protocol in patients turn out to be at a high risk of ovarian hyperstimulation syndrome (OHSS) during ovarian stimulation.

METHODS: This is a retrospective cohort study. 205 patients in the control group were recruited from August 2015 to July 2016, all using traditional GnRHant protocol. 196 patients in the study group were recruited from August 2016 to July 2017. In the study protocol (switch protocol), GnRHant was stopped and then sequentially replaced by an oral MPA of 10 mg per day till the day of ovulation trigger once freeze-all was determined.

RESULTS: Premature LH surge did not occur in both groups of patients. The switch protocol group had a significantly fewer days of GnRHant treatment (3.1 ± 1.0 vs. 6.5 ± 1.2) compared with GnRHant protocol group. The mean duration of MPA treatment was 3.6 ± 1.1 days. There was no statistically significant difference in terms of live birth, implantation, and clinical pregnancy rates.

CONCLUSIONS: This study showed that MPA could replace GnRHant and effectively prevent premature LH surge after several days of GnRHant administration in patients turn out to be at high risk of OHSS. Switch protocol resulted in similar clinical outcomes compared with those by the GnRHant protocol, but more patient friendly in terms of injection burden and costs. In contrast to PPOS, the major advantage of switch protocol is individualizing freeze-all policy.

Quan-Bin Jou 周奎銘 (Y12)



The relationship between cumulus cell gene expression and the developmental potential of the early embryo

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Objective: To study whether cumulus cells gene expression could predict early embryo developmental potential to higher-level blastocyst or arrested embryo?

Materials and Methods: Total RNA of cumulus cells collected from cumulus-oocyte complexes (COCs) for intracytoplasmic sperm injection procedures was extracted and reverse-transcribed to cDNA. The cDNA was amplified and fragmented to prepare a library for RNA sequencing (RNA-Seq). Cumulus RNA-Seq data were compared between 4AA blastocyst (n=6) and developmentally arrested embryo (n=6). A Pearson correlation test was performed to examine the relationship between the two groups. R software was used to compare the significance of the differentially expressed genes between the two groups. Quantitative real-time polymerase chain reaction (qPCR) was applied to validate the difference in gene expression.

Results: Pearson correlation test and principal component analysis showed that the gene expression profile was very similar between the 4AA and the arrested group. In total, 264 differentially expressed genes (DEGs) with two-fold change were found in cumulus cells between the two groups. However, lower expression levels of DEGs were revealed in cumulus cells surrounding mature oocytes that developed into 4AA blastocyst or arrested embryo. We then validated 14 genes, including AC008641.1, AC067930.3, AC234031.1, AL160408.2, AL354892.2, ALPL, CXCL6, GATD3A, IKBKGP1, MLXIPL, NPIPA8, PRB1, PTPN7, and VN1R83P, using qPCR; however, only the expression of PRB1 and PTPN7 were trended to be differentially expressed.

Conclusions: The similarity of the gene expression profile and the lower expression level of DEGs in cumulus cells surrounding mature oocytes that developed into 4AA blastocyst or arrested embryo indicate that cumulus cell gene expression may not differentiate the developmental potential of the early embryo. Even though PRB1 and PTPN7 may be the differentially expressed genes, further studies with large cohort samples are needed to confirm the differential expression.

Kai-Cheng Chung 鍾凱丞 (Y13)



Association between the total number of mature oocytes and live birth rate in patient with azoospermia

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BACKGROUND: Azoospermia infected around 10-15% infertile male, which cause adverse pregnancy outcome. At the same time, maternal age is an unchangeable condition which negatively affect IVF outcomes. Under the development of oocyte vitrification technology, this study is aim to evaluate the association between the total mature oocyte (MII phase) number collected before performing TESE-ICSI and the chance of having at least one live birth baby in those azoospermic couples.

METHODS: This retrospective cohort study enrolled azoospermic couples receiving TESE-ICSI treatment from 2016/1/1-2018/12/31 in Taipei veteran general hospital. We defined one cycle as every time performing ICSI-TESE, and oocytes number as total collected mature oocyte number during one cycle. Primary outcome is recorded as at least one live birth baby.

RESULTS: Total 219 couple enrolled, received 262 ICSI-TESE cycles. Mean cumulative mature oocyte number per cycle is 12.1, while at least one live birth rate per cycle is 42.7%, with total 144 live birth babies. Logistic regression revealed adjusted OR 1.08 (95% CI 1.02-1.14), each additional oocyte provides 1.08-fold chances of having at least one live birth, however has no interaction with maternal age. Live birth rate significantly increases if collecting more than 10 eggs, and reach maximum in female age form 11-15 years old (52%)

CONCLUSIONS: More mature oocytes retrieved before performing TESE-ICSI on azoospermia patients gives higher chance of at least one live birth rate per cycle.

Te-Wei Wu 吳得維
(Y14)



Effect of chronic endometritis therapy in women with recurrent implantation failure and recurrent pregnancy loss: a case series

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BACKGROUND: The aim of this case series was to investigate the effect of chronic endometritis (CE) in infertile women with a history of repeated implantation failure (RIF) and recurrent pregnancy loss (RPL) and whether there was an improvement by the treatment of oral antibiotics. RPL was defined as two or more miscarriages before 20 weeks' gestation (ASRM, 2008). RIF was defined as the failure to achieve a clinical pregnancy after transfer of at least four good-quality embryos in three or more transfer cycles (Coughlan et al., 2014). We retrospectively collected 28 women diagnosed with CE from 2015-2018 · 15 of which were cases with RPL and 13 cases with RIF.

METHODS: Endometrial biopsy was done in women with RIF or RPL. Chronic endometritis was diagnosed by pathologist with the definition of presenting plasma cells with CD138 stain under 10 high power field (Kannar et al., 2012). Then we prescribed oral antibiotics with doxycycline for two weeks and repeat endometrial biopsy was done again. If CE persisted, additional treatment using a combination of metronidazole and ciprofloxacin was given for two weeks (Kitaya et al., 2017).

RESULTS: After antibiotics treatment, 21 of 28 women (75%) finally gave live birth.

CONCLUSIONS: Chronic endometritis should be evaluated in infertile patients with RIF and RPL. The oral antibiotic treatment against CE might be a promising therapeutic option to improve live birth rate for them.

Yi-Lun Lin 林毅倫 (Y15)



Obstetrical complications and perinatal outcomes resulting from frozen embryo transfer by different way of endometrium preparation

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BACKGROUND: Frozen embryo transfer (FET) have been widely performed in the past few years and in selected cases, FET can achieve live birth rate up to 60-70%. Previous studies have reported that FET might lower the risks of placenta accidents and decrease the perinatal mortality than fresh embryo transfer (ET). However, increased risks of pregnancy-induced hypertension (PIH), large for gestational age (LGA), and postpartum hemorrhage (PPH) were also noted when compared to ET.

OBJECTIVE: The purpose of this study is to test whether these dissimilarity in obstetrical complications and perinatal outcomes are due to the different protocols that been used in endometrium preparation for FET.

STUDY DESIGN: This is a retrospective study enrolled all live births after frozen embryo transfer from 2016 to 2018 in our hospital. Only singletons were included. Patients who received nature cycle for FET were classified as group I (n=40), patients who received HRT for endometrium preparation before FET were classified as group II (n=118). Nature cycle was defined as FET after spontaneous ovulation. Hormone cycle was started at cycle day 5th with estrade (2mg) 1# tid until the thickness of endometrium was greater than 8mm with triple line appearance. Primary outcomes were preterm birth (<37 w), low birthweight (<2500 g), macrosomia (>4000g), hypertensive disorders in pregnancy, gestational diabetes mellitus (GDM), postpartum hemorrhage (>1000 mL) and other maternal outcomes including placenta previa, placenta accreta and placental abruption. Two sample t test and fisher's exact tests with 95% confidence interval were calculated made for relevant confounders.

RESULTS: A total of 158 singletons were included in this study after frozen embryo transfer (natural cycles, n = 40; programmed cycles, n = 118). No significant differences were found in preterm birth and low birthweight between two groups. There were also no statistically significance between natural and programmed frozen cycles in pregnancy induced hypertension, preeclampsia, placenta previa, placenta accrete, postpartum hemorrhage and GDM. Moreover, neonatal outcomes which including preterm birth and macrosomia were also similar in two groups.

CONCLUSION: Higher obstetrical complications and poor perinatal outcomes resulting from frozen embryo transfer might not be related to the way of endometrium preparation.

Kuan-Ying Huang 黃冠穎 (Y16)



Functional Study of the Fetal Heart – Fetal Echocardiographic Parameters in Pulmonary stenosis

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Background: An integrated assessment of the size and shape of the 4-chamber view (4-CV) and right and left ventricles (RV and LV) as well as the function of the RV and LV in fetuses with coarctation of the pulmonary stenosis (PS) has not yet been conducted.

Objectives: Initial fetal echocardiograms (1/2009–10/2019) were interpreted as pulmonary stenosis. We evaluated the size and shape of the 4-CV, RV, and LV, and function of the RV and LV, to identify a profile for fetuses with PS when compared to a control population.

Methods: 57 PS fetuses were compared to 200 controls. This was a retrospective case series comparing the 4-CV of PS fetuses and controls. The 4-CV end-diastolic area, length, width, and sphericity index were measured to determine the configuration of the 4-CV. Speckle-tracking analysis was used to compute the RV and LV end-diastolic area, length, 24-segment sphericity index, 24-segment transverse width. Using 5 and 95% reference intervals, the PS fetal measurements were classified; from these, the odds ratio was computed between the fetuses with PS and the controls. $p < 0.05$ was considered significant.

Results: In fetuses with PS, the 4-CV was spherical in shape, increased in area and width, and decreased in length. Abnormal PS sphericity indices reflected a flatter RV and a more spherical LV. The RV area, length, and width, and LV length were decreased. The transverse width of the LV was increased. RV contractility were depressed.

Conclusions: The results demonstrate previously unappreciated differences in the shape, size, and function of the heart in fetuses with PS. These differences may assist examiners in identifying fetuses with PS.

Howard Hao Lee 李浩 (Y17)



Intracervical Foley catheter plus Intravaginal misoprostol vs intravaginal misoprostol alone for cervical ripening: A Meta-analysis

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Abstract: Currently, there is no meta-analysis comparing intravaginal misoprostol plus intracervical Foley catheter versus intravaginal misoprostol alone for term pregnancy without identifying risk factors. Therefore, the purpose of this study is to conduct a systematic review and meta-analysis of randomized control trials (RCT' s) comparing concurrent intravaginal misoprostol and intracervical Foley catheter versus intravaginal misoprostol alone for cervical ripening. We systematically searched Embase, Pubmed and Cochrane Collaboration databases for randomized controlled trials (RCT' s) comparing intracervical Foley catheter plus intravaginal misoprostol and intravaginal misoprostol alone using the search terms "Foley" , "misoprostol" , "cervical ripening" , and "induction" up to Jan. 29, 2019. Data were extracted and analyzed by two independent reviewers including study characteristics, induction time, cesarean section (C/S), chorioamnionitis, uterine tachysystole, meconium stain, and neonatal intensive care unit (NICU) admissions. Data was pooled using random effects modeling and calculated with risk ratio (RR) and 95% confidence interval (CI). Pooled analysis from eight studies of 1110 women showed that labor induction using combination of intracervical Foley catheter and intravaginal misoprostol decreased induction time by 2.71 hours (95% CI -4.33 to -1.08, p=0.001), and the risk of uterine tachysystole and meconium stain (RR 0.54, 95% CI 0.30-0.99 and RR 0.48, 95% CI 0.32-0.73, respectively) significantly than those using intravaginal misoprostol alone did. However, there was no difference in C/S rate (RR 0.93, 95% CI 0.78-1.11) or chorioamnionitis rate (RR 1.22, CI 0.58-2.57) between both groups. Labor induction with combination of intracervical Foley catheter and intravaginal misoprostol may be a better choice based on advantages in shortening induction time and reducing the risk of uterine tachysystole and meconium staining compared to intravaginal misoprostol alone.

Keywords: induction; intracervical Foley catheter; intravaginal misoprostol; labor; term pregnancy

Siao-Wun Chen 陳曉雯 (Y18)



Timing of planned cesarean delivery and neonatal outcomes

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BACKGROUND: Cesarean section rates have risen over the last decade worldwide because of obstetrical indications and maternal request. However, it is not associated with clear benefit for the baby or mother. According to the previous studies, neonatal adverse outcomes in infants born before 39 weeks of gestation are increased and increase progressively as gestational age at birth declines. Therefore, it is very important to choose the correct timing for planned cesarean section to prevent unnecessary morbidities.

OBJECTIVES: Whether or not the late-term deliveries will reduce neonatal mortality and/or morbidities compare to the late-preterm and early-term deliveries.

METHODS: This is a prospective observational study. There is a birth registration system in our hospital for every live neonate born in our hospital beyond gestational age 20 weeks. We collect the data of neonates during study period from January 2017 through December 2018 a total 360 neonates delivered by planned Cesareans and were divided into two groups, those who were born (late preterm and early term) before 39 weeks of gestation (36+0 – 38+6) and those who were born (late term) at or greater than 39 weeks of gestation. The primary outcome was the composite of several adverse events, including respiratory complications, hypoglycemia, hypoglycemia feeding difficulties and admission to the sick baby nursery (SBN).

RESULTS: 1019 live births delivered by Cesarean section with obstetrical indications and maternal request. Of these only 360 neonates fulfilling the inclusion criteria were included in this study. About 74 % of them were delivered before 39 weeks of gestation (1.94% at 36 weeks, 19.17% at 37 weeks and 52.78% at 38 weeks). As compared with births after 39 weeks, we found a significant risk in the early Cesareans group for development of hypoglycemia (P=0.041), hypothermia (P=0.0003) and feeding difficulty (P=0.004).

CONCLUSIONS: Planned cesarean delivery before 39 weeks of gestation is common and significant associated with neonatal morbidities in our hospital. Further larger studies are needed to responsible for our data in neonates born electively by Cesareans before 39 completed weeks of gestation.

Kun-Long Huang 黃坤龍 (Y19)



Three-dimensional ultrasound and prophylactic transcatheter arterial embolization in conservative management of morbidly adherent placenta

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Objective: The objective of our study was to evaluate patients with morbidly adherent placenta (MAP) managed conservatively with prophylactic transcatheter arterial embolization (TAE) and three-dimensional (3-D) ultrasound by measuring the resorption rate and analyzing the correlated factors.

Methods: From April 2005 to July 2019, twenty-one women with MAP were managed conservatively after being diagnosed by magnetic resonance imaging (MRI). After delivery of the neonate, prophylactic TAE was performed immediately. The placenta was left in situ, and the residual placental volume was evaluated by 3-D ultrasound at each clinical visit. Prophylactic antibiotics were administered during the 7-day postpartum period. The patient profiles, outcomes, and complications were retrospectively reviewed. The resorption rate of residual placenta and correlated factors were statistically analyzed.

Results: Twenty-one women with MAP were included. Based on the MRI findings, 13 patients had placenta percreta, and 8 patients had placenta increta. The mean maternal age was 35.6 ± 5.6 years old, the mean gestational age was 34.9 ± 3.3 weeks, and the mean surgical blood loss was 854.7 ± 478.2 mL. Excluding 7 cases without measurements obtained by 3-D ultrasound, the mean resorption rate of residual placenta in the remaining 14 cases was 178.95 ± 169.06 cm³/month. The mean natural resorption time without surgical intervention was 4.69 ± 1.65 months. Old age was associated with a reduced resorption rate ($p = 0.014$, coefficients = 2.98, $R^2 = 43.9\%$ by Pearson correlation and linear regression model). Regarding maternal complications, 4 patients (19%) had delayed postpartum hemorrhage (PPH), 12 patients (57.1%) developed postpartum infections, 3 patients (14.3%) progressed to sepsis, 4 patients (19%) underwent surgical evacuation, and 4 patients (19%) underwent hysterectomy. No maternal mortality was reported. Regarding fertility, 16 (76.1%) patients had return of menstruation, and one (4.7%) had a subsequent pregnancy resulting in a live birth.

Conclusions: Conservative management with prophylactic TAE and 3-D ultrasound may be effective and safe for young women with MAP.