

doi: 10.13241/j.cnki.pmb.2024.12.028

# 早卵泡期长效方案联合全程重组黄体生成素 对卵巢高反应人群排卵和妊娠结局的影响\*

余晓燕<sup>1</sup> 杨惠林<sup>1</sup> 李燕子<sup>1</sup> 马英兰<sup>1</sup> 王春梅<sup>2</sup> 李琴<sup>3</sup>

(1 青海红十字医院生殖中心 青海 西宁 810000; 2 青海红十字医院妇科 青海 西宁 810000;

3 青海大学附属医院妇产科 青海 西宁 810000)

**摘要 目的:**探讨早卵泡期长效方案联合重组黄体生成素(r-LH)对卵巢高反应人群排卵和妊娠结局的影响。**方法:**选入 2019 年 1 月~2023 年 3 月在我院行早卵泡期长效方案促排卵的卵巢高反应患者 150 例,根据是否添加 r-LH 分为对照组(未添加 r-LH, n=75)和观察组(添加 r-LH, n=75)。比较两组的促排卵相关指标和妊娠结局。**结果:**观察组 Gn 天数、Gn 总量、HCG 日血清 LH 水平、优质胚胎率均显著高于对照组,获卵数显著少于对照组( $P<0.05$ )。两组降调天数、Gn 启动量以及 HCG 日  $E_2$ 、P 水平和子宫内膜厚度、临床妊娠率、活产率、流产率比较无差异( $P>0.05$ )。**结论:**卵巢高反应患者行早卵泡期长效方案促排卵时,添加 r-LH 可显著增加体内 LH 水平,提高优质卵泡率,对妊娠结局具有一定改善作用。

**关键词:**卵巢高反应;长效方案;早卵泡期;重组黄体生成素;排卵;妊娠结局

**中图分类号:**R711.6 **文献标识码:**A **文章编号:**1673-6273(2024)12-2341-05

## The Effect of Early Follicular Phase Long-acting Protocol Combined with Whole Process Recombinant Luteinizing Hormone on Ovulation and Pregnancy Outcomes of High Ovarian Response\*

YU Xiao-yan<sup>1</sup>, YANG Hui-lin<sup>1</sup>, LI Yan-zi<sup>1</sup>, MA Ying-lan<sup>1</sup>, WANG Chun-mei<sup>2</sup>, LI Qin<sup>3</sup>

(1 Reproductive Center, Qinghai Red Cross Hospital, Xining, Qinghai, 810000, China;

2 Gynecology Department, Qinghai Red Cross Hospital, Xining, Qinghai, 810000, China;

3 Department of Obstetrics and Gynecology, Qinghai University Affiliated Hospital, Xining, Qinghai, 810000, China)

**ABSTRACT Objective:** To explore the effect of early follicular phase long-acting protocol combined with whole process recombinant luteinizing hormone (r-LH) on ovulation and pregnancy outcomes of high ovarian response. **Methods:** A total of 150 cases high ovarian response patients who underwent long-term ovulation induction in our hospital from January 2021 to March 2023 were divided into Matched group (r-LH was added, n=75) and observation group (r-LH was added, n=75 according to r-LH). Ovulation-related indicators and pregnancy outcomes were compared between the two groups. **Results:** Gn days, total Gn days, HCG daily serum LH level, and high-quality embryo rate were higher than that of the observation group, and the number of eggs obtained was less than that of the Matched group ( $P<0.05$ ). There was no difference between the days of reduction, Gn initiation,  $E_2$ , P level, and endometrial thickness, clinical pregnancy rate, live birth rate, and abortion rate between the two groups ( $P>0.05$ ). **Conclusion:** The addition of r-LH significantly increased LH levels in vivo and improved the rate of high-quality follicles when ovulation was promoted in patients with ovarian hyperresponsiveness undergoing the early follicular phase of the long-acting, long-lasting regimen, which had an improved effect on pregnancy outcome.

**Key words:** High ovarian response; Long term rectangular plan; Early follicular phase; Recombinant luteinizing hormone; Ovulation; Pregnancy outcome

**Chinese Library Classification(CLC):** R711.6 **Document code:** A

**Article ID:** 1673-6273(2024)12-2341-05

### 前言

卵巢高反应人群是指在控制性超排卵(COH)过程中对外源性的促性腺激素(Gn)反应异常敏感的人群<sup>[1,2]</sup>。在临床研究中

常将 HCG 注射日  $E_2>3000$  pg/mL 或者获卵数 $>15$  个的患者定义为卵巢高反应人群<sup>[3]</sup>。研究发现,卵巢高反应是中重度卵巢过度刺激综合征发生的独立危险因素,且卵巢高反应患者存在明显的多卵泡发育,性激素水平极显著高于正常人,造成卵母

\* 基金项目:青海省卫生健康委员会指导性计划项目(2020-wjzdx-62)

作者简介:余晓燕(1982-),女,本科,副主任医师,研究方向:生殖中心相关内容,E-mail:AZ311599@163.com

(收稿日期:2023-10-21 接受日期:2023-11-17)

细胞和胚胎质量差,子宫内膜容受性降低,不利于妊娠和助孕<sup>[45]</sup>。辅助生殖技术(ART)在近年来应用越加广泛,其中 COH 是 ART 的关键环节,合适的个体化 COH 方案有助于提高患者临床妊娠率,减少卵巢过度刺激综合征的发生<sup>[6,7]</sup>。早卵泡期长效方案因卵泡发育同步性高、增加获卵数和胚胎数等优点<sup>[8,9]</sup>。促性腺激素释放激素拮抗剂(GnRH-a)方案是近年来应用较多的促排卵技术,具有促排卵时间短、Gn 用量少、卵巢过度刺激综合征发生率低等特点,在卵巢高反应人群中推荐应用<sup>[10]</sup>。但也有部分患者在降调节后发现 LH 被过度抑制进而造成临床妊娠结局不理想,因此有学者建议添加 LH 来能改善妊娠结局,但目前仍存在争议<sup>[11]</sup>。鉴于此,本文就早卵泡期长效方案联合重组黄体生成素(r-LH)对卵巢高反应患者排卵和妊娠结局的影响进行了探讨,为临床工作提供指导,现报告如下。

## 1 资料和方法

表 1 两组一般资料比较

Table 1 Comparison of General Information between Two Groups

Category	Matched group(n=75)	Observation group(n=75)	t/ $\chi^2$ -value	P-value
Age(years)	31.95± 2.47	32.16± 2.53	0.514	0.608
Infertility years	4.52± 1.91	4.48± 1.83	0.131	0.896
BMI(kg/m <sup>2</sup> )	22.03± 2.44	22.16± 2.39	0.330	0.742
Basic FSH(U/L)	6.05± 1.65	6.11± 1.62	0.225	0.823
Basic LH(U/L)	6.31± 2.01	6.47± 1.94	0.496	0.621
AMH( $\mu$ g/L)	5.98± 1.35	5.92± 1.41	0.266	0.790
AFC	26.05± 6.07	26.03± 5.35	0.021	0.983
Infertility type	Primary	22(29.33)	0.032	0.859
	Secondary	53(70.67)		

### 1.2 治疗方法

采用早卵泡期长效方案促排卵:时间点为:月经来潮 2~5 d,且非妊娠,给予皮下注射 3.75 mg 醋酸曲普瑞林(Ipsen Pharma,国药准字 HJ20140298,3.75 mg/支)进行垂体降调节,待卵泡直径<5 mm,血清 FSH 和 LH 均<5 U/L, E<sub>2</sub><50 pg/mL,子宫内膜厚度≤5 mm 时启动促排卵药物治疗,用药 4~5 d 时检查卵泡生长和血清性激素水平调整促排卵药物剂量。之后每 2~3 d 检测一次卵泡发育和血清性激素水平,卵泡发育至 17 mm 以上时调整为每日监测至 HCG 注射日。在此过程中,对照组不添加 r-LH, 观察组自启动日开始给予患者皮下注射重组人促黄体激素  $\alpha$ (Merck Europe B.V., 国药准字 SJ20181004, 75 IU/瓶), 75 IU/d, 在直径≥16 mm 的优势卵泡 >2/3 时停药并在当晚注射 250  $\mu$ g 重组 HCG(注射用重组人绒促性素,艾泽,默克雪兰诺,瑞士)+ HCG 2000IU(人绒促性素,丽申宝,珠海丽珠制药)激发排卵,注射后 36 h 后在经阴道超声引导下取卵,取出的卵母细胞进行体外受精或胞浆内单精子注射。若 16~18 h 后出现双原核或两个极体则为正常受精,在 48~72 h 选择优质胚胎移植,同时给予黄体支持(口服地屈孕酮 20 mg/日,同时黄体酮 60 mg/日肌肉注射)至移植后 14 d。通过外周血 HCG 测定

### 1.1 一般资料

本研究为回顾性分析,选择 2019 年 1 月至 2023 年 3 月行早卵泡期长效方案排卵以及 IVT/ICSI 助孕治疗的 150 例卵巢高反应患者的临床资料,其中 75 例患者在早卵泡期长效方案排卵中添加 r-LH 纳入观察组,余 75 例不添加者纳入对照组。两组一般资料见表 1,两组比较无差异( $P>0.05$ )。

纳入标准:(1)年龄在 25-40 岁;(2)月经周期第 2-4 日,基础 FSH<10IU/L;(3)COH 方案为早卵泡期长效方案;(4)COH 获卵数>15 个或 HCG 注射日 E<sub>2</sub>>3000 pg/mL;(5)临床资料完整。

排除标准:(1)自身或配偶染色体异常;(2)合并内分泌疾病;(3)子宫畸形;(4)既往有细胞毒性药物治疗或盆腔放射性治疗;(5)合并严重内外科疾病。

和超声检查确定生化妊娠和临床妊娠。

### 1.3 观察指标

1.3.1 促排情况 记录降调时间、Gn 启动量、Gn 使用天数和 Gn 总量。

1.3.2 HCG 日激素水平及子宫内膜厚度 检测 HCG 日的 LH、E<sub>2</sub> 和 P 等血清激素水平及 HCG 日子宫内膜厚度。

1.3.3 获卵、受精和胚胎获取情况 记录获卵数、正常受精率(双原核总数/总卵母细胞数×100%)、移植胚胎数和优质胚胎率(优质胚胎数/可移植胚胎数×100%)。

1.3.4 妊娠结局 记录临床妊娠、胚胎丢失(妊娠期胎停)和活产数量。

### 1.4 统计学方法

SPSS 24.0 软件,计量和计数资料组间比较分别采用 t 和  $\chi^2$  检验。以  $\alpha=0.05$  作为检验水准。

## 2 结果

### 2.1 两组促排情况比较

观察组 Gn 使用天数和总使用量较对照组多( $P<0.05$ )。两组降调天数、Gn 启动量比较无差异( $P>0.05$ ),见表 2。

表 2 两组促排情况比较( $\bar{x} \pm s$ )

Table 2 Comparison of ovulation induction between two groups ( $\bar{x} \pm s$ )

Groups	n	Days of downregulation (d)	Gn startup volume (U)	Days of Gn	Total Gn (U)
Matched group	75	34.11± 3.14	154.79± 38.09	12.03± 2.01	2106.45± 620.80
Observation group	75	34.03± 3.22	163.20± 51.77	13.39± 2.17	2459.58± 792.46
t-value		0.154	1.133	3.982	3.038
P-value		0.878	0.259	<0.001	0.003

2.2 HCG 日血清激素水平及子宫内膜厚度比较

两组 E<sub>2</sub>、P 水平及子宫内膜厚度比较无差异(P>0.05),见表 3。

与对照组相比,观察组 HCG 日血清 LH 水平高(P<0.05),

表 3 两组 HCG 日血清激素水平及子宫内膜厚度比较( $\bar{x} \pm s$ )

Table 3 Comparison of serum hormone levels and endometrial thickness between two groups on HCG day ( $\bar{x} \pm s$ )

Groups	n	LH(U/L)	E <sub>2</sub> (pg/mL)	P(nmol/L)	Endometrial Thickness (mm)
Matched group	75	1.15± 0.29	6054.68± 1179.12	3.74± 2.24	11.01± 2.27
Observation group	75	1.32± 0.36	6111.09± 1282.67	3.68± 2.39	10.79± 2.13
t-value		3.185	0.280	0.159	0.612
P-value		0.002	0.780	0.874	0.542

2.3 获卵、受精和胚胎获取情况比较

见表 4。

与对照组相比,观察组获卵数低,优质胚胎率高(P<0.05),

表 4 两组获卵、受精和胚胎获取情况比较

Table 4 Comparison of egg acquisition, fertilization, and embryo acquisition between two groups

Groups	n	Number of eggs obtained	Normal fertilization rate(%)	High quality embryo rate(%)	Number of transferred embryos
Matched group	75	17.62± 4.53	77.37(554/716)	42.06(223/554)	1.57± 0.45
Observation group	75	15.55± 4.01	79.89(457/572)	60.17(275/457)	1.64± 0.53
t/ $\chi^2$ -value		2.963	1.197	39.766	0.872
P-value		0.004	0.274	<0.001	0.385

2.4 两组妊娠结局比较

低,但比较无差异(P>0.05),见表 5。

观察组临床妊娠率及活产率较对照组高,流产率较对照组

表 5 妊娠结局比较(%)

Table 5 Comparison of pregnancy outcomes (%)

Groups	n	Clinical pregnancy rate	Embryo loss rate	Live birth rate
Matched group	53	50.94(27/53)	25.93(7/27)	37.74(20/53)
Observation group	55	56.36(31/55)	16.13(5/31)	47.27(26/55)
$\chi^2$ -value		0.319	0.844	1.004
P-value		0.572	0.358	0.316

3 讨论

COH 的最佳目标是使患者获得合适数量的优质卵细胞和胚胎,并在此过程中尽可能减少或者避免中重度卵巢过度刺激

综合征发生的发生,以最终获得理想的妊娠结局<sup>[12]</sup>。对于卵巢高反应人群的 COH 操作,更需注意避免高反应和卵巢过度刺激综合征发生。

早卵泡期长效方案是一种新的 GnRH-a 长效制剂衍生

的COH方案<sup>[13,14]</sup>,具有适用范围广、操作简单等,逐渐应用广泛。该方案利用GnRH-a长效抑制垂体功能,减少LH表达和分泌,避免卵泡在尚未成熟时排卵和黄素化,进而提高卵泡质量,增加优势卵泡数量和妊娠率;GnRH-a抑制盆腔内炎症反应,减少自身抗体,有助于卵泡募集,增加成熟卵细胞数量<sup>[15]</sup>。此外,GnRH-a具有一致内源性LH特点<sup>[16,17]</sup>,其可对早发性LH峰的出现进行预防,并使卵泡发育与内膜同步,降低因过早排卵造成的周期取消。但GnRH-a的使用会使部分患者垂体功能过度抑制,造成内源性LH水平过低<sup>[18]</sup>。而相关报道显示<sup>[19,20]</sup>,LH低表达将会减少雌激素底物合成,进而造成卵泡微环境中雌激素的缺乏,最终导致卵母细胞、胚胎质量下降、流产等不良妊娠结局。

陈彩虹等<sup>[21]</sup>研究认为,和GnRH-a方案比较,通过长效方案促排卵能够改善患者子宫内膜容受性,提高胚胎种植率、临床妊娠率,减少妊娠后流产风险。现有研究和临床实践均证实通过GnRH-a方案能够有效减少COH过程中卵巢过度刺激综合征,但不能完全避免。柯张红等<sup>[22]</sup>研究在将预期卵巢高反应人群应用长效方案,发现53.61%的患者获得了正常卵巢反应,两组临床妊娠率比较无显著差异,而高反应组流产率可达正常反应患者近2倍。这些结果提示,对于预期卵巢高反应患者,通过长效方案进行促排卵可降低高反应率,但仍有进步的巨大空间。

"两细胞-两促性腺激素"学说认为FSH、LH可参与调控卵泡正常发育、卵巢类固醇激素合成<sup>[23]</sup>,前者通过结合卵巢颗粒细胞受体提高芳香化酶水平促进雄烯二酮和雌激素合成,发挥维持卵泡和子宫内膜发育的作用;LH能够与卵巢间质细胞、卵泡膜细胞上的LH受体结合,提高雄激素水平<sup>[24]</sup>。卵泡发育中晚期,颗粒细胞表达LH受体并能够结合LH,LH作用超过FSH并进一步促进卵泡成熟<sup>[25,26]</sup>;排卵后,LH促进孕激素表达和分泌,形成并维持黄体期。因此,保持LH水平在适当范围对于卵泡发育、卵子成熟、排卵、黄体形成和维持均有重要作用。

基于上述理论,本研究在ART促排卵过程中添加r-LH,结果显示:观察组Gn使用天数、Gn总量、HCG日血清LH水平均高于对照组,两组患者在降调天数、Gn启动量以及HCG日E<sub>2</sub>水平、P水平、子宫内膜厚度等指标上无明显区别。观察组获卵数低于对照组( $P < 0.05$ ),其可能是因为在早卵泡期添加r-LH,将会增加LH的表达,进而导致卵泡闭锁或黄素化。观察组优质胚胎率高于对照组( $P < 0.05$ ),临床妊娠率及活产率较对照组高,流产率较对照组低,但比较无差异( $P > 0.05$ )。分析原因:一方面,早卵泡期补充r-LH能够改善GnRH-a降调节后内源性LH过分抑制患者的卵巢反应性,提高卵子和胚胎的质量<sup>[27,28]</sup>;另一方面,在整个过程中添加r-LH,可以弥补患者内源性LH的不足,满足卵泡发育中晚期对LH需求的不断增加,导致卵泡内雄激素大量生成,进而对卵泡内低雄激素水平、卵母细胞发育微环境起到改善作用,促进卵泡和卵子的发育成熟,改善妊娠结局<sup>[29,30]</sup>。

综上所述,卵巢高反应患者行早卵泡期长效方案促排卵时,添加r-LH可显著增加体内LH水平,提高优质卵泡率,对妊娠结局具有一定改善作用。本研究为单中心研究、纳入病例数较少,可能造成结论偏倚,另外未探究r-LH添加时间对排卵

和妊娠结局的影响。因此仍需进一步探究r-LH的应用价值。

#### 参考文献(References)

- [1] Schachter-Safrai N, Karavani G, Esh-Broder E, et al. High ovarian response to ovarian stimulation: effect on morphokinetic milestones and cycle outcomes [J]. *J Assist Reprod Genet*, 2021, 38 (12): 3083-3090.
- [2] Zeng R, Chen H, Zeng X, et al. The Essential Role of Body Weight in Adjusting Gn Dosage to Prevent High Ovarian Response for Women With PCOS During IVF: A Retrospective Study [J]. *Front Endocrinol (Lausanne)*, 2022, 13: 922044.
- [3] WU M Y, CHUNG C H, PAN S P, et al. Advantages of cumulative pregnancy outcomes in freeze-all strategy in high responders-A case-control matching analysis of a large cohort [J]. *J Formos Med Assoc*, 2018, 117(8): 676-684.
- [4] 宋娜, 朱光丽, 宋文月, 等. 中-重度卵巢过度刺激综合征对IVF-ET单/双胎妊娠患者晚期结局的影响 [J]. *重庆医科大学学报*, 2021, 46(4): 406-411.
- [5] Verberg MF, Eijkemans MJ, Macklon NS, et al. The clinical significance of the retrieval of a low number of oocytes following mild ovarian stimulation for IVF: a meta-analysis [J]. *Hum Reprod Update*, 2009, 15(1): 5-12.
- [6] Guan S, Feng Y, Huang Y, et al. Progestin-Primed Ovarian Stimulation Protocol for Patients in Assisted Reproductive Technology: A Meta-Analysis of Randomized Controlled Trials [J]. *Front Endocrinol (Lausanne)*, 2021, 12(1): 702558.
- [7] Blumenfeld Z. What Is the Best Regimen for Ovarian Stimulation of Poor Responders in ART/IVF? [J]. *Front Endocrinol (Lausanne)*, 2020, 11(4): 192.
- [8] Zhang F, Zhang H, Du H, et al. Application value of Early-Follicular Phase Long-Acting Gonadotropin-Releasing Hormone Agonist Long Protocol in patients with resistant ovary syndrome [J]. *BMC Pregnancy Childbirth*, 2023, 23(1): 178.
- [9] Ni YH, Zhang HL, Jiang WW. Analysis and prediction of risk factors of ovarian hyperstimulation caused by Long-acting GnRH agonist protocol in follicular phase [J]. *Eur Rev Med Pharmacol Sci*, 2022, 26 (9): 3261-3268.
- [10] Kol S. LH Supplementation in Ovarian Stimulation for IVF: The Individual, LH Deficient, Patient Perspective [J]. *Gynecol Obstet Invest*, 2020, 85(4): 307-311.
- [11] Xing WJ, Lin HY, Li Y, et al. Is the GnRH antagonist protocol effective at preventing OHSS for potentially high responders undergoing IVF/ICSI? [J]. *PLoS One*, 2015, 10(10): e0140286.
- [12] Pilsgaard F, Grynnerup AG, Løssl K, et al. The use of anti-Müllerian hormone for controlled ovarian stimulation in assisted reproductive technology, fertility assessment and -counseling [J]. *Acta Obstet Gynecol Scand*, 2018, 97(9): 1105-1113.
- [13] Li G, Wu Y, Niu W, et al. Analysis of the Number of Euploid Embryos in Preimplantation Genetic Testing Cycles With Early-Follicular Phase Long-Acting Gonadotropin-Releasing Hormone Agonist Long Protocol [J]. *Front Endocrinol (Lausanne)*, 2020, 11: 424.
- [14] Zhang Y, Zhao W, Han Y, et al. The follicular-phase depot GnRH agonist protocol results in a higher live birth rate without discernible

- differences in luteal function and child health versus the daily mid-luteal GnRH agonist protocol: a single-centre, retrospective, propensity score matched cohort study [J]. *Reprod Biol Endocrinol*, 2022, 20(1): 140.
- [15] Piróg M, Kacalska-Janssen O, Jach R, et al. GnRH Antagonist Protocol Enhances Coagulation During Controlled Ovarian Stimulation for IVF[J]. *Reprod Sci*, 2022, 29(12): 3521-3531.
- [16] Tian LF, Tan J, Zou Y, et al. Mild starting dosage ovarian stimulation combined with a modified prolonged GnRH-a protocol improved IVF/ICSI outcomes in normal ovarian responders [J]. *Arch Med Sci*, 2019, 15(5): 1294-1300.
- [17] Song J, Duan C, Cai W, et al. Comparison of GnRH-a Prolonged Protocol and Short GnRH-a Long Protocol in Patients with Thin Endometrium for Assisted Reproduction: A Retrospective Cohort Study[J]. *Drug Des Devel Ther*, 2020, 14: 3673-3682.
- [18] 郑露, 张红, 姚兵, 等. 早卵泡期长效方案中添加重组人黄体生成素对于 IVF/ICSI 助孕结局的影响[J]. *医学研究生学报*, 2023, 36(1): 50-55.
- [19] Luo X, Li L, Lin N, et al. Low Endogenous LH on the COS Initiation Day of a GnRH-Agonist Regimen Increases the Risk of Early Pregnancy Loss and Adverse ART Outcomes [J]. *Front Endocrinol (Lausanne)*, 2022, 13(2): 830567.
- [20] Luo Y, Liu S, Su H, et al. Low Serum LH Levels During Ovarian Stimulation With GnRH Antagonist Protocol Decrease the Live Birth Rate After Fresh Embryo Transfers but Have No Impact in Freeze-All Cycles[J]. *Front Endocrinol (Lausanne)*, 2021, 12(1): 640047.
- [21] 陈彩虹, 郭艺红. 卵泡期长效方案促排卵早期思考[J]. *生殖医学杂志*, 2019, 28(10): 1130-1132.
- [22] 柯张红, 孙艳, 刘丽荣, 等. 卵泡期长效方案在符合卵巢高反应预测指标患者中的运用及其发生高反应的危险因素分析[J]. *中华生殖与避孕杂志*, 2021, 41(3): 199-205.
- [23] Liu YX, Zhang Y, Li YY, et al. Regulation of follicular development and differentiation by intra-ovarian factors and endocrine hormones [J]. *Front Biosci (Landmark Ed)*, 2019, 24(5): 983-993.
- [24] Arat Ö, Deveci D, Özkan ZS, et al. What is the effect of the early follicular phase FSH/LH ratio on the number of mature oocytes and embryo development?[J]. *Turk J Med Sci*, 2020, 50(2): 420-425.
- [25] Oduwole OO, Huhtaniemi IT, Misrahi M. The Roles of Luteinizing Hormone, Follicle-Stimulating Hormone and Testosterone in Spermatogenesis and Folliculogenesis Revisited [J]. *Int J Mol Sci*, 2021, 22(23): 12735.
- [26] Muñoz de la Torre LP, Trujillo Hernández A, Eguibar JR, et al. Characterization of sperm motility and testosterone secretion in the taiep myelin mutant, a model of demyelination [J]. *Anim Reprod*, 2023, 20(3): e20220102.
- [27] 王琳, 王菁, 胡艳秋, 等. 不同时机添加重组黄体生成素对高龄不孕症患者早卵泡期长效方案促排卵妊娠结局的影响[J]. *中华妇产科杂志*, 2022, 57(10): 758-766.
- [28] 李元, 龚斐. 重组人黄体生成素能改善改良超长方案多囊卵巢综合征患者 IVF/ICSI 妊娠结局[J]. *生殖医学杂志*, 2015, 24(1): 21-25.
- [29] 梁秀霞, 刘丽, 贾玲玲. 早卵泡期和晚卵泡期添加黄体生成素对多囊卵巢综合征 GnRH-a 长效方案卵巢慢反应患者临床结局的影响[J]. *临床和实验医学杂志*, 2020, 19(4): 397-399.
- [30] 邢孔芸, 邓岳红, 龚婷. 重组人黄体生成素不同添加时机在早卵泡期长效方案促排卵不孕患者中的应用比较[J]. *中国性科学*, 2023, 32(6): 74-78.
- (上接第 2305 页)
- [11] Zhao XY, Teng YS, Li ZN, et al. Acquired subglottic cysts in infants with ultra-low birth weight: a case report[J]. *Chin J Otorhinolaryngol Head Neck Surg*, 2020, 55(10): 972-974.
- [12] 黄碧茵, 谭宝莹, 许小慧, 等. 极低、超低体重早产儿医院感染变化及其危险因素分析[J]. *中国现代医学杂志*, 2021, 31(5): 73-80.
- [13] Zhou J, Ba Y, Du Y, et al. The Etiology of Neonatal Intensive Care Unit Death in Extremely Low Birth Weight Infants: A Multicenter Survey in China[J]. *Am J Perinatol*, 2021, 38(10): 1048-1056.
- [14] Desorcy-Scherer K, Bendixen MM, Parker LA. Determinants of the Very Low-Birth-Weight Infant's Intestinal Microbiome: A Systematic Review[J]. *J Perinat Neonatal Nurs*, 2020, 34(3): 257-275.
- [15] 修文龙, 杨长仪, 赖淑华, 等. 极低出生体重儿晚发型败血症发生情况及其危险因素[J]. *中华围产医学杂志*, 2020, 23(5): 338-344.
- [16] Hong YM, Cho DH, Kim JK. Developmental outcomes of very low birth weight infants with catch-up head growth: a nationwide cohort study[J]. *BMC Pediatr*, 2023, 23(1): 392.
- [17] 李勇裴, 朱云霞, 吴婷, 等. 极低及超低体重儿迟发型败血症病原菌分布及其发生影响因素分析 [J]. *中华全科医学*, 2018, 16(11): 1851-1853.
- [18] Hu X, Hu W, Sun X, et al. Transmission of cytomegalovirus via breast milk in low birth weight and premature infants: a systematic review and meta-analysis[J]. *BMC Pediatr*, 2021, 21(1): 520.
- [19] Perrem L, Semberova J, O'Sullivan A, et al. Effect of Early Parenteral Nutrition Discontinuation on Time to Regain Birth Weight in Very Low Birth Weight Infants: A Randomized Controlled Trial[J]. *JPEN J Parenter Enteral Nutr*, 2019, 43(7): 883-890.
- [20] 孔雯, 蒋玮玮, 孔德川. NICU 新生儿院内感染危险因素及病原菌分布情况的研究[J]. *中国妇幼保健*, 2019, 34(18): 4240-4242.
- [21] Ferry A, Plaisant F, Ginevra C, et al. Enterobacter cloacae colonisation and infection in a neonatal intensive care unit: retrospective investigation of preventive measures implemented after a multiclinal outbreak[J]. *BMC Infect Dis*, 2020, 20(1): 682.
- [22] Tamura K, Kawasuji H, Tachi S, et al. Congenital tuberculosis in an extremely preterm infant and prevention of nosocomial infection[J]. *J Infect Chemother*, 2019, 25(9): 727-730.
- [23] 王娟, 范雅廷, 董小英. NICU 新生儿院内感染危险因素和病原菌分布情况[J]. *中国妇幼保健*, 2021, 36(5): 1136-1139.
- [24] Kim YJ, Hong MY, Kang HM, et al. Using adenosine triphosphate bioluminescence level monitoring to identify bacterial reservoirs during two consecutive Enterococcus faecium and Staphylococcus capitis nosocomial infection outbreaks at a neonatal intensive care unit[J]. *Antimicrob Resist Infect Control*, 2023, 12(1): 68.
- [25] 李笑, 吴运芹, 李贵南, 等. 极低与超低出生体重早产儿发生真菌败血症的影响因素[J]. *医学临床研究*, 2022, 39(10): 1539-1541, 1545.