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## 妊娠期卵巢过度刺激综合征合并卵巢蒂扭转行腹腔镜下保留卵巢术的可行性及安全性研究 \*

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**摘要 目的:**研究妊娠期卵巢过度刺激综合征合并卵巢蒂扭转行腹腔镜下保留卵巢术的可行性及安全性。**方法:**对本院 2010 年 1 月 -2017 年 12 月妇科住院的 9 例妊娠期卵巢过度刺激综合征合并卵巢蒂扭转患者进行腹腔镜下保留卵巢术, 观察其发病时间、卵巢扭转情况、手术时间、术中出血量、术后并发症及妊娠结局等。**结果:**9 例患者术后均无明显并发症发生, 术后随访 9 例患者妊娠结局均良好, 其中, 8 例患者足月产, 1 例早产。**结论:**腹腔镜下妊娠期卵巢过度刺激综合征合并卵巢蒂扭转保留卵巢术对患者维持妊娠及生育功能的影响小、术后并发症低, 是一种安全、可行性强的手术。

**关键词:**妊娠期; 卵巢过度刺激综合征; 卵巢蒂扭转; 腹腔镜下保留卵巢术; 可行性; 安全性

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## Feasibility and Safety of Laparoscopic Lvarian-conserving Surgery for Ovarian Hyperirritant Syndrome Combined with Ovarian Pedicle Torsion during Pregnancy\*

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**ABSTRACT Objective:** To investigate the feasibility and safety of lvarian-conserving surgery for ovarian hyperirritant syndrome combined with ovarian pedicle torsion during pregnancy. **Methods:** laparoscopic lvarian-conserving surgery was performed for 9 cases of ovarian hyperstimulation syndrome complicated with ovarian pedicle torsion during pregnancy, who were admitted to 174th Hospital of Chinese people's Liberation Army from January 2010 to December 2017. The onset time, ovarian torsion, operation time, intraoperative bleeding volume, postoperative complications and pregnancy outcome of the patients were observed. **Results:** There were no obvious complications in 9 patients, and the pregnancy outcomes were good in 9 patients, including 8 patients with full term birth and 1 patient premature birth. **Conclusion:** Laparoscopic lvarian-conserving surgery is a safe and feasible operation for ovarian hyperirritant syndrome combined with ovarian pedicle torsion during pregnancy, with little influence on maintaining pregnancy and reproductive function and low postoperative complications.

**Key words:** During pregnancy; Ovarian hyperstimulation syndrome; Ovarian pedicle torsion; Laparoscopic ovarian-conserving surgery; Feasibility; Safety

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### 前言

卵巢过度刺激综合征 (ovarian hyperstimulation syndrome, OHSS) 引起的卵巢蒂扭转于 1987 年由 Robson 等首次报道, 该病发生率约为 0.1%<sup>[1-3]</sup>, 临床表现主要包括卵巢增大、腹胀、恶心呕吐, 严重时出现血液浓缩、深静脉血栓、肺栓塞、电解质紊乱和肾功能障碍等<sup>[4-6]</sup>。卵巢过度刺激综合征以妊娠后多见, 且常发生于妊娠 12 周内, 但危害严重<sup>[7,8]</sup>。临床处理卵巢过度刺激综合征分为保守及手术治疗, 以手术治疗为主。既往临床医生常草率行患者附件切除术, 其对于年轻的育龄期妇女损失巨

大, 特别是在妊娠期切除卵巢, 对维持妊娠不利<sup>[9-11]</sup>。近年来对妊娠期卵巢过度刺激综合征合并卵巢蒂扭转保留卵巢的手术越来越受到临床医生的重视。本文旨在探索研究妊娠期卵巢过度刺激综合征合并卵巢扭转行腹腔镜下保留卵巢术的可行性及安全性, 现报道如下。

### 1 资料与方法

#### 1.1 一般资料

选取 2010 年 1 月 -2017 年 12 月本院妇科收入院且经腹腔镜探查后决定行卵巢复位手术的 9 例妊娠期卵巢过度刺激

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综合征合并卵巢蒂扭转患者作为研究对象。患者平均年龄( $27 \pm 2.4$ )岁,最大30岁,最小22岁;所有患者主要表现为下腹疼痛,以患侧疼痛尤为明显,腹痛时间最短4h,最长28h。腹痛随体位改变8例,并伴有腹胀、恶心、呕吐、肛门坠胀及发热等症状。行妇科检查和彩超检查等辅助诊断显示双侧卵巢均呈现不同程度的增大,患侧附件包块压痛明显且分隔为多房,其中6例未能探及血流信号,另3例患侧血流信号比对侧减弱。8例行院时彩超已证实为宫内妊娠,1例为移植后11d,促绒毛膜性腺激素(HCG)阳性。

## 1.2 手术方法

(1)术前准备:血常规、肝肾功能、凝血指标、心电图等,均无手术禁忌证。术前给予“间苯三酚注射液”200mg静滴。(2)手术操作步骤:气管内插管全麻,膀胱截石位低臀高位,倾斜角度不宜过低,头低 $15^\circ \sim 30^\circ$ 能暴露手术视野即可。第一穿刺孔适当上移; $\text{CO}_2$ 气腹压力为 $10 \sim 12 \text{ mmHg}$ ;在左下腹选择第二、第三个操作孔穿刺,探查盆腹腔,观察腹腔内有无明显感染迹象、卵巢大小、颜色及质地,计算卵巢扭转周数;超声刀于患侧骨盆入口处打开后腹膜,分离出骨盆漏斗韧带内血管及输尿管,7号丝线双重结扎患侧骨盆漏斗韧带血管;对卵巢进行复位后观察10min,根据卵巢的血供颜色及质地,判断能否保留

卵巢,血运很快完全恢复者,行保留卵巢术。于卵巢表面行卵泡穿刺,缩小卵巢体积;用3/0可吸收线将患侧卵巢缝合3~4针,分别固定于同侧盆壁及子宫后壁。卵巢缝合创面予以止血纱布压迫。尽可能吸尽盆腹腔内游离气体,取出穿刺套管,切口予以3/0可吸收线皮内缝合。(3)术后处理:于术后给予“黄体酮注射液”及“间苯三酚注射液”静滴抑制子宫收缩。术后24h予预防性使用青霉素类抗生素治疗,过敏者选用头孢菌素类抗生素治疗。

## 1.3 随访

9例患者出院后均接受定期随访,随访率为100%。术后每3个月随访1次,直至分娩结束。随访指标有彩超检查卵巢大小、血流情况,孕期并发症及妊娠结局等。

## 2 结果

### 2.1 术中情况

卵巢平均直径( $9.11 \pm 1.65$ )cm,最大12cm、最小7cm;6例扭转发生在右侧,3例发生在左侧;顺时针扭转5例,逆时针扭转4例,平均扭转( $560 \pm 125.49$ )°;2例卵巢基本没有颜色改变,6例卵巢蓝紫色,1例卵巢蓝黑色。详见表1。

表1 9例患者一般情况、卵巢蒂扭转及卵巢大小情况

Table 1 General condition, torsion of ovary pedicle and size of ovary of 9 patients

| Case order | Age<br>(years) | Abdominal pain time<br>(h) | Colour      | Torsional degree              | Torsional part | Ovarian line of<br>affected side(cm) |
|------------|----------------|----------------------------|-------------|-------------------------------|----------------|--------------------------------------|
| 1          | 28             | 12                         | Blue black  | Clockwise( $720^\circ$ )      | Left           | 8.2                                  |
| 2          | 22             | 5                          | Blue purple | Clockwise( $540^\circ$ )      | Right          | 7                                    |
| 3          | 29             | 10                         | Normal      | Anti-clockwise( $360^\circ$ ) | Left           | 11.5                                 |
| 4          | 24             | 28                         | Blue purple | Clockwise( $720^\circ$ )      | Right          | 12                                   |
| 5          | 30             | 12                         | Blue purple | Anti-clockwise( $630^\circ$ ) | Right          | 9.1                                  |
| 6          | 29             | 15                         | Blue purple | Anti-clockwise( $630^\circ$ ) | Left           | 8.3                                  |
| 7          | 28             | 18                         | Blue purple | Clockwise( $540^\circ$ )      | Right          | 9.5                                  |
| 8          | 27             | 4                          | Normal      | Anti-clockwise( $450^\circ$ ) | Right          | 8.5                                  |
| 9          | 30             | 6                          | Blue purple | Clockwise( $450^\circ$ )      | Right          | 7.9                                  |

### 2.2 术后情况

患者全部在腹腔镜下顺利完成手术,无中转开腹。术后保胎9例,其余无特殊处理。9例患者术后均无明显发热、异常腹痛、呼吸困难等。手术时间 $77 \sim 180$ min,平均( $114 \pm 43.49$ )min,术中出血 $5 \sim 50$ mL,平均( $31.11 \pm 18.16$ )mL。术后6h进食,拔除尿管,小便均自解;术后3d复查超声提示患侧卵巢血流信号良好;切口愈合好,无术后并发症。详见表2。

### 2.3 随访结果

9例患者均随访至分娩后1周。术后3月复查超声提示患侧卵巢血流信号均良好;术后无一例发生流产,均顺利妊娠至分娩,其中8例足月分娩,1例于26+3周因胎膜早破早产;阴道分娩6例,剖宫产3例;9例患者新生儿出生后Apgar评分为8~10分,未发现胎儿畸形。详见表2。

## 3 讨论

蒂扭转极少发生于大小正常的卵巢,促排卵后并发OHSS及妊娠是发生卵巢蒂扭转的高危因素<sup>[12,13]</sup>。其主要发生机制为:超促排卵后造成卵巢体积的增大及多个黄素囊肿形成,并发OHSS,使得卵巢的体积更为增大,腹水的产生使得卵巢的活动性加大,扭转率增加;妊娠期因大量分泌内源性hCG,卵巢体积进一步增大,合并OHSS使得持续时间延长<sup>[14,15]</sup>。临床表现主要为突发性腹痛,伴恶心、呕吐等胃肠道不适。体位突然改变常是诱发卵巢蒂扭转的主要因素,本资料中有8例患者突然体位改变是卵巢扭转的诱因,包括洗澡、起床、排尿后起身、翻身等。妇检可发现患侧卵巢扭转蒂部有明显压痛。

彩色多普勒超声是诊断卵巢扭转的一种安全、有效的方法,通过测量卵巢的体积及检测卵巢血供情况为临床诊断提供依据<sup>[16,17]</sup>。血流信号消失常提示卵巢完全性扭转,血流信号减少则提示不全扭转可能。但是,Nizar K等<sup>[18]</sup>报道在卵巢不全扭转的患者中,早期动脉血流信号仍可正常,仅表现为患侧卵巢静

表 2 9 例患者手术时间、术中出血量及术后情况

Table 2 Operative time, intraoperative bleeding volume and postoperative condition of nine patients

| Case order | Operation time(min) | Intraoperative bleeding volume(mL) | Postoperative complications | Postoperative ovarian blood flow | Pregnancy outcome after operation      |
|------------|---------------------|------------------------------------|-----------------------------|----------------------------------|--|
| 1          | 168                 | 20                                 | No                          | Good                             | Full-term normal delivery              |
| 2          | 110                 | 10                                 | No                          | Good                             | Full-term normal delivery              |
| 3          | 83                  | 5                                  | No                          | Good                             | Premature delivery of cesarean section |
| 4          | 75                  | 50                                 | No                          | Good                             | Full-term normal delivery              |
| 5          | 73                  | 50                                 | No                          | Good                             | Full-term normal delivery              |
| 6          | 180                 | 50                                 | No                          | Good                             | Premature delivery of cesarean section |
| 7          | 160                 | 45                                 | No                          | Good                             | Full-term normal delivery              |
| 8          | 100                 | 30                                 | No                          | Good                             | Premature delivery of cesarean section |
| 9          | 77                  | 20                                 | No                          | Good                             | Full-term normal delivery              |

脉血流信号的缺失或减少,因此术前仅凭普通超声术前诊断卵巢血供存在一定的缺陷。随时腹腔镜在妇产科领域的成熟应用,如今腹腔镜检查不仅有助于诊断,还可以术中同时进行治疗,因此腹腔镜探查已成为考虑卵巢蒂扭转时的首选诊治方案;且腹腔镜手术具有创伤小、出血量少、并发症少、术后康复快的优点,不会对妊娠期妇女的妊娠结局产生不良影响。姚莉<sup>[19]</sup>对 34 例行腹腔镜手术治疗的妊娠期患者资料回顾性分析发现,腹腔镜手术治疗妊娠期患者对母体和新生儿影响小,具安全可靠性。程瑶等<sup>[20]</sup>人的报道显示,行腹腔镜手术与开腹手术妊娠期妇女,其妊娠结局及新生儿远期预后等指标等指标组间无明显差异,表明行腹腔镜手术对孕妇妊娠结局不会造成不良影响。

临床医生常根据卵巢颜色黑紫、发病时间长短来决定是否行卵巢切除是不合理的,Oelsner G 等<sup>[21]</sup>的报道表明术后卵巢的功能与术中扭转的附件颜色无关。也有观点认为,卵巢蒂扭转后易形成血栓,为避免卵巢静脉血栓脱落造成肺动脉栓塞而提倡行卵巢切除术;吴夏筠<sup>[22]</sup>等人随机将 40 例卵巢肿瘤蒂扭转患者分为卵巢切除和保留卵巢两组,并选取 20 例腹式卵巢良性肿瘤剥除术患者为参照,结果发现三组凝血酶原时间(PT)、活化部分凝血活酶时间(APTT)及血浆纤维蛋白原(Fg)术前与术后均无显著差异,表明保留卵巢手术对患者凝血功能无明显影响,不会增加血栓的发生率。因此,仅根据卵巢颜色、发病时间及对血栓发生的顾虑来决定卵巢切除并不科学,还需结合扭转周数、松紧、复位后卵巢颜色等来作出进一步判断。

Bider<sup>[23]</sup>在 1989 年首次报道妊娠合并卵巢肿瘤蒂扭转剥除肿瘤后直接行保留卵巢术,患者术后恢复良好,复查卵巢功能均正常。国内张碧云<sup>[24]</sup>等也报道了术中卵巢扭转圈数较少或扭转程度较轻,可以直接行卵巢复位、固定术。吴忧<sup>[25]</sup>等报道 18 例卵巢囊肿蒂扭转腹腔镜下保留卵巢手术,所有患者均完成手术,术中卵巢外观未见明显坏死,术后无肺栓塞、腹膜炎等并发症发生,表明卵巢囊肿蒂扭转患者行腹腔镜保留卵巢手术具有一定的可行性,且具创伤小,并发症少的特点。手术过程中,通过先高位结扎卵巢动静脉,再进行卵巢复位,可保留患者卵巢,同时还可防止扭转卵巢内栓子脱落导致肺动脉栓塞。张斌<sup>[26]</sup>等

对 62 例卵巢囊肿蒂扭转患者行腹腔镜下高位结扎卵巢动静脉,再将扭转的卵巢复位,既保留了卵巢,又避免血栓脱落,整个手术过程中妊娠患者生命体征稳定且无流产发生,无血栓形成或其他感染等。可见,妊娠合并卵巢蒂扭转患者可通过先高位结扎卵巢动静脉,预防肺栓塞,后将患侧卵巢复位并行固定术,保留卵巢,术后母儿均可获得较好的妊娠结局<sup>[27-30]</sup>。

综上所述,结合大量的文献报道以及我们的临床经验来看,腹腔镜下妊娠期卵巢过度刺激综合征合并卵巢蒂扭转保留卵巢术可行、安全。但本研究为我院近年 9 例患者诊治的回顾性分析,病例数少及随访时间短是本研究的局限,在未来的研究中还需要扩大样本量及对患者的远期生存率、复发率进行长期随访。

#### 参 考 文 献(References)

- [1] Shin JJ, Jeong Y, Nho E, et al. Clinical outcomes of frozen embryo transfer cycles after freeze-all policy to prevent ovarian hyperstimulation syndrome[J]. Obstet Gynecol Sci, 2018, 61(4): 497-504
- [2] Namavar Jahromi B MD, Parsanezhad ME MD, Shomali Z MD, et al. Ovarian Hyperstimulation Syndrome: A Narrative Review of Its Pathophysiology, Risk Factors, Prevention, Classification, and Management[J]. Iran J Med Sci, 2018, 43(3): 248-260
- [3] Ozgur S, Oktem M, Altinkaya SO, et al. The effects of resveratrol on ovarian hyperstimulation syndrome in a rat model[J]. Taiwan J Obstet Gynecol, 2018, 57(3): 383-388
- [4] Szkodziak PR, Czuczwar P, Wrona W, et al. Ascites Index - a novel technique to evaluate ascites in ovarian hyperstimulation syndrome: a concept-proof study[J]. Ginekol Pol, 2018, 89(4): 182-188
- [5] 魏代敏,潘烨,石玉华.多囊卵巢综合征辅助生殖治疗策略的优化[J].中华妇产科杂志,2018,65(1): 58-61
- [6] 董朝彤.卵巢过度刺激综合征发病机制研究进展[J].中国计划生育学杂志,2017,25(11): 791-794
- [7] 宁琼,张蒙夏,曾海涛.卵巢过度刺激综合征发病机制及预防[J].中南医学科学杂志,2017,45(2): 189-192
- [8] Abbara A, Islam R, Clarke SA, et al. Clinical parameters of ovarian hyperstimulation syndrome following different hormonal triggers of

- oocyte maturation in IVF treatment[J]. Clin Endocrinol (Oxf), 2018, 88(6): 920-927
- [9] Aghahosseini M, Aleyasin A, Chegini V, et al. Low-dose hCG as trigger day and 35 hr later have different ovarian hyperstimulation syndrome occurrence in females undergoing In vitro fertilization: An RCT[J]. Int J Reprod Biomed (Yazd), 2017, 15(11): 735-740
- [10] Thoreau A, Tran PL, Gabriele M, et al. Ureteral obstruction and ruptured kidney following ovarian hyperstimulation syndrome [J]. J Gynecol Obstet Hum Reprod, 2018, 47(4): 167-169
- [11] 刘伟信,曾琴,徐红.卵巢过度刺激综合征防治研究进展[J].中国计划生育和妇产科,2017,9(1): 20-23, 28
- [12] Asfour V, Varma R, Menon P. Clinical risk factors for ovarian torsion [J]. J Obstet Gynaecol, 2015, 35(7): 721-725
- [13] Dhanda S, Quek ST, Ting MY, et al. CT features in surgically proven cases of ovarian torsion-a pictorial review [J]. Br J Radiol, 2017, 90 (1078): 20170052
- [14] Seyam E, Hefzy E. Laparoscopic ovarian drilling versus GnRH antagonist combined with cabergoline as a prophylaxis against the re-development of ovarian hyperstimulation syndrome[J]. Gynecol Endocrinol, 2018, 34(7): 616-622
- [15] Zech J, Brandao A, Zech M, et al. Elective frozen-thawed embryo transfer (FET) in women at risk for ovarian hyperstimulation syndrome[J]. Reprod Biol, 2018, 18(1): 46-52
- [16] Choux C, Barberet J, Ginod P, et al. Severe ovarian hyperstimulation syndrome modifies early maternal serum beta-human chorionic gonadotropin kinetics, but obstetrical and neonatal outcomes are not impacted[J]. Fertil Steril, 2017, 108(4): 650-658.e2
- [17] Artur Czekierdowski. Comment on: Case report of ovarian torsion mimicking ovarian cancer as an uncommon late complication of laparoscopic supracervical hysterectomy [J]. Prz Menopauzalny, 2017, 16(1): 26-28
- [18] Nizar K, Deutsch M, Filmer S, et al. Doppler studies of the ovarian venous blood flow in the diagnosis of adnexal torsion[J]. J Clin Ultrasound, 2009, 37(8): 436-439
- [19] 姚莉. 妊娠期附件行腹腔镜手术的可行性及对妊娠结局的影响分析[J]. 国际医药卫生导报, 2017, 23(12): 1902-1904
- [20] 程瑶,张晓玲.腹腔镜手术治疗妊娠期妇科疾病的临床分析[J].江西医药, 2017, 52(9): 888-890, 910
- [21] Oelsner G, Cohen SB, Soriano D, et al. Minimal surgery for the twisted ischemic adnexa can preserve ovarian function [J]. Hum Reprod, 2003, 18(12): 2599-2602
- [22] 吴夏筠,黄宏伟.保留卵巢的卵巢肿瘤蒂扭转手术对患者凝血功能的影响[J].岭南急诊医学杂志, 2017, (4): 388-389
- [23] Bider D, Ben-Rafael Z, Goldenberg M, et al. Pregnancy outcome after unwinding of twisted ischaemic-haemorrhagic adnexa[J]. Br J Obstet Gynaecol, 1989, 96(4): 428
- [24] 张碧云,王蓓,胡炳真.妊娠合并卵巢囊肿蒂扭转手术治疗 18 例临床分析[J].现代实用医学, 2011, 23(4): 451-452
- [25] 吴忧,胡君,朱丽荣.卵巢囊肿蒂扭转患者腹腔镜下保留卵巢手术 18 例临床分析[J].中国妇产科临床杂志, 2016, 17(4): 302-304
- [26] 张斌,郭艳,李静静.卵巢囊肿蒂扭转保留卵巢腹腔镜手术 62 例报告[J].中国微创外科杂志, 2014, 19(7): 600-602
- [27] 黄晶,张明铭,邓曦和,等.腹腔镜下卵巢囊肿蒂扭转复位手术对卵巢储备功能影响[J].医学临床研究, 2018, 35(3): 435-437
- [28] 孙媛媛.妊娠合并卵巢囊肿蒂扭转的诊断和处理[J].中国微创外科杂志, 2017, 17(11): 1039-1041
- [29] 王萍.卵巢囊肿蒂扭转手术中保留卵巢的治疗效果及安全性探究[J].实用妇科内分泌电子杂志, 2018, 4(12): 23, 26
- [30] 胡志芳,郑建军.保留患侧输卵管及卵巢的良性卵巢肿瘤蒂扭转复位及肿瘤剥除术临床分析 [J]. 医学临床研究, 2017, 34(10): 1930-1932

(上接第 1250 页)

- [21] Martinova L, M S Field, J L Finkelstein, et al. Maternal dietary uridine causes, and deoxyuridine prevents, neural tube closure defects in a mouse model of folate-responsive neural tube defects[J]. Am J Clin Nutr, 2015, 101(4): 860-869
- [22] Lucock M, Z Yates, L Boyd, et al. Vitamin C-related nutrient-nutrient and nutrient-gene interactions that modify folate status[J]. Eur J Nutr, 2013, 52(2): 569-582
- [23] Huang Y, Y He, X Sun, et al. Maternal high folic acid supplement promotes glucose intolerance and insulin resistance in male mouse offspring fed a high-fat diet[J]. Int J Mol Sci, 2014, 15(4): 6298-6313
- [24] Duplessis M, H Lapierre, B Ouattara, et al. Whole-body propionate and glucose metabolism of multiparous dairy cows receiving folic acid and vitamin B12 supplements [J]. J Dairy Sci, 2017, 100(10): 8578-8589
- [25] Salari P, M Abdollahi, R Heshmat, et al. Effect of folic acid on bone metabolism: a randomized double blind clinical trial in postmenopausal osteoporotic women[J]. Daru, 2014, 22: 62
- [26] Crider K S, L B Bailey, R J Berry. Folic acid food fortification-its history, effect, concerns, and future directions [J]. Nutrients, 2011, 3 (3): 370-384
- [27] 翁玉蓉,房静远,孙丹凤,等.叶酸受体  $\alpha$  在胃癌组织中的表达及其与叶酸、亚甲基四氢叶酸还原酶基因多态性以及胃癌生物学行为的关系[J].胃肠病学, 2006, 11(4): 198-201
- [28] McGlynn A P, G R Wasson, S L O'Reilly, et al. Low colonocyte folate is associated with uracil misincorporation and global DNA hypomethylation in human colorectum[J]. J Nutr, 2013, 143(1): 27-33
- [29] Chang S, L Wang, Y Guan, et al. Long interspersed nucleotide element-1 hypomethylation in folate-deficient mouse embryonic stem cells[J]. J Cell Biochem, 2013, 114(7): 1549-1558
- [30] Wang L, S Chang, Z Wang, et al. Altered GNAS imprinting due to folic acid deficiency contributes to poor embryo development and may lead to neural tube defects [J]. Oncotarget, 2017, 8 (67): 110797-110810
- [31] van Uitert E M, R P Steegers-Theunissen. Influence of maternal folate status on human fetal growth parameters [J]. Mol Nutr Food Res, 2013, 57(4): 582-595
- [32] Farrell C J, S H Kirsch, M Herrmann. Red cell or serum folate: what to do in clinical practice? [J]. Clin Chem Lab Med, 2013, 51 (3): 555-569
- [33] Marchetta C M, H C Hamner. Blood folate concentrations among women of childbearing age by race/ethnicity and acculturation, NHANES 2001-2010[J]. Matern Child Nutr, 2016, 12(1): 39-50
- [34] Crider K S, O Devine, L Hao, et al. Population red blood cell folate concentrations for prevention of neural tube defects: Bayesian model [J]. BMJ, 2014, 349: g4554