Efficacy and Safety of *In Vitro* Fertilization (IVF)/Intracytoplasmic Sperm Injection (ICSI) Among Patients with Endometriosis After a Shortened Protocol of Long-Term Pituitary Downregulation

**Background:** Patients with endometriosis (EMs) are routinely advised to take GnRH-a for 3–6 months to improve the internal reproductive environment, but this may not be necessary.

**Material/Methods:** This retrospective study examined the effects of *in vitro* fertilization (IVF)/intracytoplasmic sperm injection (ICSI) with shortened (n=311) or conventional (n=213) long-term pituitary downregulation in EMs patients between January 2013 and July 2017.

**Results:** The 2 groups showed no significant differences in gonadotropin (Gn) dose, number of oocytes retrieved, or miscarriage rate. Follicle-stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (E2) levels on the initiation day and the LH level on human chorionic gonadotropin (hCG) day (1.22±1.39 vs. 0.74±0.55 P=0.0026) were higher in the study group than in the control group. The cumulative live birth rates in the second cycle were 69.13% in the study group (95% confidence interval (CI), 64–74.27%) vs. 68.54% in the control group (95% CI, 62.31–74.78%, P=0.88, respectively).

**Conclusions:** This study showed that the shortened regimen and the ultralong regimen did not produce different pregnancy outcomes after ART, and the single-application, long-term GnRH-a protocol may serve as a cost-effective and safe treatment protocol for EMs patients.

**MeSH Keywords:** Endometriosis • Fertilization *In Vitro* • Gonadotropin-Releasing Hormone • Pregnancy Rate

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Background

Endometriosis is a common disease known to be detrimental to fertility [1]. Evidence has demonstrated that EMs has deleterious effects on fecundity [2]. A Cochrane systematic review based on 3 small studies showed that GnRH-a for 3–6 months improved the internal reproductive environment of patients with EMs [3–5]. However, many relevant studies had small sample sizes and drastic differences in success rates, causing uncertainty regarding the ultimate effectiveness of the treatment [6,7]. Notably, GnRH-a causes women to be in a low-estrogen state and to have a poor oocyte response, and long-term use is associated with osteoporosis.

However, a recent systematic review and meta-analysis examined 30 retrospective studies and 3 RCTs and found that, compared with patients without EMs, women with endometriosis had similar IVF/ICSI outcomes, fewer oocytes, and a higher cancellation rate [8]. Recent studies have compared GnRH antagonists or oral contraceptives [9] and short-acting GnRH agonists [10] and reported comparable outcomes. Surrey demonstrated that a 2-month course of GnRH-a therapy is also effective [11]. Thus, whether a GnRH-a is administered for 3–6 months should be considered carefully. The optimum duration of long-term pituitary downregulation remains unknown [5,7]. Ren et al. reported that pregnancy rates were improved by long-term pituitary downregulation for women without endometriosis [12]. These findings may extend to patients with endometriosis.

Based on the above data, we hypothesized that one-time, long-term pituitary downregulation of D2 can produce outcomes comparable to those of the conventional prolonged course in terms of the IVF clinical pregnancy rate and the cumulative live birth rate in EMs patients.

Material and Methods

Patients

From January 2013 to July 2017, patients diagnosed with surgically confirmed endometriosis who were treated with IVF-embryo transfer (ET) consecutively assigned long-term GnRH-a regimen were included. A total of 311 patients who received a one-time regimen were assigned to the study group, and 213 patients who received the repeated ultralong regimen were assigned to the control group. Basic demographic and assisted reproductive technology (ART) data for this study were collected from the Clinical Reproductive Medicine Management System/Electronic Medical Record Cohort Database (CCRM/EMRCD) in the Reproductive Medical Center, the First Affiliated Hospital of Zhengzhou University.

Inclusion criteria were: (1) EMs diagnosed through laparoscopy/laparotomy; (2) age ≤42 years; (3) normal menstrual cycle; and (4) basal FSH (bFSH) ≤12 mIU/mL.

Exclusion criteria were: (1) endocrine-related diseases such as polycystic ovary syndrome or hyperprolactinemia; (2) uterine malformations; (3) previous history of recurrent miscarriages; (4) preimplantation genetic diagnosis/preimplantation genetic screening; (5) adenomyosis; (6) hydrosalpinx.

Ethics approval and consent to participate

The study received approval from the Zhengzhou University Research Ethics Board (Research-2017-LW-69).

Controlled ovarian stimulation protocols

The study group were treated with the standard full dose (3.75 mg) of triptorelin depot (Diphereline 3.75; Ipsen Pharma) on days 2–3 of the cycle, and 28 days later, transvaginal sonography as well as serum hormone levels of FSH, LH, E2, and progesterone (P) were monitored. The control group was treated with depot every 28 days for 56 days. Twenty days after the second administration, downregulation was confirmed. Ovary stimulation, oocyte retrieval, and embryo transfer were conducted as previously described [13]. Briefly, the dose of recombinant FSH (Gonal-F; Merck, Germany) was determined according to the subject’s age, antral follicle count (AFC), body mass index (BMI), and levels of base FSH and anti-Mullerian hormone (AMH). The Gn dose was increased or decreased in a timely manner according to response. When the antral follicle size was 12–14 mm, human menopausal gonadotropin (hMG; Livzon, China) was added. When the dominant follicle size was ≥20 mm and at least 3 follicles were ≥18 mm, hCG (Ovidrel; Merck Serono), either alone or combined with the hCG 2000IU, was injected as a trigger. In the case of frozen embryos, the endometrium was prepared through the natural cycle, an artificial cycle, or pituitary downregulation combined with an artificial cycle, according to ovulation.

Clinical follow-up

Pregnancy outcomes were determined according to the terms revised by the International Committee Monitoring Assisted Reproductive Technologies (ICMART) [14]. In calculating the CLB rate, 1 cycle was defined as the process from the start of ovarian stimulation to completion of transplantation of all fresh and frozen embryos [15].

End-points

The primary end-points of this study were clinical pregnancy rate and cumulative live birth rate. The secondary end-points...
were hormone test results during ovarian stimulation, the total stimulating hormone dose, the mean number of oocytes retrieved, the fertilization rate, the miscarriage rate, and any adverse effects such as transplantation cancelation and associated complications during treatment.

**Statistical analysis**

All data were analyzed using SAS 9.3 statistical software. Measurement data are described as the means (standard deviation), and count data are described as frequencies (proportions). The means were compared using the \( t \) test or Wilcoxon rank sum test, and intergroup comparisons were performed using the chi-square test or Fisher's exact test. \( P<0.05 \) was considered statistically significant.

**Results**

A total of 245 patients underwent 1 ovarian stimulation cycle and 60 patients underwent 2 cycles in the study group, resulting in 461 ET cycles, including cryopreserved ETs. A total of 213 patients in the control group underwent 288 ET cycles (Table 1).

The overall demographic and cycle characteristics of the patients, including the average maternal age, infertility duration (years), basal hormonal test results, and BMI, were similar between the 2 groups. The total gonadotropin (Gn) dose used in the study group was 2845.22±1082.62 IU, while in the control group it was 3025.89±1002.08 IU (\( P=0.0464 \)). The control group required more time (13.86±2.48 days vs. 13.77±2.32 days) for stimulation, although no significant differences were detected between the 2 groups (\( P>0.05 \)). P and E2 levels and endometrial thickness on the hCG day were similar in both groups. The dominant follicles ratio was lower (79.79% vs. 82.88%, \( P=0.0045 \)) and FSH, LH, and E2 levels on the initiation day and the LH level on the hCG day were significantly higher in the study group (1.22±1.39 vs. 0.74±0.55, \( P=0.0026 \)) (Table 1). However, the biological parameters of the fresh cycles – the transplantation ratio (78.15% vs. 78.14%), the high response-induced cancelation ratio (10.28% vs. 10.93%), IVF/ICSI rank, the number of retrieved oocytes, the fertilization rate, and the numbers of transplantable embryos and high-quality embryos – were comparable between the 2 groups (Table 2).

The clinical outcomes of ET cycles are summarized in Table 3. No differences in the miscarriage rate, ectopic pregnancy rate, 

| Characteristics                      | Study group (n=311) | Control group (n=213) | \( P \)-value |
|--------------------------------------|--------------------|-----------------------|---------------|
| Maternal age at cycle start (y)*     | 30.37±4.36         | 29.94±3.74            | 0.5159        |
| infertility duration(y)              | 4.30±3.15          | 3.99±3.01             | 0.1392        |
| BMI (Kg/m\(^2\))*                   | 22.14±2.89         | 22.05±2.81            | 0.8072        |
| D2 FSH (mIU/ml)                      | 7.24±3.51          | 7.52±3.25             | 0.0804        |
| D2 E2 (pmol/l)                       | 47.06±41.60        | 59.92±66.23           | 0.2156        |
| D2 P (ng/ml)                         | 0.77±1.01          | 0.84±0.75             | 0.8754        |
| D2 LH(mIU/ml)                        | 4.89±3.76          | 4.86±2.15             | 0.4350        |
| Total Gn dose administered           | 2845.22±1082.62    | 3025.89±1002.08       | 0.0464        |
| Days of Gn                           | 13.77±2.32         | 13.86±2.48            | 0.8098        |
| E2 on initiation day (pmol/l)        | 8.92±6.74          | 26.71±170.69          | <0.0001       |
| LH on initiation day (mIU/ml)        | 0.64±0.39          | 0.57±0.59             | 0.0007        |
| FSH on initiation day (mIU/ml)       | 3.56±1.91          | 4.07±1.68             | 0.0021        |
| P on initiation day (ng/ml)          | 0.47±0.23          | 0.45±0.25             | 0.5842        |
| Endometrial thickness (mm)           | 12.60±2.66         | 13.08±2.82            | 0.0945        |
| E2 on day hCG (pmol/l)               | 3338.14±2093.43    | 3803.20±2426.87       | 0.049         |
| LH on day hCG (mIU/ml)               | 1.22±1.39          | 0.74±0.55             | 0.0026        |
| P on day hCG (ng/ml)                 | 1.05±0.67          | 1.03±0.68             | 0.3228        |
| Dominant follicles ratio, %          | 79.79              | 82.88                 | 0.0045        |

* \( t \)-test, the else Wilcoxon rank sum test; values are mean ±SD or n (%); NS – not statistically.

Table 1. Demographic and cycle characteristics of the 2 groups.

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Table 2. Comparison of oocyte retrieval outcomes between the 2 groups.

| Outcome                                | Study group (n=311) | Control group (n=213) | P-value* |
|----------------------------------------|---------------------|-----------------------|----------|
| Oocyte retrieval cycles                |                     |                       |          |
| 1                                      | 245 (78.78)         | 190 (89.2)            |          |
| 2                                      | 60 (19.29)          | 18 (8.45)             |          |
| 3                                      | 3 (0.96)            | 1 (0.47)              |          |
| 4                                      | 3 (0.96)            | 4 (1.88)              |          |
| Oocyte retrieval outcome               |                     |                       | 0.1536   |
| No oocytes after oocyte retrieval      | 5 (1.60)            | 4 (1.88)              |          |
| Total unfertilization                  | 3 (0.96)            | 1 (0.47)              |          |
| Abornamal fertilization               | 3 (0.96)            | 0 (0.00)              |          |
| Uncleavage                            | 3 (0.96)            | 0 (0.00)              |          |
| Transplantation cancelleda            | 58 (18.64)          | 44 (20.66)            |          |
| High response                         | 40 (12.86)          | 27 (12.68)            |          |
| No transplantable embryo              | 13 (4.18)           | 5 (2.34)              |          |
| Embryo transfer cycles                 | 226 (72.67)         | 193 (78.14)           |          |
| Total oocytes, n (SD)*                | 10.46±6.47          | 10.31±6.77            | 0.6285   |
| Fertilization, %                     | 63.52               | 64.97                 | 0.5982   |
| Total embryos, n (SD)*               | 3.91±2.71           | 4.39±3.16             | 0.1744   |
| High quality embryos, n (SD)*       | 3.45±2.51           | 4.08±3.13             | 0.053    |
| Fertilization protocol               |                     |                       | 0.1805   |
| ICSI                                  | 65 (16.71)          | 38 (15.38)            |          |
| IVF                                   | 308 (79.18)         | 205 (83)              |          |
| IVF+ICSI                              | 16 (4.11)           | 4 (1.62)              |          |

* Reasons: high response; personal reasons; presence of intra-cavity fluid due to a hydrosalpinx; high P on day of embryo transfer. 
# Chi-square test, a Wilcoxon rank sum test, Values is mean ±SD, n (%) or median (range).

Table 3. Comparison of clinical outcomes of embryo transfer cycles* between the 2 groups.

| Outcome                                | Study group (n=460) | Control group (n=288) | P-value |
|----------------------------------------|---------------------|-----------------------|---------|
| Embryo transfer                        |                     |                       | 0.0884  |
| Single-embryo transfer                 | 69 (15.00)          | 57 (19.79)            |         |
| Double-embryo transfer                 | 391 (85.00)         | 231 (80.21)           |         |
| Implantation rate, %                   | 43.36               | 48.40                 | 0.3664  |
| Clinical pregnancy rate, n (%)*        | 262 (56.83)         | 175 (60.55)           | 0.3146  |
| Ectopic pregnancy rate, n (%)*         | 3 (0.67)            | 3 (1.04)              | 0.3664  |
| Miscarriage, n (%)*                    | 35 (11.25)          | 22 (8.30)             | 0.7383  |

* Chi-square test; values are mean ±SD, n (%) or median (range); NS – not statistically; * include thaw-ET.
or clinical pregnancy rate were found between the groups (Table 3). The live birth rates of the 2 groups after the first treatment were similar (40.00% vs. 41.00%, P=0.81); no significant difference was found. The cumulative live birth rates of both groups showed an upward trend, with significant changes in the first cycle (59.81% (95% CI, 54.36–65.26%)) in the study group vs. 65.73% (95% CI, 59.35–72.1%) in the control group, P=0.17) and second cycle (69.13% (95% CI, 64–74.27%) in the study group vs. 68.54% (95% CI, 62.31–74.78%) in the control group, P=0.88), but no significant differences between the groups were observed (Table 4).

**Discussion**

To the best of our knowledge, this is the first study investigating the ultralong downregulation protocol in EMs patients. Although this retrospective study has limited power to draw strong conclusions regarding the proper dose for long-term pituitary downregulation before IVF, our findings may provide a new perspective. Our study supports the hypothesis that a single-application, long-term downregulation regimen can achieve comparable clinical outcomes to those of the conventional ultralong regimen. More importantly, shortening the downregulation duration minimizes patient costs and excessive pituitary suppression.

The proportions of poor cycle outcomes, such as failed oocyte retrieval and fertilization, abnormal fertilization, and no transplantable embryos, were similar in the 2 groups. The proportions of patients undergoing different fertilization methods did not differ between the groups, indicating that the baseline data of the 2 groups were not different.

Long-term pituitary downregulation is beneficial to endometrial receptivity. EMs alters endometrial receptivity by increasing estrogen exposure through CYP enzymes [19] and inflammation-dependent resistance to the effects of progesterone [17]. Many researchers have attempted to overcome this obstacle using either oral contraceptive pills [18] or levonorgestrel-releasing IUDs [19], but these methods cannot directly facilitate IVF. Two retrospective studies reported that GnRH antagonist (GnRH-ant) protocols can achieve comparable results to those of long-term GnRH-a protocols in EMs patients [20,21]. However, a Cochrane meta-analysis by Al-Inany and Aboulghar suggested that GnRH-ant protocols negatively affected pregnancy rates [22]. Khan et al. showed that long-term pituitary downregulation decreased the microvessel density of endometriotic lesions, reducing blood flow into the lesions [23]. With long-term amenorrhea, pinopodes can be restored [24]. Thus, long-term pituitary downregulation is useful for EMs. However, no data suggest that improved endometrial receptivity with long-term pituitary downregulation occurred in a dose-dependent manner. All CLB rates showed an upward trend and were higher than 66% after 2 cycles in the 2 groups, indicating that the effectiveness of the dose-reduced long-term regimen is not inferior to that of the conventional regimen.

Conflicting results have been reported regarding oocyte quality between patients with EMs and controls [25]. A randomized controlled trial showed that 3-month GnRH agonist treatment for peritoneal EMs prior to IVF did not produce a better outcome, such as a greater number of MII oocytes, compared with a longer protocol [26]. Van der Houwen found that ultralong pituitary downregulation can achieve a limited favorable effect in ongoing pregnancy in women who had experienced severe EMs during fresh cycles [27]. These results are generally consistent with ours, indicating the ultralong protocol may be unnecessary.

Moreover, long-term GnRH-a has been reported to result in a longer time to recovery of the pituitary gland [11]. The results obtained here are consistent with the above findings, with a higher LH level on hCG day in the study group than in the control group. When pituitary-ovarian function is excessively suppressed, egg and embryo quality are affected [28]. Our study showed no clear negative effect of the lower LH level in the control group. When pituitary-ovarian function is excessively suppressed, GnRH-a protocols can achieve comparable results to those of long-term GnRH-a protocols in EMs patients [20,21]. Our study showed no clear negative effect of the lower LH level in the control group. However, ultralong pituitary downregulation may suppress the ovarian response to Gn [26], and our results are consistent with this finding. The control group required a higher Gn dose and longer time for stimulation. More importantly, the live birth rate decreased with increasing FSH levels in the control group, but this trend was not observed in the study group. Therefore, the ultralong protocol may be unnecessary.

| Table 4. Comparison of cumulative live birth rate outcomes between the 2 groups. |
|---------------------------------------------------------------|
| Study group (n=330) | control group (n=261) | P-value* |
| First treatment | 42.12 (36.63–47.61) | 47.89 (41.18–54.6) | 0.1921 |
| First cycle* | 59.81 (54.36–65.26) | 65.73 (59.35–72.1) | 0.1698 |
| Second cycle | 69.13 (64–74.27) | 68.54 (62.31–74.78) | 0.8866 |
| ≥3 cycles | 69.45 (64.33–74.57) | 69.01 (62.8–75.22) | 0.9147 |

*First treatment plus thaw embryo transfer; * Chi-square test; CI – confidence interval.
doses [29]. All these data suggest an inherent negative effect of ultralong pituitary downregulation.

This study had some limitations. The main limitation is the retrospective study design, which limits the robustness of the findings. The results of this study support the necessity of further prospective studies [13]. The sample sizes of the study are small. IVF-ET has become the first choice for the treatment of EMs patients with infertility. However, all therapies were administered in a single large IVF center that passed standard operation tests, thus ensuring the uniformity of the treatment paradigms. The study is limited by the lack of information on some patients’ detailed surgical records. Thus, r-FS scoring was not performed, and the severity of the EMs of the patients was not analyzed in subgroups. However, the causal link between endometriosis and subfertility remains elusive except for bilateral tubal blockage [30]. Many patients with Ems of ASRM stage III and IV after surgery had poor ovarian reservation and limited number of oocytes [31], which might be exaggerated by longer downregulation.

Conclusions

A modified long-term downregulation regimen may serve as a cost-effective and safe treatment protocol for patients with EMs to improve the quality of care in assisted reproduction.

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Conflict of interest

None.

References:

1. Giudice LC. Clinical practice. Endometriosis. N Engl J Med, 2010; 362(25): 2389–98
2. Barnhart K, Dunsmoor-Su R, Coutifaris C: Effect of endometriosis on in vitro fertilization. Fertil Steril, 2002; 77(6): 1148–55
3. Sallam HN, Garcia-Velasco JA, Dias S, Arici A: Long-term pituitary down-regulation before in vitro fertilization (IVF) for women with endometriosis. Cochrane Database Syst Rev, 2006; 4(1): CD004635
4. Nasiri N, Moini A, Eftekhari-Yazdi P et al: Oxidative stress statuses in serum and follicular fluid of women with endometriosis. Cell J, 2017; 18(4): 582–87
5. Dicker D, Goldman IA, Levy T et al: The impact of long-term gonadotropin-releasing hormone analogue treatment on preclinical abortions in patients with severe endometriosis undergoing in vitro fertilization-embryo transfer. Fertil Steril, 1992; 57(3): 597–600
6. Vercellini P, Viganò P, Somigliana E, Fedele L: Endometriosis: pathogenesis and treatment. Nat Rev Endocrinol, 2014; 10(5): 261–75
7. de Ziegler D, Borghese B, Chapron C: Endometriosis and infertility: Pathophysiology and management. Lancet, 2010; 376(9742): 730–38
8. Hamdan M, Dunselman G, Li TC, Cheong Y: The impact of endometrioma on IVF/ICSI outcomes: A systematic review and meta-analysis. Hum Reprod Update, 2015; 21(6): 809–25
9. de Ziegler D, Gayet V, Aubriot FX et al: Use of oral contraceptives in women with endometriosis before assisted reproduction treatment improves outcomes. Fertil Steril, 2010; 94(7): 2796–99
10. Nakamura K, Osawawa M, Kondou I et al: Menotropin stimulation after prolonged gonadotropin releasing hormone agonist pretreatment for in vitro fertilization in patients with endometriosis. J Assist Reprod Genet, 1992; (2): 113–17
11. Surrey ES, Katz-Jaffe M, Kondapalli LV et al: GnRH agonist administration prior to embryo transfer in freeze-all cycles of patients with endometriosis or anterior endometrial integrin expression. Reprod Biomed Online, 2017; 35(2): 145–51
12. Ren J, Sha A, Han D et al: Does prolonged pituitary down-regulation with gonadotropin-releasing hormone agonist improve the live-birth rate in in vitro fertilization treatment? Fertil Steril, 2014; 102(1): 75–81
13. Kong H, Hu L, Nie L et al: A multi-center, randomized controlled clinical trial of the application of a shortened protocol of long-acting triptorelin down-regulated prior to IVF/ICSI among patients with endometriosis: A protocol. Reprod Health, 2018; 15(1): 213
14. Zegers-Hochschild F, Adamson GD, de Mouzon J et al., International Committee for Monitoring Assisted Reproductive Technology, World Health Organization: International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology, 2009. Fertil Steril, 2009; 92(5): 1520–24
15. Smith A, Tilling K, Nelson SM, Lawlor DA: Live-birth rate associated with repeat in vitro fertilization treatment cycles. JAMA, 2015; 314(24): 2654–62
16. Bulun SE: Aromatase and estrogen receptor alpha deficiency. Fertil Steril, 2014; 101(2): 323–29
17. Yoo JY, Kim TH, Fazleabas AT et al: KRAS Activation and over-expression of SIRT1/BCL6 contributes to the pathogenesis of endometriosis and progesterone resistance. Sci Rep, 2017; 7(1): 6765
18. Maia H Jr., Casoy J, Pimentel K et al: Effect of oral contraceptives on vascular endothelial growth factor, Cox-2 and aromatase expression in the endometrium of uteri affected by myomas and associated pathologies. Contraception, 2008; 78(6): 479–85
19. Engemise SL, Willets JM, Taylor AH et al: Changes in glandular and stromal estrogen and progesterone receptor isoform expression in eutopic and ectopic endometrium following treatment with the levonorgestrel-releasing intrauterine system. Eur J Obstet Gynecol Reprod Biol, 2011; 157(1): 101–6
20. Bastu E, Yasa C, Dural O et al: Comparison of ovulation induction protocols after endometrioma resection. JLS, 2014; 18(3): pii: e2014.00128
21. Rodriguez-Purata J, Coroleu B, Tur R et al: Endometriosis and IVF: are agonists really better? Analysis of 1180 cycles with the propensity score matching. Gynecol Endocrinol, 2013; 29(9): 859–62
22. Al-Imany H, Aboulghar M: GnRH antagonist in assisted reproduction: A Cochrane review. Hum Reprod, 2002; 17(4): 874–85
23. Khan KN, Kitajima M, Hiraki K et al: Changes in tissue inflammation, angiogenesis and apoptosis in endometriosis, adenomyosis and uterine myoma after GnRH agonist therapy. Hum Reprod, 2010; 25(3): 642–53
24. Abdalla HI, Wren ME, Thomas A, Korea L: Age of the uterus does not affect pregnancy or implantation rates; A study of egg donation in women of different ages sharing oocytes from the same donor. Hum Reprod, 1997; 12(4): 827–29
25. Sanchez AM, Vanni VS, Bartiromo L et al: Is the oocyte quality affected by endometriosis? A review of the literature. J Ovarian Res, 2017; 10(1): 43
26. Declere W, Osmanagagil K, Verschuere K et al: RCT to evaluate the influence of adjuvant medical treatment of peritoneal endometriosis on the outcome of IVF. Hum Reprod, 2016; 31(9): 2017–23
27. van der Houwen LE, Mijatovic V, Leemhuis E et al: Efficacy and safety of IVF/ICSI in patients with severe endometriosis after long-term pituitary down-regulation. Reprod Biomed Online, 2014; 28(1): 39–46
28. Tesarik J, Mendoza C: Effects of exogenous LH administration during ovarian stimulation of pituitary down-regulated young oocyte donors on oocyte yield and developmental competence. Hum Reprod, 2002; 17(12): 3129–37
29. Baker VL, Brown MB, Luke B et al: Gonadotropin dose is negatively correlated with live birth rate: Analysis of more than 650,000 assisted reproductive technology cycles. Fertil Steril, 2015; 104(5): 1145–52e1141–45
30. Kasapoglu I, Ata B, Uyaniklar O et al: Endometrioma-related reduction in ovarian reserve (ERROR): A prospective longitudinal study. Fertil Steril, 2018; 110(1): 122–27
31. Tao X, Chen L, Ge S, Cai L: Weigh the pros and cons to ovarian reserve before stripping ovarian endometriomas prior to IVF/ICSI: A meta-analysis. PLoS One, 2017; 12(6): e0177426