doi: 10.13241/j.cnki.pmb.2019.11.023

丙种球蛋白联合地屈孕酮治疗复发性流产的效果及对患者免疫功能和血清炎症因子水平的影响*

邰迎春 赵爱妮△ 王 晶 赵丽华 孙丽娜

（陕西中医药大学附属医院妇产科 陕西 咸阳 712000）

摘要 目的：探讨丙种球蛋白联合地屈孕酮治疗复发性流产的效果及对患者免疫功能和血清炎症因子水平的影响。**方法：**选择2016年1月-2017年12月我院收治的82例复发性流产患者为研究对象，将其随机分为两组。对照组采用单纯口服地屈孕酮，每次10 mg，每天2次；观察组在对照组基础上联合静脉滴注丙种球蛋白500 mg/(kg·d)。比较两组治疗前后的血清白介素-6(IL-6)、肿瘤坏死因子-α(TNF-α)以及白介素-10(IL-10)水平，$CD4^+/CD8^+$、$CD8^+$以及$CD4^+$及保胎成功率。**结果：**治疗后，观察组治愈14例，有效18例，无效9例，治疗有效率为78.05%(32/41)，明显高于对照组[60.98%(25/41)](P<0.05)；两组治疗后的血清TNF-α、$CD8^+$水平较治疗前明显降低(P<0.05)，血清IL-6、IL-10、$CD4^+/CD8^+$以及$CD4^+$水平较治疗前明显升高(P<0.05)，且观察组血清TNF-α、$CD8^+$水平明显低于对照组(P<0.05)，血清IL-6、IL-10、$CD4^+/CD8^+$以及$CD4^+$水平明显高于对照组(P<0.05)。观察组的保胎成功率为82.93%(34/41)，明显高于对照组[31.71%(13/41)](P<0.05)。**结论：**丙种球蛋白联合地屈孕酮可以有效增强复发性流产患者体内的免疫功能，减少调节炎症因子的表达，提高保胎成功率.

关键词：丙种球蛋白；地屈孕酮；复发性流产；疗效；血清细胞因子；免疫功能

中图分类号：R714.21 **文献标识码：**A **文章编号：**1673-6273(2019)11-2112-04

Effect of Gamma Globulin Combined with Megestrol Acetate on the Recurrent Spontaneous Abortion and Its Influence on the Immune Function and Serum Inflammatory Cytokines Levels*

TAI Ying-chun, ZHAO Ai-ni△, WANG Jing, ZHAO Li-hua, SUN Li-na

(Gynaecology and obstetrics department, Affiliated Hospital of Shaanxi University of traditional Chinese Medicine, Xianyang, Shaanxi, 712000, China)

ABSTRACT Objective: To investigate the effect of gamma globulin combined with megestrol acetate in the treatment of recurrent spontaneous abortion and its influence on immune function and serum inflammatory factors. **Methods:** 82 patients with recurrent spontaneous abortion admitted to our hospital from January 2016 to December 2017 were randomly divided into two groups. The control group was treated with oral megestrol acetate only, and the observation group was given intravenous gamma globulin [500 mg/ (kg·d)] on the basis of the control group. The serum levels of IL-6, TNF-α and IL-10, $CD4^+/CD8^+$, $CD8^+$, $CD4^+$, and the success rate of pregnancy preservation were compared between the two groups. **Results:** After treatment, 14 cases were cured, 18 cases were effective and 9 cases were ineffective in the observation group. The effective rate was 78.05%(32/41), which was significantly higher than that in the control group [60.98% (25/41)](P<0.05). And the levels of serum TNF-α and $CD8^+$ in the two groups were significantly lower than those be- fore treatment (P<0.05), the levels of serum IL-6, IL-10, $CD4^+/CD8^+$ and $CD4^+$ were significantly higher than those before treatment (P<0.05). The levels of serum TNF-α and $CD8^+$ in the observation group were significantly lower than those in the control group (P<0.05). The levels of serum IL-6, IL-10, $CD4^+/CD8^+$ and $CD4^+$ in the observation group were significantly higher than those in the control group (P<0.05). The success rate of the observation group was 82.93%(34/41), which was significantly higher than that of the control group [31.71% (13/41)] (P<0.05). **Conclusion:** Gamma globulin combined with megestrol acetate can effectively enhance the immune function of patients with recurrent spontaneous abortion, reduce the expression of inflammatory factors, and improve the success rate of pregnancy preservation.

Key words: Gamma globulin; Megestrol acetate; Recurrent spontaneous abortion; Curative effect; Serum cytokines; Immunologic function

Chinese Library Classification(CLC): R714.21 Document code: A

Article ID:1673-6273(2019)11-2112-04

* 基金项目：陕西省自然科学基础研究计划项目(2010JQ4008)

作者简介：邰迎春(1974-)，女，硕士，副主任医师，研究方向：子痫前期，复发性流产早产，妊娠期血栓前状态、肺栓塞的防治，电话：13892967000，E-mail：Taiyingchun1974@163.com

△ 通讯作者：赵爱妮(1974-)，女，本科，副主任医师，研究方向：流产早产，电话：13991008263，E-mail：Taiyingchun1974@163.com

(收稿日期：2018-11-07 接受日期：2018-11-30)

前言

随着环境污染的日益加剧和社会竞争压力的加大,复发性流产的发病率呈逐年升高的趋势,对患者及家庭造成严重的压力,不利于社会以及家庭的和谐稳定。复发性流产的发病机制比较复杂,主要与遗传因素、环境理化因素、免疫因素、感染因素、解剖因素和内分泌因素紧密相关[1-3],临床上主要采取黄体酮治疗。虽然黄体酮对黄体功能不全导致的流产具有较好的治疗效果,但对病因不明或者其他病因引发的复发性流产的疗效并不佳[4,5]。

地屈孕酮能促进子宫内膜转变为完全的分泌相,有效预防由雌激素导致的子宫内膜增生以及癌变[6]。有研究显示复发性流产与免疫调节作用和自身免疫抑制密切相关[7]。丙种球蛋白作为人免疫球蛋白中最主要的一种成分,是临床上广泛使用的免疫抑制剂,由于其包含有健康人群血清所需要的各种抗体,能显著增强机体的免疫功能,使患者的病情获得迅速改善[8]。本研究将丙种球蛋白以及地屈孕酮联合使用,以探讨其对复发性流产的效果及对患者血清细胞因子的影响,现报道如下。

1 资料与方法

1.1 一般资料

选择 2016 年 1 月 -2017 年 12 月我院收治的 82 例复发性流产患者,诊断标准:反复自然流产超过 2 次,无死产、死胎和活产史;性激素、空腹血糖、黄体功能等内分泌检查结果均为正常;封闭抗体检查结果为阴性,抗子宫内膜抗体以及抗精子抗体检查结果为阴性;子宫内膜正常,排卵正常,丈夫的精液正常。排除标准:异位妊娠患者,子宫发育异常、月经周期异常和子宫颈功能异常患者,染色体异常、血型不符、遗传因素、解剖因素、免疫性因素、感染因素等导致复发性流产的患者。将所有患者随机分为两组。观察组 41 例,年龄 23~40 岁,平均(28.45± 4.37) 岁;流产时孕周 5~12 w,平均(7.38± 1.29) w;清宫次数 1~5 次,平均 (1.73± 0.52) 次;自然流产次数 2~6 次,平均 (3.57± 1.09) 次;体重指数 20~29 kg/m^2,平均 (24.38± 2.75) kg/m^2。对照组 41 例,年龄 23~40 岁,平均(28.57± 3.29) 岁;流产时孕周 5~12 w,平均(7.24± 1.05) w;清宫次数 1~5 次,平均(1.76± 0.49) 次;自然流产次数 2~6 次,平均(3.42± 0.97) 次;体重指数 20~29 kg/m^2,平均(24.53± 2.69) kg/m^2。两组患者的年龄、流产时孕周、清宫次数、自然流产次数以及体重指数相比差异均无统计学意义(P>0.05),具有可比性。所有反复性流产患者均签署了知情同意书。

1.2 治疗方法

对照组单纯口服地屈孕酮(批号:H20110075,生产厂家:荷兰 Solvay Pharmaceuticals B.V.,规格:10 mg),每次 10 mg,每天 2 次,连续给药至妊娠 12 w;观察组联合静脉滴注丙种球蛋白(批号:国药准字 S20043007,生产厂家:深圳市卫武光明生物制品有限公司,规格:5.0 g(5 %,100 mL)/ 瓶)500 mg/(kg·d),每周连续给药 3 d,共给药至 11~14 w。在进行治疗的过程中,给予心理辅导,当妊娠成功后应禁止性生活。

1.3 观察指标

比较两组的临床治疗有效率:① 治愈:患者的妊娠时间 > 20 w,而且孕 20 w 时,B 超检查结果表明胎儿正常发育,伴随的症状明显改善或基本消失;② 有效:患者的妊娠时间超过以前流产的最长孕周,但是未超过 20 周即发生流产,伴随的症状有所缓解;③ 无效:妊娠时间尚未超过以前流产的最长孕周即出现流产,伴随的症状无任何好转甚至加重。

分别在治疗前和治疗后,于清晨采集 5 mL 静脉血,使用 ELISA 双抗体夹心法测定血清 IL-6、TNF-α 以及 IL-10 水平,试剂盒均购自北京奇松生物科技有限公司。

采用美国 BD Accuri C6 流式细胞仪检测两组治疗前后的 CD4$^+$/CD8$^+$、CD8$^+$ 以及 CD4$^+$ 等细胞免疫功能。

记录两组的早产胎儿存活率、足月产率、早产胎儿死亡率、保胎成功率以及流产率。

1.4 统计学分析

采用 SPSS19.0 软件进行数据分析,计量资料以 $\bar{x}\pm s$ 表示,组间和组内对比采用单因素方差分析和 t 检验,组间率的比较用 χ^2 检验,以 P<0.05 表明差异有统计学意义。

2 结果

2.1 两组临床疗效对比

治疗后,观察组治愈 14 例,有效 18 例,无效 9 例,治疗有效率为 78.05%(32/41),明显高于对照组 [60.98%(25/41)](P<0.05),见表 1。

表 1 两组临床疗效的比较[例(%)]

Table 1 Comparison of the clinical effect between two groups [n(%)]

Group	n	Cure	Valid	Invalid	The total effect rate
Observation group	41	14 (34.15)	18 (43.90)	9 (21.95)	78.05*
Control group	41	10 (24.39)	15 (36.58)	16 (39.02)	60.98

Note: Compared with the control group, *P<0.05.

2.2 两组治疗前后血清炎症因子水平对比

两组治疗后的血清 TNF-α 水平均较治疗前明显降低(P<0.05),且观察组显著低于对照组血清(P<0.05);两组血清 IL-6 以及 IL-10 水平均较治疗前明显升高(P<0.05),且观察组明显高于对照组(P<0.05),见表 2。

2.3 两组治疗前后免疫功能指标对比

两组治疗后的 CD4$^+$/CD8$^+$ 以及 CD4$^+$ 水平均较治疗前明显升高(P<0.05),CD8$^+$ 水平较治疗前明显降低(P<0.05),且观察组 CD4$^+$/CD8$^+$ 以及 CD4$^+$ 水平明显高于对照组 (P<0.05),而 CD8$^+$ 水平显著高于对照组,见表 3。

2.4 两组保胎成功率对比

两组早产胎儿存活率比较,差异无统计学意义(P>0.05)。观察组足月产率和保胎成功率均显著高于对照组(P<0.05),早产胎儿死亡率和流产率均显著低于对照组(P<0.05)。见表 4。

3 讨论

复发性流产作为一种产科常见的并发症,是指女性连续出现 2 次或大于 2 次的自然流产,但不包含生化妊娠[9,10]。复发性

表 2 两组治疗前后血清炎症因子水平对比($\bar{x}\pm s$)

Table 2 Comparison of the Serum inflammatory factor levels between two groups before and after treatment ($\bar{x}\pm s$)

Groups	n	IL-6 (ng/L)		IL-10 (pg/mL)		TNF-α (pg/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	41	3.82± 0.45	6.24± 0.59*#	7.31± 1.49	11.57± 2.34*#	151.94± 16.25	49.33± 6.27*#
Control group	41	3.81± 0.52	4.73± 0.62#	7.32± 1.25	9.32± 2.28#	152.58± 17.32	85.29± 7.41#

Note: Compared with the control group, *P<0.05; compared with before treatment, #P<0.05.

表 3 两组治疗前后免疫功能指标对比($\bar{x}\pm s$)

Table 3 Comparison of the immune index between two groups before and after treatment ($\bar{x}\pm s$)

Group	n	$CD4^+/CD8^+$		$CD8^+$(%)		$CD4^+$(%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	41	1.03± 0.15	1.58± 0.34*#	30.54± 6.25	23.41± 5.19*#	29.16± 6.27	37.28± 8.14*#
Control group	41	1.04± 0.16	1.32± 0.27#	30.31± 6.38	26.25± 6.38#	29.35± 6.44	33.53± 7.64#

Note: Compared with the control group, *P<0.05; compared with before treatment, #P<0.05.

表 4 两组保胎成功率对比[例(%)]

Table 4 Comparison of the success rate of embryo protection between two groups [n(%)]

Groups	n	Preterm fetal survival rate	Full term yield	Premature birth death rate	Success rate of embryo protection	Abortion rate
Observation group	41	6(14.63)	28(68.29)*	3(7.32)*	34(82.93)*	4(9.76)*
Control group	41	6(14.63)	7(17.07)	13(31.71)	13(31.71)	16(39.02)

Note: Compared with the control group, *P<0.05.

流产不仅会对妇女的身体健康和生育健康造成严重的危害，还会对其家庭带来极大的压力和精神痛苦。临床上常常采用肌肉注射人绒毛膜促性腺激素以及黄体酮进行治疗，但是其保胎效果并不满意，而且极易导致硬结、皮疹以及感染等不良反应。因而，探索复发性流产的有效治疗策略具有重要的临床价值。封闭抗体缺乏以及 T 辅助淋巴细胞亚群平衡失调是引发复发性流产的主要原因。免疫疗法是治疗复发性流产的主要疗法，即通过诱导母体对胚胎出现免疫耐受，有效发挥确保胚胎存活的效果[11-13]。地屈孕酮作为一种口服孕激素，具有副作用低、用药方便、易于被患者所接受等优点，其可以诱导淋巴细胞生成阻滞因子，对花生四烯酸的释放进行明显的抑制，还可以诱导机体合成封闭抗体，抑制 NK 细胞的活性，从而有助于维持妊娠[14-16]。

丙种球蛋白作为一种临床上广泛使用的包括广谱抗细菌、病毒以及其他病原菌的免疫球蛋白 G 抗体的免疫增强剂，可以有效发挥免疫调节于免疫替代的双重治疗效果，静脉滴注给药后能快速升高血液免疫球蛋白 G 水平[17-19]。本研究结果显示丙种球蛋白联合地屈孕酮治疗的复发性流产的有效率明显高于单纯口服地屈孕酮者，表明丙种球蛋白联合地屈孕酮可以提高复发性流产患者的疗效。有研究表明免疫因素是导致复发性流产发生的一个重要因子[20,21]。丙种球蛋白是临床上治疗丙种球蛋白缺乏症以及免疫缺陷病的一种免疫疗法，可以通过把免疫球蛋白所包含的大量抗体输送至患者体内，发挥免疫保护作用[22,23]。

IL-6 可以明显促进机体免疫细胞抗体的产生，有助于胚胎的发育以及卵泡的着床，对母体的免疫排斥反应进行较为显著的抑制，从而提高妊娠的成功率[24-26]。TNF-α 可以对胎盘滋养层细胞的增殖分化造成影响，妨碍胚胎着床，损伤蜕膜血管，导致妊娠不良反应的发生[27,28]。IL-10 作为人体较为重要的一种抗炎因子，可以有效抑制母体的免疫排斥反应，具有维持妊娠以及保护胎儿的效果[29]。有研究发现，复发性妊娠患者的血清 IL-10 水平显著低于正常妊娠女性[30]。产妇血清 IL-10 水平的降低不仅会大大减弱母体的抗炎作用，使机体的免疫失衡，诱发流产，还可以引发妊娠高血压疾病和早产等妊娠并发症。本研究结果显示丙种球蛋白联合地屈孕酮治疗的复发性流产者治疗后血清 TNF-α、$CD8^+$ 水平明显低于单纯口服地屈孕酮者，血清 IL-6 以及 IL-10 水平、$CD4^+/CD8^+$ 以及 $CD4^+$ 明显高于单纯口服地屈孕酮者，表明丙种球蛋白联合地屈孕酮可以有效调节复发性流产患者体内的免疫状态。丙种球蛋白联合地屈孕酮治疗的复发性流产者的保胎成功率为 82.93%，明显高于单纯口服地屈孕酮者，表明丙种球蛋白联合地屈孕酮在保护胚胎、提高复发性流产患者正常妊娠率方面具有明显的临床优势。

在治疗复发性流产患者的过程中，必须注意以下几个事项：① 指导习惯性流产患者必须定期按时到医院开展相关方面的检查，且严格遵照医嘱服用药物进行治疗；② 当孕妇出现流产后，心情应当尽量保持放松状态，短时间内必须禁止一切的性生活；③ 孕妇必须尽可能地避免到肺炎、伤寒以及流行性感冒等区域进行活动，不要被动或主动吸烟，禁止到人群拥挤的公共场所进行活动，以免对胎儿造成不良影响；④ 当孕妇再次怀孕时，应禁止进行重体力的活动，特别是提举重物以及用力大便，在妊娠的早期禁止接触 X 线、超声波以及放射性同位素，以避免胎儿出现畸形。

综上所述，丙种球蛋白联合地屈孕酮可以有效增强复发性流产患者体内的免疫功能，减少调节炎症因子的表达，提高保胎成功率。

参 考 文 献(References)

[1] Dong X, Long Y, Hui W. miR-520 promotes DNA-damage-induced trophoblast cell apoptosis by targeting PARP1 in recurrent spontaneous abortion (RSA) [J]. Gynecological Endocrinology, 2017, 33(4): 274-278

[2] Sun Q, Zhang X L. Research on apoptotic signaling pathways of recurrent spontaneous abortion caused by dysfunction of trophoblast infiltration [J]. European Review for Medical & Pharmacological Sciences, 2017, 21(3 Suppl): 12

[3] Ramu D, Venkatesan V, Paul S F D, et al. Genetic variation in matrix metalloproteinase MMP2, and MMP9, as a risk factor for idiopathic recurrent spontaneous abortions in an Indian population[J]. Journal of Assisted Reproduction & Genetics, 2017, 34(2): 1-5

[4] Barišić A, Pereza N, Hodžić A, et al. A Single Nucleotide Polymorphism of DNA methyltransferase 3B gene is a risk factor for recurrent spontaneous abortion [J]. American Journal of Reproductive Immunology, 2017, 78(953-963): e12765

[5] Li J, Xu D, Li H L. Evaluation of failed immunotherapy among patients with negative APLA recurrent spontaneous abortion by serum anticardiolipin antibodies and mononuclear cell of Tim-1[J]. European Review for Medical & Pharmacological Sciences, 2017, 21(5): 908

[6] Lee H J, Park T C, Kim J H, et al. The Influence of Oral Dydrogesterone and Vaginal Progesterone on Threatened Abortion: A Systematic Review and Meta-Analysis [J]. BioMed Research International, 2017, 2017(9): 1-10

[7] Quan X, Yang X. Correlation between unexplained recurrent spontaneous abortion with $CD4^{+}CD25^{+}$ regulatory T-cell and killer cell immunoglobulin-like receptor levels [J]. Experimental & Therapeutic Medicine, 2017, 14(2): 1459-1462

[8] Barmettler S, Otani I M, Minhas J, et al. Gastrointestinal Manifestations in X-linked Agammaglobulinemia [J]. Journal of Clinical Immunology, 2017, 37(3): 287-294

[9] Wang G, Sun J. Interactive Effects of Snps Located Within CD28/B7Pathway and Environment on Susceptibility to Recurrent Spontaneous Abortion[J]. Cellular Physiology & Biochemistry, 2017, 43(6): 2185-2199

[10] Ning L, Li S, Wang Y, et al. Decreased expression of WNT2 in villi of unexplained recurrent spontaneous abortion patients may cause trophoblast cell dysfunction via downregulated Wnt/β- catenin signaling pathway[J]. Cell Biology International, 2017, 41(8): 898

[11] Nonaka T, Tominaga M, Takahashi M, et al. Immunotherapy with paternal lymphocytes for patients with unexplained recurrent abortion and association with blocking antibodies: Comparison between patient groups with primary and secondary unexplained recurrent abortion[J]. Journal of Reproductive Medicine, 2018, 63(3): 285-291

[12] Petrányi G, Simsa P, á. Padányi, et al. Intravenous immunoglobulin and partner specific thrombocyte transfusion immunotherapy in selected cases of recurrent miscarriage [J]. Journal of Reproductive Medicine, 2018, 63(1): 13-20

[13] Zhao X, Jiang Y, Wang L, et al. Advances in Understanding the Immune Imbalance between T-Lymphocyte Subsets and NK Cells in Recurrent Spontaneous Abortion[J]. Geburtshilfe Und Frauenheilkunde, 2018, 78(07): 677-683

[14] Healy M, Patounakis G, Zanelotti A, et al. Does premature elevated progesterone on the day of trigger increase spontaneous abortion rates in fresh and subsequent frozen embryo transfers [J]. Gynecological Endocrinology, 2017, 33(6): 472-475

[15] Khalid A, Qureshi H J, Nazir S, et al. Effect of second hand smoke exposure on serum estradiol and progesterone levels in women having first trimester spontaneous abortions [J]. Pakistan Journal of Medical & Health Sciences, 2017, 11(1): 163-167

[16] Moffuouk S, Yahia M, Mouffouk C, et al. Accuracy of serum markers, progesterone and vitamins measurements for early screening of abortions in the eastern region of Algeria (Batna)[J]. 2018, 90(2): 126-129

[17] Weinberger T, Maglione P, Cunningham-Rundles C. Differences in Pulmonary Complications in Common Variable Immunodeficiency and X-Linked Agammaglobulinemia[J]. Journal of Allergy & Clinical Immunology, 2017, 139(2): AB111

[18] Benali M, Yang J, Chan K W, et al. Homozygous TCF3 mutation is associated with severe hypogammaglobulinemia and B-cell acute lymphoblastic leukemia [J]. J Allergy Clin Immunol, 2017, 140(4): 1191

[19] Pac M, Bernatowska E A, Kierkuś J, et al. Gastrointestinal disorders next to respiratory infections as leading symptoms of X-linked agammaglobulinemia in children-34-year experience of a single center[J]. Archives of Medical Science Ams, 2017, 13(2): 412-417

[20] Li J, Xu D, Li H L. Evaluation of failed immunotherapy among patients with negative APLA recurrent spontaneous abortion by serum anticardiolipin antibodies and mononuclear cell of Tim-1[J]. European Review for Medical & Pharmacological Sciences, 2017, 21(5): 908

[21] Ye S L, Gu X K, Tao L Y, et al. Efficacy of Different Treatment Regimens for Antiphospholipid Syndrome-related Recurrent Spontaneous Abortion[J]. Chinese Medical Journal, 2017, 130(12): 1395-1399

[22] Eaa C, Giardino G, Worth A, et al. Risk factors predisposing to the development of hypogammaglobulinemia and infections post-Rituximab[J]. International Reviews of Immunology, 2017, 36(6): 1-8

[23] Kempf B, Edgar J D, Mc C C, et al. Nitazoxanide Is an Ineffective Treatment of Chronic Norovirus in Patients With X-Linked Agammaglobulinemia and May Yield False-Negative Polymerase Chain Reaction Findings in Stool Specimens [J]. Journal of Infectious Diseases, 2017, 215(3): 486-487

[24] Jing S, Liu F, Zhai J, et al. Alteration of Th17 and Foxp3+ regulatory T cells in patients with unexplained recurrent spontaneous abortion before and after the therapy of hCG combined with immunoglobulin [J]. Experimental & Therapeutic Medicine, 2017, 14(2): 1114-1118

[25] Zhu L, Chen H, Liu M, et al. Treg/Th17 Cell Imbalance and IL-6 Profile in Patients With Unexplained Recurrent Spontaneous Abortion[J]. Reproductive Sciences, 2017, 24(6): 882-890

[26] Chen Z, Li Y X, Fu H J, et al. Hepatitis B Virus Core Antigen Stimulates IL-6 Expression via p38, ERK and NF-κB Pathways in Hepatocytes[J]. Cellular Physiology & Biochemistry International Journal of Experimental Cellular Physiology Biochemistry & Pharmacology, 2017, 41(1): 91

[27] Li S, Wang L, Xing Z, et al. Expression level of TNF-α in decidual tissue and peripheral blood of patients with recurrent spontaneous abortion [J]. Central-European Journal of Immunology, 2017, 42(2): 156-160

[28] Rahmani S A, Paknejad Z, Mohammadkhanlou M. The effects of tumor necrosis factor-α (TNF-α) and IL-1 receptor antagonist (IL-1Ra) polymorphisms on recurrent abortion in Azari women[J]. Ginekologia Polska, 2017, 88(8): 421-427

[29] Blois S M, Freitag N, Tiradogonzález I, et al. NK cell-derived IL-10 is critical for DC-NK cell dialogue at the maternal-fetal interface[J]. Scientific Reports, 2017, 7(1): 2189

[30] Vidyadhari M, Sujatha M, Krupa P, et al. Haplotype analysis of IL-10 gene polymorphism in couples with spontaneous abortions and aborted fetuses[J]. Immunologic Research, 2017, 65(4): 853-861