

·编者按·

随着我国辅助生殖技术水平的不断提高,体外受精-胚胎移植治疗需求也持续扩大,寻求安全、有效的促排卵方案成为患者和临床医生共同追求的治疗选择。在众多的促排卵方案中,促性腺激素释放激素(GnRH)拮抗剂方案因其用药时间短、简单方便等优势越来越受青睐。为进一步明确 GnRH 拮抗剂方案在中国人群中的应用效果,探讨并优化其临床用药方案,本刊 2015 年刊出了“促性腺激素释放激素拮抗剂方案在辅助生殖领域中使用的专家共识”,2017 年 3 月发起了《HOPE 源动力——GnRH 拮抗剂方案病例征集》项目,现已完成此项目的相关工作,刊出优秀论文,希望能对临床医生的诊疗工作带来帮助。

·临床研究·

促性腺激素释放激素拮抗剂在防治早发型中重度卵巢过度刺激综合征的应用

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【摘要】目的 探讨促性腺激素释放激素拮抗剂(GnRH-A)在防治体外受精-胚胎移植(IVF-ET)助孕过程中并发早发型中、重度卵巢过度刺激综合征(OHSS)的效果,旨在寻找防治早发型中重度 OHSS 的有效措施。**方法** 回顾性队列研究分析本院生殖中心接受 IVF-ET 助孕治疗具有 OHSS 高风险而取消新鲜周期胚胎移植行全部胚胎冷冻的患者共 138 例。其中 hCG 注射日血清雌二醇(E_2) $\geq 4\ 000$ ng/L 且 $<6\ 000$ ng/L 和 / 或获卵数 ≥ 15 个为对照组,在取卵当日给予来曲唑 5 mg,口服, qd; 溴隐亭 2.5 mg, 直肠给药, qd, 共 76 例;血清 $E_2 \geq 6\ 000$ ng/L 为试验组,在取卵当日给予以上治疗措施的同时另给予思则凯 0.25 mg 单次皮下注射,共 62 例。两组患者均在取卵后第 3 日及第 5 日复查血清 E_2 水平、血常规及阴道 B 超,比较两组患者在使用两种治疗措施前后的变化,计算两组患者中、重度 OHSS 的发生率。**结果** 两组患者中均无重度 OHSS 发生。试验组中度 OHSS 发生率(3.23%)低于对照组(7.90%)($P=0.243$)。使用 GnRH-A 后 E_2 水平下降快、卵巢恢复快($P=0.00$)。试验组白细胞、红细胞、红细胞压积、血小板水平与对照组差异无统计学意义($P>0.05$)。**结论** OHSS 高风险患者取卵日单次给予 GnRH-A 不受促排卵方案的影响,可显著降低早发型中重度 OHSS 的发生率,减轻了患者的症状及经济负担,可作为防治早发型中重度 OHSS 的有效措施。

【关键词】 促性腺激素释放激素拮抗剂(GnRH-A); 体外受精-胚胎移植(IVF-ET); 卵巢过度刺激综合征(OHSS)

· 临床研究 ·

Application of gonadotropin-releasing hormone antagonist in the prevention and treatment of early ovarian hyperstimulation syndrome Song Rong, Li Shoumei, Shi Jinyue, Long Yan, Zhou Yuyan

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【Abstract】 Objective To investigate the effect of gonadotropin-releasing hormone antagonist (GnRH-A) in the prevention and treatment of early moderate and severe ovarian hyperstimulation syndrome (OHSS) during *in vitro* fertilization-embryo transfer (IVF-ET) cycles. **Methods** A retrospective cohort analysis was performed at our center. A total of 138 infertile women undergoing reproductive technique with high risk of OHSS were enrolled in this clinical trial and were divided into two groups. The treatment was given from the day of oocytes retrieved and fresh transplantation was cancelled in the two groups. Control group with 76 patients [serum estradiol (E_2) level $\geq 4\ 000$ ng/L and $<6\ 000$ ng/L and/or the number of oocytes retrieved ≥ 15 on the day of hCG injection] was given routine preventative treatment. GnRH-A group with 62 patients (serum E_2 level $\geq 6\ 000$ ng/L on the day of hCG injection) was given the routine preventative treatment and 0.25 mg cetrotorelix at a time. The incidence of moderate and severe OHSS was surveyed and the clinical data of patients in the two groups were analyzed. **Results** There were no severe OHSS in the two groups. The incidence of moderate OHSS was lower in GnRH-A group than control group ($P=0.243$). The serum E_2 level in the GnRH-A group dropped faster when using GnRH-A ($P=0.00$). **Conclusion** GnRH-A can reduce the incidence of moderate and severe OHSS. GnRH-A used at a time on the day of oocytes retrieved to the patients with high risk of OHSS could significantly reduce the incidence of moderate and severe OHSS, reduce the symptoms and economic burden of patients, it can be used as an effective measure to prevent and treat early moderate and severe OHSS.

【Key words】 Gonadotropin-releasing hormone antagonist (GnRH-A); *In vitro* fertilization-embryo transfer (IVF-ET); Ovarian hyperstimulation syndrome (OHSS)

促性腺激素释放激素激动剂联合低剂量人绒毛膜促性腺激素扳机在高反应患者体外受精治疗中的应用

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【摘要】目的 探索低剂量人绒毛膜促性腺激素(hCG)双扳机在高反应患者中应用的安全性及有效性。方法 回顾性分析2014年1月1日—2015年12月31日期间采取促性腺激素释放激素(GnRH)拮抗剂方案进行控制性促排卵行体外受精/卵胞质内单精子显微注射(IVF/ICSI)助孕的患者,因卵巢高反应采用低剂量hCG扳机的患者(A组, $n=431$),同期采用标准hCG扳机的患者,以年龄和获卵数1:2配对(B组, $n=862$)进行队列研究。比较分析患者的一般资料及治疗结局。结果 患者年龄等一般情况差异无统计学意义,两组患者促性腺激素(Gn)启动剂量及用药时间比较等差异无统计学意义($P>0.05$)。A组患者hCG扳机日血清雌二醇(E_2)水平 $[(16\ 261\pm\ 6\ 561)\text{ pmol/L}]$ 显著高于B组患者 $[(12\ 795\pm\ 6\ 133)\text{ pmol/L}]$ ($P=0.000$)。ICSI受精率、MII卵比率组间比较差异均无统计学意义($P>0.05$),A组患者双原核(2PN)率(56.0%)显著高于B组(54.7%)($P=0.001$)。临床妊娠率、胚胎着床率、早期流产率及活产率组间比较差异均无统计学意义($P>0.05$)。A组有5例患者发生重度卵巢过度刺激综合征(OHSS)。结论 使用拮抗剂方案的高反应患者,使用减量联合扳机,得到满意临床结局的同时,不增加OHSS发生率,新鲜周期也得到了满意的治疗结局。

【关键词】 GnRH拮抗剂(GnRH-A); 高反应; 控制性卵巢刺激(COS); GnRH激动剂(GnRH α)扳机; 联合扳机

Application of gonadotropin-releasing hormone agonist combined with low dose human chorionic gonadotropin trigger in the *in vitro* fertilization of high responder

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【Abstract】 Objective To investigate the effectiveness and safety of low dose human chorionic gonadotropin (hCG) dual trigger, by comparing the *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) outcomes of high responders using low dose hCG dual trigger or standard hCG trigger. **Methods** This was a retrospective cohort study. The patients accepted IVF/ICSI treatment in Reproductive Medical Center of Peking University, between Jan. 1st 2014 and Dec. 31st 2015, with gonadotropin-releasing hormone antagonist (GnRH-A) flexible protocol. The research group was high responders using low dose hCG dual trigger (group A, $n=431$), paired by age and number of oocytes retrieved (1 : 2), over the same period (group B, $n=862$). The general characteristics and treatment outcomes were compared between the two groups. **Results** There were no significant differences between the two groups refer to general characteristics, and gonadotropin (Gn) used dosage ($P>0.05$). The serum E_2 level on hCG trigger day in group A [$(16\ 261 \pm 6\ 561\ \text{pmol/L})$] was significantly higher than that in group B [$(12\ 795 \pm 6\ 133)\ \text{pmol/L}$, $P=0.000$]. The fertilization rate of ICSI and M_{II} oocyte rate were comparable between two groups ($P>0.05$). The rate of two pronucleus (2PN) oocytes was significantly higher in group A (56.0%) than that in group B (54.7%) ($P=0.001$). The clinical pregnancy rate, the implantation rate, the miscarriage rate and live birth rate were comparable between two groups ($P>0.05$). There were 5 patients in group A who suffered severe ovarian hyperstimulation syndrome (OHSS). **Conclusion** For high responders, besides of GnRH antagonist protocol, using low dose hCG dual trigger, will get satisfied clinical outcomes and do not increase the incidence of OHSS, and get satisfied clinical outcomes in fresh cycle.

【Key words】 GnRH antagonist (GnRH-A); High responder; Controlled ovarian stimulation (COS); GnRH agonist (GnRH α) trigger; Dual trigger

三种促排卵方案在体外受精 / 卵胞质内单精子注射卵巢低反应患者中的应用

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【摘要】目的 探讨克罗米芬(CC)+来曲唑(LE)微刺激、安宫黄体酮(MPA)微刺激与拮抗剂方案在卵巢低反应(POR)患者体外受精/卵胞质内单精子注射(IVF/ICSI)周期中的应用效果。方法 应用回顾性队列研究分析2015年10月—2016年12月期间接受IVF/ICSI助孕的POR患者共1427个周期的临床资料,分别采用CC+LE+人绝经期促性腺激素(hMG)方案(A组,674个周期)、MPA+hMG方案(B组,496个周期)和拮抗剂方案(C组,257个周期)促排卵,常规行IVF/ICSI。观察上述3组患者临床、实验室的各项指标的变化。结果 A组Gn用量 $[(2\ 590.88 \pm 742.85)\text{ IU}]$ 、Gn使用时间 $[(9.3 \pm 2.3)\text{ d}]$ 低于B组 $[(2\ 739.11 \pm 862.84)\text{ IU}]$, $[(9.8 \pm 2.9)\text{ d}]$ $(P=0.006, P=0.002)$ 和C组 $[(2\ 765.22 \pm 714.43)\text{ IU}]$, $[(9.9 \pm 2.8)\text{ d}]$ $(P=0.003, P=0.007)$,获卵数 (3.6 ± 2.7) 、2PN数 $[2\ (1,3)]$ 高于B组 $[(3.0 \pm 2.6), 1\ (1,3)]$ $(P=0.002, P=0.015)$;C组的获卵数 (4.4 ± 2.7) 、2PN数 $[2\ (1,4)]$ 、可利用胚胎数 $[2\ (1,3)]$ 、优质胚胎数 $[1\ (0,2)]$ 均高于A组 $[3.6 \pm 2.7, 2\ (1,3), 1\ (1,2.25), 0\ (0,1)]$ $(P<0.001)$ 和B组 $[3.0 \pm 2.6, 1\ (1,3), 1\ (0,2), 0\ (0,1)]$ $(P<0.001)$;A组扳机日LH值 $[(7.96 \pm 5.76)\text{ mIU/L}]$ 高于B组 $[(3.74 \pm 3.54)\text{ mIU/L}]$ $(P<0.001)$ 和C组 $[(2.76 \pm 3.88)\text{ mIU/L}]$ $(P<0.001)$,但A组的提前排卵率与其余两组差异无统计学意义 $(P>0.05)$;A组的未获卵率(4.5%)低于B组(8.2%) $(P=0.008)$ 和C组(9.7%) $(P=0.002)$;A、B、C3组的临床妊娠率分别为27.3%、24.5%、29.7%,累积妊娠率分别为34.6%、29.6%、35.2%,活产率分别为22.7%、20.2%、25.7%,组间比较差异无统计学意义 $(P>0.05)$ 。**结论** 微刺激方案中CC、MPA与拮抗剂方案相似,均已起到明显的降调节作用。对POR患者而言,拮抗剂方案较微刺激方案临床效果好,获卵数、可利用胚胎数及优质胚胎数较多。微刺激方案中CC+LE方案与MPA方案比较,Gn用量及使用时间少,获卵数及可利用胚胎数多。3种方案的临床妊娠率、累积妊娠率及活产率差异均无统计学意义。

【关键词】 卵巢低反应(POR);来曲唑(LE);克罗米芬(CC);安宫黄体酮(MPA);促性腺激素释放激素拮抗剂(GnRH-A)

Application of three kinds of ovulation induction in *in vitro* fertilization/intracytoplasmic sperm injection patients with poor ovarian response

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【Abstract】 Objective To investigate the effect of clomiphene (CC)+letrozole (LE) microstimulation protocol, medroxyprogesterone acetate (MPA) microstimulation protocol and antagonist protocol in *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) cycles of patients with poor ovarian response (POR). **Methods** All data were collected from October 2015 to December 2016. A retrospective cohort study was used to analyze 1 427 infertile women with POR, who underwent IVF/ICSI cycle with CC+LE+human menopausal gonadotropin (hMG) protocol (group A, 674 cycles), MPA+hMG protocol (group B, 496 cycles) and antagonist protocol (group C, 257 cycles). Then we observed and compared the the clinical and laboratory outcomes of the 3 groups. **Results** Gn used dosage [(2 590.88±742.85) IU] and duration [(9.3±2.3) d] in group A were significantly lower than that in group B [(2 739.11±862.84) IU, (9.8±2.9) d] ($P=0.006$, $P=0.002$) and group C [(2 765.22±714.43) IU, (9.9±2.8) d] ($P=0.003$, $P=0.007$). In group A, the number of eggs (3.6±2.7) and two pronucleus (2PN) [2 (1,3)] were significantly more than those of group B [(3.0±2.6), 1 (1,3)] ($P=0.002$, $P=0.015$). Antagonist protocol resulted in the highest number of eggs (4.4±2.7), 2PN [2 (1,4)], available embryos [2 (1,3)] and high-quality embryos [1 (0,2)] than group A [3.6±2.7, 2 (1,3), 1 (1,2.25), 0 (0,1)] ($P<0.001$) and group B [3.0±2.6, 1 (1,3), 1 (0,2), 0 (0,1)] ($P<0.001$). The level of LH on trigger day in group A [(7.96±5.76) mIU/L] were significantly higher than that in group B [(3.74±3.54) mIU/L] ($P<0.001$) and group C [(2.76±3.88) mIU/L] ($P<0.001$). There was no significant difference in the rate of advanced ovulation between the 3 groups ($P>0.05$). But the oocyte free rate of group A (4.5%) was significantly lower than that of group B (8.2%) ($P=0.008$) and group C (9.7%) ($P=0.002$). The rate of clinical pregnancy in groups A-C were separately 27.3%, 24.5%, 29.7%, the cumulative pregnancy rate was separately 34.6%, 29.6%, 35.2%, and the live birth rate was separately 22.7%, 20.2%, 25.7%, there were no significant differences among 3 groups ($P>0.05$). **Conclusion** Similarly to GnRH-A protocol, CC+LE+hMG protocol and MPA+hMG protocol have a better effect of down-regulation. For patients with POR, the antagonist protocol was better than microstimulation protocol in the number of retrieved oocytes, available embryos and the high-quality embryos. In the 2 microstimulation protocols, CC+LE protocol used less Gn but obtained more oocytes compared with MPA protocol. The clinical pregnancy rate, the cumulative pregnancy rate and the live birth rate are not significantly different among the 3 protocols.

【Key words】 Poor ovarian response (POR); Letrozole (LE); Clomiphene (CC); Medroxyprogesterone acetate (MPA); Gonadotropin-releasing hormone antagonist (GnRH-A)

拮抗剂方案中卵泡期促黄体生成素水平对不同卵巢反应者体外受精 - 胚胎移植结局的影响

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【摘要】 目的 探寻拮抗剂方案中添加拮抗剂的最佳时机及人绒毛膜促性腺激素 (hCG) 注射日合理的促黄体生成素 (LH) 水平区间。方法 回顾性队列研究分析 1 327 例拮抗剂方案的取卵周期资料, 根据基础窦卵泡数 (AFC) 将卵巢反应性依次分为卵巢低反应组 ($AFC \leq 5$, $n=278$)、卵巢正常反应组 ($6 \leq AFC \leq 15$, $n=756$)、卵巢高反应组 ($AFC \geq 16$, $n=293$), 并根据拮抗剂添加日及 hCG 注射日的 LH 水平再分组比较临床结局。结果 ①在拮抗剂添加日, 不同卵巢反应者 $LH < 5$ IU/L 及 ≥ 5 IU/L 组的妊娠结局差异均无统计学意义, 但卵巢低反应者在 $LH \geq 5$ IU/L 时开始添加拮抗剂可能获得较高的优质胚胎率, 卵巢正常反应者在 $LH \geq 5$ IU/L 时开始添加拮抗剂 Gn 使用时间较少。②在 hCG 注射日不同卵巢反应者的 LH 水平对其妊娠结局均无影响。结论 拮抗剂添加日 LH 水平及 hCG 注射日 LH 水平均不影响拮抗剂方案的临床妊娠率, 但不同卵巢反应者卵泡期适合的 LH 水平可能有所不同。

【关键词】 拮抗剂方案; 卵泡期促黄体生成素 (LH) 水平; 卵巢反应性; 妊娠结局

Effect of luteinizing hormone level on the outcome of *in vitro* fertilization and embryo transfer in the different ovarian response patients with gonadotrophin-releasing hormone antagonist protocol

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【Abstract】 Objective To explore the optimal time of adding antagonist and the reasonable range of luteinizing hormone (LH) level on the human chorionic gonadotropin (hCG) injection day. **Methods** The data of 1 327 cases of GnRH-A protocol were retrospectively analyzed. According to the antral follicle count (AFC), the patients were divided into three groups: 1) poor ovarian responder ($AFC \leq 5$, $n=278$); 2) normal ovarian responder ($6 \leq AFC \leq 15$, $n=756$); 3) high ovarian responder ($AFC \geq 16$, $n=293$), and then each group was divided into two or three subgroups according to the LH level on antagonist administered day or the hCG injection day, the clinical outcomes were compared among the groups. **Results** 1) There were no significant differences in pregnancy outcomes between $LH < 5$ IU/L and ≥ 5 IU/L groups on the day of antagonist addition, but for the poor ovarian responders, administration of the antagonist when $LH \geq 5$ IU/L could get higher high-quality embryos rate; for the normal ovarian responders, administration of the antagonist when $LH \geq 5$ IU/L could reduce the duration of Gn used. 2) Regardless of ovarian response, the serum LH level on the hCG injection day did not affect the pregnancy outcome. **Conclusion** The LH level on the antagonist administered day and the hCG injection day did not affect the pregnancy outcomes. However, the optimum LH level of follicular phase may vary in different ovarian responders.

【Key words】 GnRH antagonist (GnRH-A) protocol; Luteinizing hormone (LH) level of follicular phase; Ovarian response; Pregnancy outcome

多囊卵巢综合征患者体外受精 / 卵胞质内单精子显微注射周期中拮抗剂和全程克罗米芬方案的妊娠结局比较

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【摘要】 目的 比较对多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者进行体外受精 / 单精子卵胞质内注射 (*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI) 辅助生殖技术助孕时, 使用拮抗剂或全程克罗米芬 (CC) 的温和刺激方案促排卵的妊娠结局及风险。方法 回顾性队列分析 2014 年 1 月—2015 年 12 月期间接受 IVF/ICSI 助孕的 PCOS 患者, 符合纳入标准的共 361 个取卵周期, 其中拮抗剂方案 224 个周期, 全程 CC 方案 137 个周期。比较使用 2 种不同卵巢刺激方案每取卵周期的累积活产率 (cumulative live birth rate, CLBR)、获卵数、促性腺激素 (Gn) 用量及刺激时间、受精率、优质胚胎率和卵巢过度刺激综合征 (OHSS) 的发生率。结果 拮抗剂方案的 CLBR 为 75.4%, 高于全程 CC 方案的 64.2%, 差异有统计学意义 ($P=0.022$)。全程 CC 方案组的促性腺激素使用总剂量 [$1\ 140.5 \pm 474.8$] IU 及刺激时间 [9.4 ± 1.8] d 显著少于拮抗剂方案组 [$1\ 380.7 \pm 498.1$] IU, (10.1 ± 2.3) d] ($P=0.000$, $P=0.002$), hCG 注射日内膜厚度 [8.5 ± 2.2] mm 低于拮抗剂方案组 [10.0 ± 1.9] mm] ($P=0.000$)。两组的获卵数和受精率无显著性差异 ($P>0.05$), 但拮抗剂方案的优质胚胎率 [78.4%(1 285/1 639)] 高于全程 CC 方案 [71.6%(643/898)] ($P=0.000$)。拮抗剂方案的中重度 OHSS 的发生率为 8.9%, 高于全程 CC 方案组的 5.1%, 但差异无统计学意义 ($P>0.05$)。结论 PCOS 患者进行 IVF/ICSI 助孕使用不同的温和刺激方案时, 拮抗剂方案的 CLBR 和优质胚胎率较全程 CC 方案更高, 但是全程 CC 方案的药物用量更低, OHSS 的风险降低。全程 CC 方案在高反应人群中的应用价值, 还需要更大样本的前瞻性随机对照研究来得出结论。

【关键词】 多囊卵巢综合征 (PCOS); 累积活产率 (CLBR); 拮抗剂方案 (GnRH-A); 克罗米芬 (CC); 温和刺激方案; 卵巢过度刺激综合征 (OHSS); 体外受精 / 单精子卵胞质内注射 (IVF/ICSI)

Comparison of pregnancy outcomes using gonadotrophin-releasing hormone antagonists and clomiphene citrate mild stimulation approaches in *in vitro* fertilization patients with polycystic ovary syndrome

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【Abstract】 Objective To validate the use of clomiphene citrate (CC) in *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) when mild stimulation approaches are chosen compared with gonadotrophin-releasing hormone antagonist (GnRH-A) approaches in patients with polycystic ovary syndrome (PCOS). **Methods** Of the PCOS patients who underwent IVF/ICSI from January 1, 2014 to December 31, 2015 in our reproductive center, a total of 361 oocytes retrieved cycles were included, among them, 224 cycles were stimulated using the antagonist protocol while 137 cycles were stimulated with CC and gonadotropin (Gn). The clinical and laboratory parameters of different ovarian stimulation protocols were analyzed. **Results** The cumulative live birth rate (CLBR) of antagonist group (75.4%) was significantly higher than that of clomiphene-based protocol (64.2%) ($P=0.022$). Compared with antagonist protocol, the amount of Gn used ($P=0.000$) and stimulation day ($P=0.002$) of clomiphene-based cycles were significantly lower. The endometrial thickness on the day of human chorionic gonadotropin (hCG) trigger was thinner than that of antagonist protocol ($P=0.000$). Although the number of oocytes retrieved and fertility rate were non significantly higher, the good-quality embryo rate was higher in the antagonist protocol compared with the clomiphene-based protocol. The incidence rate of OHSS in clomiphene group (5.1%) was slightly lower than that of antagonist protocol (8.9%), in spite of no significant difference was found. **Conclusion** Medication cost per cycle for clomiphene group were significantly less, but it should be viewed in the context of reduced CLBR. Whether mild stimulation using CC in combination with low dose of Gn used can be considered a realistic option for good-prognosis patients undergoing IVF still questioned.

【Key words】 Polycystic ovary syndrome (PCOS); Cumulative live birth rate (CLBR); Gonadotrophin-releasing hormone antagonist (GnRH-A); Clomiphene citrate (CC); Mild stimulation; Ovarian hyperstimulation syndrome (OHSS); *In vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET);

醋酸加尼瑞克拮抗剂方案在多囊卵巢综合征患者体外受精 - 胚胎移植中的应用

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【摘要】目的 探讨体外受精 - 胚胎移植 (IVF-ET) 助孕中更适合多囊卵巢综合征 (PCOS) 患者的治疗方案。**方法** 回顾 2012—2017 年期间行 IVF-ET 助孕新鲜周期移植的 PCOS 患者, 比较应用长方案 ($n=130$) 和拮抗剂方案 ($n=133$) PCOS 患者的临床资料和妊娠相关指标。**结果** 患者年龄、不孕年限、体质量指数 (BMI) 值、取卵周期数和移植胚胎数差异均无统计学意义 ($P>0.05$), 垂体促性腺激素 (Gn) 总用量及 Gn 使用总时间, 组间比较差异均有统计学意义 ($P<0.05$), 长方案组 Gn 总用量 [$2\ 208.65 \pm 575.56$ IU] 较拮抗剂方案组多 [$2\ 089.10 \pm 312.42$ IU], Gn 使用总时间长 [(11.1 ± 1.6) d, (10.6 ± 1.5) d]; 长方案组患者的获卵数 [14(2)], 扳机日血雌激素 [$3\ 831.73 \pm 501.22$ ng/L] 大于拮抗剂组 [13(1), $(3\ 133.83 \pm 410.01)$ ng/L], 并且较拮抗剂方案组有较高的卵巢过度刺激综合征 (OHSS) 发生率 (3.8%, 0.0%), 且差异均有统计学意义 ($P<0.05$); 扳机日子宫内膜厚度、扳机日血孕激素、可移植胚胎比率、生化妊娠率、胚胎种植率、临床妊娠率差异均无统计学意义 ($P>0.05$)。**结论** 拮抗剂方案因无前期降调节过程, 使药物注射时间缩短, 患者经济负担减轻, 依从性增加, 且有较低 OHSS 发生率, 更适合 PCOS 患者。

【关键词】多囊卵巢综合征 (PCOS); 不孕症; 体外受精 - 胚胎移植 (IVF-ET); 拮抗剂; 醋酸加尼瑞克

· 临床研究 ·

Efficacy of ganirelix in *in vitro* fertilization-embryo transfer of infertile patients with polycystic ovary syndrome

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【Abstract】 Objective To provide insights into a suitable protocol in patients with polycystic ovary syndrome (PCOS) in *in vitro* fertilization-embryo transfer (IVF-ET). **Methods** This study reviewed patients with PCOS who underwent IVF-ET from 2012 to 2017 in our hospital. The pregnancy and clinical data after matching were analyzed between the long GnRH agonist protocol ($n=130$) and antagonist protocol ($n=133$). **Results** There were no significant differences in age, infertility, body mass index (BMI), cycle number and number of transplanted embryos between the two groups ($P>0.05$). On the basis of this match, there was a significant difference in gonadotropin (Gn) usage and Gn used days between the two groups ($P<0.05$), that is, the total usage of Gn [$(2\ 208.65 \pm 575.56)$ IU] and Gn used days [(11.1 ± 1.6) d] in the long GnRH agonist protocol was more and longer than those in the antagonist protocol [$(2\ 089.10 \pm 312.42)$ IU, (10.6 ± 1.5) d]. The number of ovaries [14 (2)] and blood estrogen [(831.73 ± 501.22) ng/L] on trigger day in the long GnRH agonist protocol were higher than those in the antagonist protocol [13 (1), $(3\ 133.83 \pm 410.01)$ ng/L], and the long GnRH agonist protocol (3.8%) had a higher incidence of ovarian hyperstimulation syndrome (OHSS) than the antagonist protocol (0.0%), and these differences were statistically significant ($P<0.05$). There was no significant difference in endometrial thickness and blood progesterone on trigger day, transplantable embryo ratio, biochemical pregnancy rate, embryo implantation rate and clinical pregnancy rate ($P>0.05$). **Conclusion** As the antagonist protocol without pre-adjustment process, it shortens the number of days of drug injection, increases patients' compliance and reduces the financial burden of the patients. So the antagonist protocol has a lower incidence of OHSS and more suitable for PCOS patients.

【Key words】 Polycystic ovary syndrome (PCOS); Infertility; *In vitro* fertilization-embryo transfer (IVF-ET); Antagonist protocol; Ganirelix

拮抗剂方案中晚卵泡期高孕酮暴露时间对临床妊娠率的影响

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【摘要】目的 分析探讨拮抗剂方案中晚卵泡期早发孕酮升高 (PPR) 暴露时间与临床妊娠率的关系。

方法 回顾性分析 2015—2017 年间本中心卵巢储备功能正常患者行拮抗剂方案促排卵, 比较停药日孕酮 (P) $\leq 1.5 \mu\text{g/L}$ 与 $P > 1.5 \mu\text{g/L}$ 组的妊娠率; 根据促排卵晚卵泡期 P 达到 $1.5 \mu\text{g/L}$ 至停药日暴露时间, 将促排卵停药日 $P < 1.5 \mu\text{g/L}$ 患者定为高 P 暴露 0 d, 纳入 A 组, 促排卵停药日 $P = 1.5 \mu\text{g/L}$ 定为高 P 暴露 1 d, 纳入 B 组, 促排卵晚卵泡期 P 达到 $1.5 \mu\text{g/L}$ 至停药日暴露 2 d、3 d、 ≥ 4 d 分别纳入 C 组、D 组、E 组, 分析 5 组患者的基线资料、促排卵药物使用及实验室数据及临床妊娠率。**结果** hCG 注射日 $P \leq 1.5 \mu\text{g/L}$ 与 $P > 1.5 \mu\text{g/L}$ 组临床妊娠率差异无统计学意义 ($P > 0.05$); A 组、B 组、C 组临床妊娠率差异无统计学意义, E 组妊娠率 (35.29%) 显著低于 A~C 组 (57.69%、58.92%、57.57%, $P = 0.007$); 停药日 P 水平在 A~E 组间差异均有统计学意义 [(1.34 \pm 0.14) $\mu\text{g/L}$ 、(1.76 \pm 0.23) $\mu\text{g/L}$ 、(2.01 \pm 0.25) $\mu\text{g/L}$ 、(2.47 \pm 0.71) $\mu\text{g/L}$ 、(2.56 \pm 0.77) $\mu\text{g/L}$, $P = 0.005$]; 停药日 E_2 水平 A~E 组间比较差异均有统计学意义 [(3 472.42 \pm 1 686.26) $\mu\text{g/L}$ 、(4 160.82 \pm 2 197.45) $\mu\text{g/L}$ 、(5 250.63 \pm 2 292.16) $\mu\text{g/L}$ 、(5 291.71 \pm 2 084.86) $\mu\text{g/L}$ 、(5 139.90 \pm 2 756.57) $\mu\text{g/L}$], 其中 A 组显著低于 C 组、D 组、E 组 ($P = 0.000$)。促排卵 Gn 使用总量 E 组 [(2 094.40 \pm 759.75) IU] 显著高于 B 组、C 组、D 组 [(1 701.45 \pm 639.15) IU、(1 527.65 \pm 424.98) IU、(1 622.34 \pm 416.30) IU, $P = 0.000$]; 5 组间获卵数差异有统计学意义 (10.9 \pm 6.7、14.9 \pm 8.2、19.0 \pm 9.2、18.9 \pm 9.2、15.8 \pm 9.4, $P = 0.000$), 5 组间 M_{II} 卵数差异有统计学意义 (9.3 \pm 6.8、12.6 \pm 8.0、16.6 \pm 8.7、16.1 \pm 7.6、11.8 \pm 7.8, $P = 0.000$)。**结论** PPR 常伴发 hCG 注射日高雌激素水平和获卵数增高, 卵巢储备正常的年轻患者, 拮抗剂方案促排卵过程中晚卵泡期 P 升高可能与多卵泡发育累计效应有关。晚卵泡期血清 P 达到 1.5 ng/mL 暴露 0~2 d 的临床妊娠率差异无统计学意义, 暴露超过 4 d 的临床妊娠率显著下降, 建议取消移植。患者子宫内膜容受性不仅需参考 hCG 注射当日的 P 水平, 而且充分考虑到高 P 暴露时间长短对子宫内膜容受性的影响。

【关键词】 早发孕酮升高 (PPR); 暴露时间; 拮抗剂方案; 临床妊娠率; 体外受精 / 卵胞质内单精子注射 (IVF/ICSI)

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Correlation of the exposure time of progesterone elevation with pregnancy outcome of gonadotropin-releasing hormone antagonist cycles in women undergoing *in vitro* fertilization Yang Ting, Wang Wei,

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【Abstract】 Objective To evaluate the clinical pregnancy rate of the exposure time of progesterone (P) elevation ≥ 1.5 ng/mL from 0 d to 4 d in gonadotropin-releasing hormone antagonist (GnRH-A) cycles.

Methods In this retrospective study, the data of 364 IVF GnRH-A cycles performed in our hospital from 2015 to 2017 were analyzed. According to the day of the exposure time of P elevation ≥ 1.5 $\mu\text{g/L}$, the patients were divided into five groups (groups A–E) of the exposure time 0–4 d, the clinical outcomes were compared among the groups.

Results The clinical pregnancy rate was not significantly different between the P levels ≤ 1.5 $\mu\text{g/L}$ on hCG injection day group and >1.5 $\mu\text{g/L}$ on hCG injection day group; the clinical pregnancy rates in groups A–C were not significantly different, it was significantly lower in group E (35.29%) than in groups A–C (57.69%, 58.92%, 57.57%); the dosage of Gn used, No. of oocytes retrieved and M_{II} oocytes were significantly different among five groups ($P < 0.05$). Serum E_2 and P levels of the trigger day were significantly different among five groups ($P < 0.05$). **Conclusion** Premature P rise was related to the total FSH dosage and number of the oocytes, not only the absolute P level on the day of hCG injection as an indicator of endometrial receptivity, but also the time of the exposure time of P elevation should be considered, the clinical pregnancy rate was significantly lower with the exposure time of 4 d of P elevation 1.5 $\mu\text{g/L}$ and should be cancelled the cycle at all.

【Key words】 Premature progesterone rise (PPR); Exposure time; Gonadotropin-releasing hormone antagonist (GnRH-A) protocol; Clinical pregnancy rate; *In-vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI)

Fund program: The Innovative Entrepreneurial Project of Lanzhou City (2016-RC-51)

控制性超促排卵时未添加拮抗剂患者的临床结局分析

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【摘要】目的 分析探讨促性腺激素释放激素 (GnRH) 拮抗剂方案中不需要添加拮抗剂患者的相关因素及其促排卵结局。方法 回顾性队列研究本院生殖医学中心 2015 年 3 月—2016 年 9 月期间行 GnRH 拮抗剂方案超促排卵中未添加拮抗剂的 141 例患者 (A 组) 及添加拮抗剂的 282 例患者 (B 组) 的治疗过程中的激素变化及促排卵结局。结果 刺激周期中雌二醇 (E_2) 以及孕酮 (P) 水平差异均无统计学意义。A 组患者促性腺激素 (Gn) 第 6 日黄体生成素 (LH) 水平 $[(1.97 \pm 1.81) \text{ IU/L}]$ 显著低于 B 组患者 $[(4.08 \pm 5.37) \text{ IU/L}]$, $P < 0.001$, A 组 Gn 第 6 日直径 $< 11 \text{ mm}$ 的卵泡数 (14.7 ± 10.4) 显著高于 B 组 (12.0 ± 8.9) , $P = 0.004$; A 组 Gn 第 8 日 LH 水平 $[(2.48 \pm 1.61) \text{ IU/L}]$ 显著低于 B 组患者 $[(4.04 \pm 3.45) \text{ IU/L}]$, $P < 0.001$, Gn 第 8 日 A 组直径 $< 11 \text{ mm}$ 的卵泡数 (7.1 ± 8.9) 也显著高于 B 组 (4.9 ± 6.3) , $P = 0.008$ 。获卵数、成熟卵子数、双原核 (2PN) 受精数、优质胚胎数以及形成优质囊胚数差异均无统计学意义 ($P > 0.05$)。结论 在拮抗剂方案超促排卵过程中, 部分患者即使不添加拮抗剂也不会出现 LH 峰或提前排卵, 且这部分患者与常规添加拮抗剂患者相比能获得相似的促排卵结局。

【关键词】 拮抗剂方案; 黄体生成素 (LH) 峰; 控制性超促排卵 (COH)

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Clinical analysis on patients without gonadotrophin-releasing hormone antagonist suppression in controlled ovarian hyperstimulation

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【Abstract】 Objective To explore related factors in patients without routine pituitary suppression in gonadotrophin-releasing hormone antagonist (GnRH-A) protocol and the clinical outcomes. **Methods** A retrospective cohort study of hormone changes and clinical outcomes in patients with *in vitro* fertilization (IVF) cycles were performed at Reproductive Medicine Centre, Fuzhou General Hospital from March 2015 to September 2016, including group A (141 patients without GnRH-A) and group B (282 patients with GnRH-A). **Results** No significant differences were found in terms of the level of estradiol (E₂) or progesterone (P) between group A and group B. The level of luteinizing hormone (LH) in group A [(1.97±1.81) IU/L] was significantly lower than that in group B [(4.08±5.37) IU/L, *P*<0.001] on day 6 of gonadotrophin (Gn) stimulation, and the number of follicles which diameter < 11 mm in group A (14.7±10.4) was significantly more than that in group B on this day (12.0±8.9, *P*=0.004). Similarly, the level of LH in group A [(2.48±1.61) IU/L] was significantly lower than that in group B on day 8 of Gn stimulation [(4.04±3.45) IU/L, *P*<0.001], and the number of follicles which diameter < 11 mm in group A (7.1±8.9) was significantly more than that in group B on this day (4.9±6.3, *P*=0.008). No significant differences were found in terms of the number of oocytes retrieved, number of mature oocytes, number of 2 pronuclear (PN) fertilization, number of high-quality embryos and high-quality blastocysts. **Conclusion** Similar clinical outcomes were required in patients without routine pituitary suppression in GnRH-A protocol with no occurrence of LH in these patients.

【Key words】 Gonadotrophin-releasing hormone antagonist (GnRH-A) protocol; Luteinizing hormone (LH) surge; Controlled ovarian hyperstimulation (COH)

Fund program: Fujian Natural Science Foundation Project (2016J01589)

比较长方案与拮抗剂方案在正常反应人群中的应用

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【摘要】目的 探讨正常反应人群拮抗剂方案临床妊娠结局及影响因素。方法 检索本院生殖中心临床辅助生殖技术管理系统软件 (CCRM) 数据库, 收集 2015 年 1 月—2016 年 1 月期间进行体外受精-胚胎移植 (IVF-ET) 共 1 264 例采用激动剂长方案 (长方案组) 与拮抗剂方案 (拮抗剂组) 超促排卵患者的临床资料, 回顾性队列研究分析采用 2 种不同超促排卵方案患者的临床结局, 包括胚胎种植率、临床妊娠率、活产率及中重度卵巢过度刺激综合征 (OHSS) 发生率等; 在此基础上, 进一步分析拮抗剂方案组获得妊娠与未获得妊娠患者的临床资料, 探讨拮抗剂方案与妊娠相关的因素。**结果** ①拮抗剂组与长方案组患者的基础资料差异无统计学意义 ($P>0.05$), 胚胎种植率、临床妊娠率、活产率、中重度 OHSS 发生率组间差异均无统计学意义 ($P>0.05$); 然而拮抗剂组在促性腺激素 (Gn) 使用总量 [(1 483.84±453.79) IU]、刺激时间 [(9.4±1.5) d]、hCG 注射日雌激素水平 [(15 321.29±7 272.67) pmol/L] 显著低于长方案组 [(1 616.10±490.04) IU、(9.7±1.6) d、(17 293.82±7 690.00) pmol/L, $P<0.001$], hCG 注射日 LH 水平 [(4.28±2.28) IU/L] 及孕激素水平 [(3.16±2.64) pmol/L] 显著高于长方案组 [(3.78±1.74) IU/L, (2.51±1.33) pmol/L, $P<0.001$]; ②比较拮抗剂组新鲜周期移植妊娠与未获得妊娠患者临床资料, 妊娠组 hCG 注射日 LH 水平 [(3.49±2.47) IU/L] 显著高于未妊娠组 [(2.80±1.82) IU/L, $P<0.05$], 进一步根据 hCG 注射日 LH 水平分为 LH<2 IU/L 组及 LH≥2 IU/L 两组, 显示 LH≥2 IU/L 组的种植率 (47.78%)、临床妊娠率 (63.72%) 及活产率 (58.41%) 显著高于 LH<2 IU/L 组 (31.51%、45.45%、36.36%, $P<0.05$), 但 Gn 的用药时间 [(9.1±1.4) d]、拮抗剂的用量 [(1.17±0.23) mg] 及用药时间 [(4.7±0.9) d]、获卵数 [(7.5±3.2) d] 显著少于 LH<2 IU/L 组 [(9.7±1.5) d、(1.26±0.31) mg、(5.1±1.2) d、(8.6±3.0) d, $P<0.05$]。**结论** 正常反应人群, 较长方案刺激排卵, 拮抗剂方案更加温和、友好、高效, 有效降低患者 Gn 用药及刺激时间, 拮抗剂可以达到与激动剂类似的种植率、妊娠率及活产率, 合理控制 hCG 注射日 LH 水平可能有利于拮抗剂方案新鲜胚胎移植临床结局。

【关键词】长方案; 拮抗剂方案; 正常反应人群; 体外受精-胚胎移植 (IVF-ET); 黄体生成素

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Comparison of the agonist protocol and antagonist protocol in normal responders Li Xuan, Liu Jiayin,

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【Abstract】 Objective To investigate the clinical pregnancy outcome and influencing factor of the antagonist protocol in normal responders. **Methods** From January 2015 to January 2016, 1 264 cases of good-prognosis patients with GnRH agonist long protocol and antagonist protocol in *in-vitro* fertilization and embryo transfer (IVF-ET) were collected using the clinical assisted reproductive technologies management system software (CCRM) database of the Reproductive Medicine Center of Jiangsu Province Hospital. Patients were divided into agonist long protocol and antagonist protocol groups. The clinical outcomes of the two groups were analyzed retrospectively, including the implantation rate, clinical pregnancy rate, live birth rate and the incidence of severe ovary hyperstimulation syndrome (OHSS); on this basis, to explore the factors associated with pregnancy, clinical data of pregnant and non pregnant patients in the antagonist group were further analyzed. **Results** 1) Comparing antagonist group and agonist long protocol group, the based data did not exhibit remarkable difference, and there was no significant difference in implantation rate, clinical pregnancy rate, the live birth rate and severe hyperstimulation rate ($P>0.05$). However, the dosage of gonatrophin (Gn) used [$(1\ 483.84\pm 453.79)$ IU], days of stimulation [(9.4 ± 1.5) d] and estrogen (E_2) level [$(15\ 321.29\pm 7\ 272.67)$ pmol/L] on the day of hCG injection in antagonist group were significantly less than agonist long protocol group [$(1\ 616.10\pm 490.04)$ IU, (9.7 ± 1.6) d, $(17\ 293.82\pm 7\ 690.00)$ pmol/L, $P<0.001$], luteinizing hormone (LH)[(4.28 ± 2.28) IU/L] and progesterone (P) levels [(3.16 ± 2.64) pmol/L] on the day of hCG injection were significantly higher compared with the agonist long protocol [(3.78 ± 1.74) IU/L, (2.51 ± 1.33) pmol/L, $P<0.05$]. 2) Comparing the clinical data of the pregnant patients and non pregnant patients with fresh transplantation cycle in the antagonist group, LH level [(3.49 ± 2.47) IU/L] on the day of hCG injection in the pregnant group was significantly higher than that in non pregnant group [(2.80 ± 1.82) IU/L, $P<0.05$]. Patients were further divided into LH <2 IU/L group and LH ≥ 2 IU/L group, according to LH level on the day of hCG injection, it showed that the implantation rate (47.78%), clinical pregnancy rate (63.72%) and live-birth rate (58.41%) in LH ≥ 2 IU/L group increased significantly (31.51%, 45.45%, 36.36%, $P<0.05$), but the days of Gn used [(9.1 ± 1.4) d], the dosage [(1.17 ± 0.23) mg] and duration [(4.6 ± 0.9) d] of antagonist and retrieved oocytes (7.5 ± 3.2) significantly reduced compared with LH <2 IU/L group [(9.7 ± 1.5) d, (1.26 ± 0.31) mg, (5.0 ± 1.2) d, (8.6 ± 3.0) d, $P<0.05$]. **Conclusion** In normal responders, comparing with long protocol to stimulate ovulation, antagonist protocol is more moderate, friendly and efficient, reducing the dose and stimulation days of Gn effectively. Antagonist can also achieve similar implantation rate, pregnancy rate and live birth rate compared with agonist protocol, a reasonable control of LH level on the day of hCG injection may have a beneficial effect on the clinical outcome in fresh embryo transplantation cycle with antagonists protocol.

【Key words】 Agonist long protocol; Antagonist protocol; Normal ovary responders; *In-vitro* fertilization and embryo transfer (IVF-ET); Luteinizing hormone (LH)

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多囊卵巢综合征患者体外受精中促性腺激素释放激素拮抗剂方案安全性分析

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【摘要】 目的 探讨多囊卵巢综合征 (PCOS) 患者应用促性腺激素释放激素拮抗剂 (GnRH-A) 方案的可行性、安全性及预防中重度卵巢过度刺激综合征 (OHSS) 的方法。方法 回顾性病例对照研究使用 GnRH-A 方案 PCOS 患者的 304 个取卵周期的临床资料。取卵后评估有无 OHSS 高风险, 无 OHSS 风险者纳入 A 组, 有 OHSS 高风险者纳入 B 组。比较患者的基本特征、促性腺激素 (Gn) 启动剂量及使用总量、Gn 使用时间、获卵数、优质胚胎率、妊娠率、OHSS 发生率等。结果 PCOS 患者的年龄、体质量指数 (BMI)、平均不孕年限组间比较差异均无统计学意义 ($P>0.05$) 的情况下, OHSS 高风险与基础高黄体生成素 (LH)、高 LH/ 卵泡刺激素 (FSH)、高睾酮 (T) 水平有关, 组间比较差异均有统计学意义 (P 均 =0.000)。A 组进行新鲜移植共 197 个周期, 临床妊娠率为 58.89%(106/197)。B 组行全部胚胎冷冻 93 个周期, 首次冻融胚胎移植的临床妊娠率为 81.81%(72/88)。分析可见, 卵巢的反应性与启动日血清 LH/FSH 比值有相关性, LH/FSH 比值越高, 其促排卵的反应性就越好。总体中重度 OHSS 发生率为 6.91%(21/304), A 组的中重度 OHSS 发生主要是迟发型, 与妊娠及多胎妊娠相关, B 组的中重度 OHSS 发生主要是早发型。结论 GnRH-A 方案应用于 PCOS 患者, 可以通过减少启动剂量, 新鲜周期移植前评估 OHSS 风险; 如有 OHSS 风险者全部胚胎冷冻, 期待冻融周期移植, 可获得安全有效的结局。

【关键词】 促性腺激素释放激素拮抗剂 (GnRH-A); 多囊卵巢综合征 (PCOS); 体外受精 (IVF); 卵巢过度刺激综合征 (OHSS)

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Security of gonadotropin-releasing hormone antagonist protocol in patients with polycystic ovary syndrome undergoing *in vitro* fertilization Zhou Hong, Shu Jinhui, Gan Xianyou, Luo Zhaowen, Li Shuang

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【Abstract】 Objective To explore the feasibility and security of the gonadotropin-releasing hormone antagonist (GnRH-A) protocol and the prevention methods of the moderate-severe ovarian hyperstimulation syndrome (OHSS) in polycystic ovary syndrome (PCOS) patients. **Methods** The clinical data of 304 oocyte retrieval cycles undergoing GnRH-A protocol in PCOS patients were retrospectively analyzed. According to whether high risk of OHSS after oocyte retrieval, 304 oocyte retrieval cycles were divided into low risk of OHSS group (group A, 197 cycles) and high risk of OHSS group (group B, 93 cycles). We analyzed the basic characteristic, the initial and total dosage of gonadotropin (Gn) used, the duration of Gn used, the number of retrieved oocytes, rate of high-quality embryos, clinical pregnancy rate, the incidence of OHSS, etc. **Results** The high risk of OHSS was related to high basic luteinizing hormone (LH), high ratio of LH and follicle-stimulating hormone (LH/FSH) and high level of testosterone (T), when there were no statistical significances in ages, basic mass index (BMI), and the duration of infertility among patients with PCOS ($P>0.05$). Group A was treated with fresh embryo transfer, and the clinical pregnancy rate was 58.89% (106/197). Group B was treated with all embryos vitrified, and the clinical pregnancy rate of first frozen-thawed embryo transfer cycle was 81.81% (72/88). Comparing the two groups, there was a positive relation between the ovarian reactivity and LH/FSH on the initial day of Gn used. Overall, the accident rate of moderate-severe OHSS was 6.91% (21/304). The moderate-severe OHSS in group A was mainly delayed type, which was related to singleton or multiple pregnancy. While the moderate-severe OHSS in group B was mainly early-onset type. **Conclusion** Reducing the initial dose of Gn used, assessing the properly occurrence rate of OHSS before fresh embryo transference, GnRH-A protocol is suitable and secure for PCOS population. Patients with high risk of OHSS should select all embryos vitrified, and expect frozen-thawed embryo transfer.

【Key words】 Gonadotropin-releasing hormone antagonist (GnRH-A); Polycystic ovary syndrome (PCOS); *In vitro* fertilization (IVF); Ovarian hyperstimulation syndrome (OHSS)

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拮抗剂方案在卵巢储备功能低下患者中的临床应用及费效比

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【摘要】目的 探讨拮抗剂方案在卵巢储备功能低下 (DOR) 患者中的临床应用和费效比。方法 回顾性病例对照研究分析 2014 年 10 月—2016 年 10 月期间在我院接受体外受精 - 胚胎移植 (IVF-ET) 治疗的 DOR 患者, 按年龄分层随机抽取 DOR 患者 302 例, 将其分为 <35 岁组 (153 例) 及 ≥ 35 岁组 (149 例), 再将 <35 岁组分为 3 小组, 其中拮抗剂方案 62 例 (A 组), 超长方案 43 例 (B 组), 微刺激方案 48 例 (C 组); ≥ 35 岁组也分为 3 小组, 拮抗剂方案 45 例 (D 组), 微刺激方案 48 例 (E 组), 拮抗剂联合温和刺激方案组 56 例 (F 组)。比较不同年龄段 DOR 患者拮抗剂方案与其它控制性超促排卵 (COH) 方案的临床结局及费效比。**结果** 在 <35 岁的 DOR 患者中, 新鲜胚胎移植临床妊娠率 B 组 (41.93%) 高于 A 组 (33.33%) 及 C 组 (25.00%) ($P < 0.05$); 累积临床妊娠率和累积活产率 A 组 (66.13%, 56.45%) 优于 B 组 (51.17%, 46.51%) 及 C 组 (43.75%, 39.58%) ($P < 0.05$); 每一启动周期总费用以 C 组 [(23 563 ± 2 133) 元] 最低 ($P < 0.05$), 但每获一成熟卵子所需费用、每获一枚优质胚胎所需费用及每获一活产所需费用 A 组较 B 组及 C 组低 ($P < 0.05$); ≥ 35 岁 DOR 患者中, 累积临床妊娠率、累积活产率方面, E 组 (33.33%, 25.00%) 低于 D 组 (44.44%, 35.56%) 及 F 组 (46.42%, 39.29%) ($P < 0.05$), D 组与 F 组相近 ($P > 0.05$); 每一启动周期总费用以 E 组 [(19 311 ± 2 238) 元] 最低, 但每获一成熟卵子所需费用、每获一枚优质胚胎所需费用及每获一活产所需费用 F 组最低 ($P < 0.05$)。**结论** 在 <35 岁的 DOR 患者中, 从临床结局及费效比方面综合考虑, 拮抗剂方案是比较理想的 COH 方案; 在 ≥ 35 岁患者中, 拮抗剂联合温和刺激方案可以获得理想的临床结局和费效比。

【关键词】GnRH 拮抗剂 (GnRH-A) 方案; 拮抗剂联合温和刺激方案; 费效比; 卵巢储备功能低下 (DOR)

Clinical application and economic analysis of gonadotropin-releasing hormone antagonist protocol in patients with decreased ovarian reserve Zhang Yan, Bao Junhua, Yao Hairong, Li Ping, Liu Li

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【Abstract】 Objective To investigate the clinical application and cost effectiveness of gonadotropin-releasing hormone antagonist (GnRH-A) protocol in the patients with decreased ovarian reserve (DOR). **Methods** A retrospective analysis of clinical outcomes and costs was performed in 302 infertile patients with DOR after *in vitro* fertilization-embryo transfer (IVF-ET) in our hospital from October 2014 to October 2016. According to different ages, patients were divided into <35 years old group (153 cases) and ≥ 35 years old group (149 cases). And according to the different protocol, <35 years old group was divided into 3 groups, which included 62 cycles of GnRH-A protocol (group A), 43 cycles of ultra-long protocol (group B), 48 cycles of minimal ovarian stimulation protocol (group C), and ≥ 35 years old group was divided into 3 groups, which included 45 cycles of GnRH-A protocol (group D), 48 cycles of minimal ovarian stimulation protocol (group E), 56 cycles of mild stimulation protocol with GnRH-A (group F), clinical outcomes and the cost-effective ratio were compared between GnRH-A protocol and other protocols. **Results** In the patients <35 years old with DOR, the clinical pregnancy rate of fresh embryo transplantation in group B was the highest than that in the other two groups ($P<0.05$), the cumulative pregnancy rate and the cumulative live birth rate were the highest in group A (66.13%, 56.45%) than in groups B (51.17%, 46.51%) and C (43.75%, 39.58%) ($P<0.05$). Total cost per start-up cycle was the lowest in group C than that in the other two groups ($P<0.05$), but other economic indicators including the each mature eggs cost and the each good embryo cost and the each live birth cost were the lowest in group A ($P<0.05$). In the patients ≥ 35 years of DOR, the cumulative pregnancy rate and the cumulative live the yield were the lowest in group E (33.33%, 25.00%) than in group D (44.44%, 35.56%) and group F (46.42%, 39.29%) ($P<0.05$), while those indicators in the group D were similar to group F ($P>0.05$). These economic indicators including the each mature eggs cost, the each good embryo cost and the each live birth cost were the lowest in group F ($P<0.05$). **Conclusion** The GnRH-A protocol was an ideal solution in less than 35 years patients with DOR; the mild stimulation protocol with GnRH-A was better than the other protocols in more than 35 years patients with DOR.

【Key words】 Gonadotropin-releasing hormone antagonist (GnRH-A) protocol; Mild stimulation protocol with GnRH antagonist; Cost efficiency ratio; Decreased ovarian reserve (DOR)

促性腺激素释放激素拮抗剂方案控制性促排卵过程中雌激素水平下降

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【摘要】 血清雌激素 (E_2) 水平是评估控制性促排卵 (COS) 中卵泡发育及对促性腺激素 (Gn) 反应的重要指标。 E_2 水平的下降能否预测妊娠结局, 目前尚无定论。本文分析了 1 例促性腺激素释放激素拮抗剂 (GnRH-A) 促排卵方案中出现 E_2 下降的案例, 患者的获卵率明显下降, 受精率和卵裂率正常, 仅获得 1 枚优质胚胎, 未成功妊娠, 因此 GnRH-A 方案中 E_2 下降, 可能会导致卵母细胞回收率下降。

【关键词】 拮抗剂方案; 雌二醇下降; 临床结局

· 个案报道 ·

Case analysis of drop in estradiol during gonadotropin-releasing hormone antagonists protocol *in vitro* fertilization Li Caihua, Wu Huan, Zhou Ping, Cao Yunxia

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【Abstract】 Serum estradiol (E_2) levels is an important marker for evaluating follicular development and response to gonadotropins in controlled ovarian stimulation (COS). Whether the decline in E_2 levels can predict outcomes still remains inconclusive. The study analyzed a case of drop in estradiol in the gonadotropin releasing hormone antagonist (GnRH-A) protocol. In the case, the patient had decreasing oocyte rates significantly, normal fertilization rates and normal cleavage rates, finally an excellent embryo but not pregnancy. So the decrease of E_2 in the GnRH-A protocol may lead to a decrease in the recovery rate of oocyte.

【Key words】 Antagonist protocol; Estradiol (E_2) decline; Clinical outcome

拮抗剂方案在高危多囊卵巢综合征患者体外受精超促排卵中的应用及病例分享——附 1 例成功病例分析

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【摘要】 **目的** 探讨高危多囊卵巢综合征 (PCOS) 患者体外受精 (IVF) 超促排卵的方法, 应用拮抗剂方案的优势及临床结局。**方法** 1 例卵巢最大径为 46 mm, 单侧卵巢体积 >20 mL 的 PCOS 患者应用拮抗剂方案行超促排卵, 并应用拮抗剂方案达必佳和人绒毛膜促性腺激素 (hCG) 进行双扳机 (trigger), 成功妊娠且无重度卵巢过度刺激综合征 (OHSS) 发生。**结果** 该患者解冻移植后成功受孕, 且无重度 OHSS 发生。**结论** 对于行 IVF 的 PCOS 患者, 可选用拮抗剂方案, 应用双 trigger 及适当选择全部胚胎冷冻, 此法灵活方便。

【关键词】 多囊卵巢综合征 (PCOS); 拮抗剂; 体外受精 (IVF)

· 个案报道 ·

The using and case sharing of gonadotropin-releasing hormone antagonist protocol in infertile patients with polycystic ovary syndrome of *in vitro* fertilization cycle—one successful case Wang Haiyan,

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【Abstract】 Objective To explore the way of gonadotropin-releasing hormone antagonist (GnRH-A) protocol in infertile patients with polycystic ovary syndrome (PCOS) *in vitro* fertilization (IVF) cycle. **Methods** An infertile women with PCOS whose the biggest diament of ovary was 46 mm and the volume was 20 mL underwent IVF, using GnRH-A protocol and double trigger, and was pregnant successfully, and no OHSS occurred. **Results** Pregnancy was in the thaw transfer cycle and no serious OHSS occurred. **Conclusion** The patients with PCOS in IVF cycle can use GnRH-A protocol and double trigger which was flexible.

【Key words】 Polycystic ovary syndrome (PCOS); Antagonist; *In vitro* fertilization (IVF)

拮抗剂方案在卵巢高反应患者中的安全性探讨

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【摘要】 目的 探讨了接受体外受精 - 胚胎移植 (IVF-ET) 技术的卵巢高反应患者使用拮抗剂方案的安全性。方法 共分析 3 例卵巢高反应者, 均使用拮抗剂方案行超促排卵, 观察患者是否发生中 - 重度卵巢过度刺激综合征 (OHSS)。结果 3 例患者中有 2 例未发生 OHSS, 1 例发生重度 OHSS。结论 在卵巢高反应患者中, 应用拮抗剂方案并不能完全避免 OHSS 的发生。为了有效避免中 - 重度 OHSS 的发生, 应该制定合适的 Gn 起始剂量, 选择恰当的诱发排卵的药物和剂量。

【关键词】 卵巢高反应; 拮抗剂方案; 卵巢过度刺激综合征 (OHSS)

Safety of gonadotropin-releasing hormone antagonist protocol absolutely for high ovarian responders

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【Abstract】 Objective To evaluate the safety of gonadotropin-releasing hormone (GnRH) antagonist protocol for high ovarian responders during *in vitro* fertilization-embryo transfer (IVF-ET). **Methods** GnRH antagonist protocol was used for three high ovarian responders. The incidence of moderate-severe ovarian hyperstimulation syndrome (OHSS) was observed. **Results** One case of moderate OHSS occurred in three patients. **Conclusion** Utilization of GnRH antagonist protocol can not absolutely prevent the occurrence of OHSS. Suitable starting doses of gonadotropins and appropriate trigger drugs should be used for avoiding the occurrence of moderate-severe OHSS.

【Key words】 High ovarian responders; gonadotropin-releasing hormone (GnRH) antagonist protocol; Ovarian hyperstimulation syndrome (OHSS)

控制性超促排卵中出现早发黄体生成素峰后加倍使用拮抗剂的效果——1 例报道

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【摘要】目的 探讨在控制性超促排卵中早发黄体生成素 (LH) 峰对卵泡发育及胚胎质量的影响。

方法 分析同一患者 2 个促排卵周期的获卵数及胚胎质量。**结果** 促排卵过程中出现的早发 LH 峰在加倍使用拮抗剂后对卵泡发育及胚胎质量未见明显影响。**结论** 单一性早发 LH 峰出现时给予加量拮抗剂控制 LH 水平下降至安全范围之内, 可挽救该助孕周期, 获得较优质的胚胎。

【关键词】 拮抗剂方案; 早发黄体生成素 (LH) 峰; 胚胎质量

· 个案报道 ·

Effect of double use of gonadotropin-releasing hormone antagonist after premature luteinizing hormone surge during controlled ovarian hyperstimulation cycles *Li Jiachen, Zou Hongyan*

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【Abstract】 Objective To discuss the impact of premature luteinizing hormone (LH) surge on the follicle development and embryo quality during controlled ovarian hyperstimulation (COH). **Methods** The number of retrieved oocytes and embryo quality in two different COH cycles on the same patient were analyzed. **Results** The impact of premature LH surge during COH cycles was not significantly different on the follicle development and embryo quality after the double-dose gonadotropin-releasing hormone (GnRH) antagonist administration. **Conclusion** A double-dose of GnRH-antagonist administration could decrease the level of single premature LH surge to safe range, which might rescue this COH cycle and get high-quality embryos.

【Key words】 Gonadotropin-releasing hormone (GnRH) antagonist protocol; Premature luteinizing hormone (LH) surge; Embryo quality

拮抗剂方案中出现早发性黄体生成素峰的处理—— 病案报道 3 例

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【摘要】 **目的** 探讨拮抗剂方案促排卵过程中出现早发黄体生成素 (LH) 峰的患者实施紧急取卵是否有效。**方法** 3 例患者均采用拮抗剂促排卵方案, 促排卵过程中密切监测卵泡发育情况及血激素水平变化, 当卵泡期监测到早发性 LH 峰或扳机次日雌激素水平快速下降时, 根据具体情况安排提前取卵。**结果** 3 例患者均能取到成熟卵子, 并获得优质胚胎。**结论** 拮抗剂方案也可能出现“LH 逃逸”现象, 需在促排卵过程中密切监测血清 LH 水平, 当出现早发性 LH 峰时, “抢收”可增加体外受精-胚胎移植 (IVF-ET) 的获卵率, 不失为一种有效的处理措施。

【关键词】 早发性黄体生成素 (LH) 峰; 拮抗剂方案; 提前取卵

· 个案报道 ·

The treatment of premature luteinizing hormone rise in the gonadotrophin-releasing hormone antagonist protocol —3 cases report

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【Abstract】 Objective To determine whether emergency oocyte retrieval strategy (rush in the harvest) is effective when a premature rise in the level of luteinizing hormone (LH) in gonadotrophin-releasing hormone antagonists (GnRH-A) protocol *in vitro* fertilization (IVF) cycles. **Methods** Three cases were undertaken GnRH-A protocol for ovarian stimulation protocol, during the the process of ovarian stimulation, the development of follicles and the changes of blood hormone levels were monitored closely, when premature LH rising during the follicular phase and estrogen levels decreasing were found in the next day of hCG injection, emergency oocyte retrieval strategy was carried out. **Result** Mature eggs and high-quality embryos were obtained from 3 patients. **Conclusion** Premature LH rise is also present in GnRH-A protocol, when the premature LH peak is monitored, “rush in the harvest” can increase the oocytes retrieved rate of IVF-embryo transfer (ET), so it is an effective treatment measure.

【Key words】 Premature luteinizing hormone (LH) rise; Gonadotrophin-releasing hormone antagonist (GnRH-A) protocol; Emergency oocyte retrieval

宫腔粘连的治疗策略及进展

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【摘要】 随着不孕症发病率的增加, 宫腔粘连作为继发性不孕的重要原因之一, 在生殖领域逐渐引起人们注意。宫腔粘连常见的临床表现是月经量减少、不孕、周期性腹痛等。其治疗目的是恢复宫腔解剖学形态及宫腔容积, 治疗相关症状, 预防再粘连形成, 促进子宫内膜再生修复, 恢复生育能力。宫腔镜是诊断和治疗宫腔粘连的金标准, 术后尽管有多种预防再粘连的方法, 但其粘连复发率仍较高, 妊娠率仍不理想。现将其研究近况作一综述。

【关键词】 宫腔粘连; 宫腔镜; 治疗; 预防再粘连

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【Abstract】 With the increase in the incidence of infertility, intrauterine adhesions as an important cause of secondary infertility, in the field of reproduction gradually attracted attention. Intrauterine adhesions common clinical manifestations of menstrual reduction, infertility, cyclical abdominal pain, etc. The purpose of treatment is to restore intrauterine anatomical morphology and uterine volume, treatment-related symptoms, prevention of re-adhesion formation, promote endometrial regeneration repair and restore fertility. Hysteroscopy is the gold standard for diagnosis and treatment of intrauterine adhesions, although there are a variety of ways to prevent re-adhesion, but the recurrence rate is still high, pregnancy rate is still not ideal. Now its research status to do a review.

【Key words】 Intrauterine adhesions; Hysteroscopy; Treatment; Prevent re-adhesion

热休克蛋白 70 在不孕不育症中的研究进展

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【摘要】 不孕不育症在近十几年发病率呈上升趋势, 其病因复杂多样, 包括女性因素、男性因素和男女双方因素。热休克蛋白 (HSP)70 是 HSP 家族中最保守、最具特征性、研究最多的一类, 具有参与免疫反应、抗细胞凋亡、分子伴侣、保护细胞免受应激损害等功能。研究表明 HSP70 与导致女性不孕和男性不育相关疾病有密切联系, 本文就 HSP70 与不孕不育相关病因作一综述。

【关键词】 HSP70; 不孕不育; 多囊卵巢综合征 (PCOS); 子宫内膜异位症 (EMS); 卵巢早衰 (POF); 男性不育; 复发性流产

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· 综述 ·

Research progress on the role of heat shock protein 70 in infertility *Hu Xue, Mu Yang, Wu Gengxiang, Yang Jing*
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【Abstract】 The incidence of infertility is on rise in the past decade, and its etiology is complex and diverse, including female factors, male factors and both factors. Heat shock protein 70 (HSP70) is the most conservative and most characteristic of HSP family. It is involved in immune response, anti-apoptosis, molecular chaperone, protect cells from stress and other functions. Studies show that HSP70 is closely related to these diseases caused infertility. The article reviews the relationship between HSP70 and infertility.

【Key words】 Heat shock protein 70 (HSP70); Infertility; Poly cystic ovary syndrone (PCOS); Endometriosis (EMS); Premature ovarian failure (POF); Male infertility; Recurrent spontaneous abortion (RSA)

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醋酸氯地孕酮的临床应用进展

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【摘要】 作为 17- α - 羟孕酮衍生物, 醋酸氯地孕酮 (chlormadinone acetate, CMA) 具有较强的孕激素活性、抗雌激素活性及较弱的糖皮质激素活性, 无雄激素活性及抗盐皮质激素活性。其与炔雌醇 (ethinylestradiol, EE) 组成的复方口服避孕药在欧洲、拉美等国家广泛应用。除主要用于避孕外, CMA 还兼具治疗痛经、雄激素过剩相关疾病 (痤疮、脂溢性皮炎、女性型脱发、多毛症、良性前列腺增生) 及改善经前或经期不适等非避孕益处。本文就 CMA 的上述临床应用进展作一综述, 为其今后在临床上发挥更充分而合理的应用提供依据。

【关键词】 醋酸氯地孕酮 (CMA); 避孕; 痛经; 雄激素过剩; 经前或经期不适

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Progress on clinical applications of chlormadinone acetate Lin Na, Huang Ting, Zeng Jia

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【Abstract】 As a 17α -Hydroxyprogesterone derivative, chlormadinone acetate (CMA) exerts a potent progestagenic effect, anti-estrogen effect and a mild glucosteroidal effect, showing noandrogenic effect and anti-mineralocorticoid effect. It is widely used for oral contraception combined with ethinylestradiol (EE) in Europe, Latin America and other countries. Except for the main use of contraception, it also has many non-contraceptive benefits for dysmenorrhea, androgen excess related diseases (such as acne, seborrheic dermatitis, female hair loss, hirsutism and benign prostatic hyperplasia) and improvement of premenstrual or menstrual discomfort. This article gives a review on the above clinical applications of CMA, so as to provide the evidence for its further and reasonable application in clinical treatment.

【Key words】 Chlormadinone acetate(CMA); Contraception; Dysmenorrhea; Androgen excess; Premenstrual or menstrual discomfort

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