

多胎及多胎合并单绒毛膜双胎减胎后妊娠结局的分析

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摘要 目的 探讨多胎及多胎合并单绒毛膜双胎妊娠行孕早期经阴道多胎妊娠负压抽吸减胎术的安全性及对妊娠结局的影响。**方法** 收集350例孕早期多胎妊娠减胎术者及297例同期未减胎者的临床资料,分析不同减胎对象妊娠结局的差异。**结果** 减胎术后各组间完全流产率、围产儿严重并发症发生率、出生缺陷、男女出生性别百分率比较,差异均无统计学意义($P > 0.05$)。非单绒毛膜性多胎组中,减为单胎组相对于减为双胎组,早产率、低体重儿出生率下降,平均出生体重升高,差异有统计学意义($P < 0.05$);减胎组与对照组比较,早产率、低出生体重儿出生率差异均无统计学意义($P > 0.05$)。减单绒毛膜双胎孕囊组相对于保留单绒毛膜双胎孕囊组,早产率及低出生体重儿出生率降低,平均出生体重升高,差异有统计学意义($P < 0.05$)。**结论** 孕早期经阴道负压抽吸减胎术可安全、有效的改善多胎及多胎合并单绒毛膜双胎的妊娠结局;选择单绒毛膜双胎孕囊做为减胎对象且减为单胎可获得更好的妊娠结局。

关键词 绒毛膜性;多胎妊娠;负压抽吸减胎术;妊娠结局

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近年来随着促排卵药物的应用及人类辅助生殖技术(assisted reproductive technology, ART)的发展,导致多胎妊娠发生率呈迅速增长的趋势^[1]。多胎妊娠明显增加了早产、流产、低出生体重儿、出生缺陷等风险,严重影响母婴结局。多胎妊娠减胎术(multifetal pregnancy reduction, MPR)作为控制多胎妊娠的重要补救措施已被广泛应用,有效降低了多胎妊娠并发症及母婴风险^[2]。有关减胎有效性安全性的报道较多,该研究进一步探讨不同绒毛膜性多胎行经阴道减胎术对妊娠结局的影响。

1 材料与方法

1.1 病例资料 搜集2006年6月~2014年6月,在安徽医科大学第一附属医院生殖中心行辅助生殖治疗后获得多胎妊娠的患者中接受孕早期经阴道MPR的350例患者的临床资料;孕妇年龄22~41(30.28±3.63)岁;获得妊娠方式主要为体外受精-胚胎移植(*in vitro* fertilization and embryo transfer, IVF-ET)和单精子卵胞浆内注射(intracytoplasmic sperm injection, ICSI);根据绒毛膜性的不同分为:①非单绒毛膜性多胎减胎组:双胎减为单胎(2-1组)

left ventricular end-systolic diameter (LVESD) were compared among three groups. The correlation of plasma BNP and echocardiographic parameters was also evaluated. Most importantly, the abilities of plasma BNP and LVEF in the diagnosis of patients with NYHA III ~ IV grade were analyzed. **Results** The age of DCM patients with NYHA II, III and IV grade was gradually increased ($P < 0.05$), while there was no significant difference in sex, smoking, drinking and complications including hypertension, hyperlipidemia and diabetes mellitus in three groups. The plasma level of BNP was highest in patients with NYHA IV grade that was increased to >3-fold compared to patients with NYHA II grade ($P < 0.001$). LA was augmented in NYHA IV grade patients compared to II grade group ($P < 0.05$), whereas no significant difference was detected in LVEF, LVEDD and LVESD in NYHA II ~ IV grade patients. Linear correlation analysis revealed that the plasma BNP was not correlated to LVEF, LA, LVEDD or LVESD. To assess severe heart failure, the receiver operating characteristic (ROC) curve analysis demonstrated that plasma BNP ≥ 521.5 pmol/L was the best threshold value in the identification of in NYHA III and IV grade patients (AUC = 0.888, $P < 0.001$), but not LVEF (AUC = 0.408). **Conclusion** The increased plasma concentration of BNP may be of importance to determine cardiac function in DCM patients with CHF, and it is also a crucial parameter to evaluate severe heart failure (NYHA III and IV grade).

Key words dilated cardiomyopathy; heart failure; brain natriuretic peptide

78例,三胎减为双胎(3-1组)176例,三胎减为单胎(3-2组)44例;②合并单绒毛膜性多胎减胎组:减单绒毛膜双胎孕囊组为45例,其中4胎组(4-单卵双胎组)10例,3胎组(3-单卵双胎组)35例,保留单绒毛膜双胎孕囊组(留单卵双胎组)7例;③对照组:双胎中未减胎患者(对照双胎组)197例,单胎患者(对照单胎组)100例。

1.2 减胎方法 患者及家属签署《减胎知情同意书》,术前准备完善,于移植后5~7周,阴道超声引导下,选择靠近宫颈便于穿刺或原始心管搏动较弱、胎芽小的孕囊做为减胎对象;合并单绒毛膜双胎孕囊时,选取单绒毛膜双胎孕囊作为减胎对象,当仅存两个单绒毛膜双胎孕囊或非单绒毛膜双胎孕囊发育不良时,保留一个单绒毛膜双胎孕囊。穿刺针刺入目标孕囊内胚芽心管搏动处,负压抽吸至心管搏动消失。术后1、3、7d复查超声,观察减胎孕囊内胚芽心管搏动消失情况和保留胎孕囊内胚芽心管搏动情况。若无异常,30d后再次超声检查,之后门诊及电话随访至分娩后1周。

1.3 统计学处理 采用SPSS 19.0软件处理,计量资料以 $\bar{x} \pm s$ 表示,采用方差分析;计数资料用率表示,采用 χ^2 检验。

2 结果

2.1 减胎情况 350例被减胎患者,共减胎440个,均一次减胎成功,减胎成功率100%;其中2-1组78个,3-1组176个,3-2组88个;4-单卵双

胎组20个,3-单卵双胎组70个;留单卵双胎组8个,1例由两个单绒毛膜双胎孕囊组成的4胎妊娠患者术后流产,其余6个非单绒毛膜双胎孕囊因发育不良而作为减胎对象。术后完全流产率为7.43%(26/350),妊娠成功率92.57%(324/350),共分娩婴儿478个。324例成功妊娠患者中,早产率25.93%(84/324);478个分娩婴儿中,低出生体重儿出生率33.26%(159/478)。

2.2 含单绒毛膜性多胎减胎妊娠结局的比 4-单卵双胎组、3-单卵双胎组相对于留单卵双胎组,完全流产率、出生性别比差异无统计学意义($P > 0.05$),早产率及低出生体重儿出生率降低($P < 0.05$),平均出生体重升高($P < 0.05$),见表1。

2.3 减为单胎组与对照单胎组妊娠结局的比较 2-1组、3-2组、3-单卵双胎组与对照单胎组比较,完全流产率、出生性别比、早产率、低出生体重儿出生率差异均无统计学意义($P > 0.05$),2-1组平均出生体重低于对照单胎组($P < 0.05$)见表2。

2.4 减为双胎组与对照双胎组妊娠结局的比较 3-1组、4-单卵双胎组与对照双胎组比较,完全流产率、出生性别比、早产率、低出生体重儿出生率差异均无统计学意义($P > 0.05$),3-1组平均出生体重低于对照双胎组($P < 0.05$),见表3。

2.5 非单绒毛膜减胎组减为单胎组与减为双胎组的比较 减为单胎组相对于减为双胎组,平均出生体重升高,早产率、低出生体重儿出生率下降,差异有统计学意义($P < 0.05$)。

表1 含单绒毛膜性多胎减胎妊娠结局的比较

项目	4-单卵双胎组	3-单卵双胎组	留单卵双胎组	F/ χ^2 值
完全流产率(%)	0	2.86(1/35)	14.29(1/7)	1.680
早产率(%)	20(2/10)*	8.82(3/34)*	66.67(4/6)	11.819
平均出生体重(g, $\bar{x} \pm s$)	2 555.26 \pm 519.59*	3 314.71 \pm 420.09*	2 237.3 \pm 380.11	44.312
低体重儿出生率(%)	47.37(9/19)*	5.88(2/34)*	72.73(8/11)	21.486
出生性别(%)	男 52.63(10/19)	44.12(15/34)	36.36(4/11)	0.205
	女 47.37(9/19)	55.88(19/34)	63.64(7/11)	

与留单卵双胎组比较: * $P < 0.05$

表2 减为单胎组及对照单胎组妊娠结局的比较

项目	2-1组	3-2组	3-单卵双胎组	对照单胎组	F/ χ^2 值
完全流产率(%)	5.13(4/78)	9.09(4/44)	2.86(1/35)	9.00(9/100)	1.426
早产率(%)	14.86(11/74)	5.00(2/40)	8.82(3/34)	14.29(13/91)	0.662
平均出生体重(g, $\bar{x} \pm s$)	3 180.43 \pm 519.52*	3 365.38 \pm 632.95	3 314.71 \pm 420.09	3 435.71 \pm 570.69	44.312
低体重儿出生率(%)	9.46(7/74)	10.00(4/40)	5.88(2/34)	4.40(4/91)	0.120
出生性别(%)	男 44.59(33/74)	45.00(18/40)	44.12(15/34)	42.86(39/91)	0.030
	女 55.41(41/74)	55.00(22/40)	55.88(19/34)	58.24(53/91)	

与对照单胎组比较: * $P < 0.05$

表3 减为双胎组及对照双胎组妊娠结局的比较

项目	3-1组	4-单卵双胎组	对照双胎组	F/ χ^2 值
完全流产率(%)	9.09(16/176)	0	8.12(16/197)	0.148
早产率(%)	38.75(62/160)	20(2/10)	39.23(71/181)	0.008
平均出生体重(g, $\bar{x} \pm s$)	2 529.59 \pm 527.40*	2 555.26 \pm 519.59	2 702.96 \pm 585.40	44.312
低体重儿出生率(%)	43.00(129/300)	47.37(9/19)	32.34(98/303)	46.360
出生性别(%)	男	46.67(140/300)	52.63(10/19)	1.043
	女	53.33(160/300)	47.37(9/19)	

与对照双胎组比较: *P < 0.05

表4 各组间围产儿并发症及出生缺陷的比较(%)

组别	新生儿重度窒息	死胎	死产	新生儿死亡	出生缺陷
2-1	0	0	0	0	0
3-1	1.33(4/300)	0.67(2/300)	1(3/300)	0.67(2/300)	0.67(2/300)
3-2	2.5(1/40)	0	0	0	0
4-单卵双胎	0	0	0	0	0
3-单卵双胎	0	0	0	0	0
留单卵双胎	9.09(1/11)	0	0	0	18.18(2/11)
对照单胎	0	0	0	0	1.1(1/99)
对照双胎	1.32(4/303)	0.33(1/303)	0.33(1/303)	0.33(1/303)	0.33(1/303)

注:本文涉及的出生缺陷患儿主要包括先天性心脏病、先天性耳聋及失明患儿

2.6 各组间围产儿严重并发症及出生缺陷的比较

各组围产儿严重并发症及出生缺陷与对照组比较,差异均无统计学意义,见表4。

3 讨论

3.1 绒毛膜性与减胎结局 Stone et al^[2]对比了多胎减至双胎组与减至单胎组的妊娠结局,发现减为单胎可以获得更好妊娠结局,但是其研究中减为双胎者为3胎及3胎以上妊娠,减为单胎者却为3胎及双胎占多数,而关于双胎减胎与否及3胎减一胎还是两胎,由于减胎前后流产率无明显改变,且多胎本就存在自减现象,因此至今仍存在争议^[3]。本研究通过双胎减胎组与非减胎组及3胎减为单胎组和减为双胎组妊娠结果的对比发现,对于双胎及3胎,减胎后流产率虽无明显变化,但早产率及低出生体重儿出生率降低,新生儿平均出生体重升高,表明减为单胎可以获得更好的妊娠结局,因此我们建议对于双胎及3胎妊娠减为单胎更为合适。

单绒毛膜双胎易发生双胎输血综合征,选择性生长受限等严重并发症^[4],而辅助生殖技术后的单绒毛膜双胎妊娠发生率较自然妊娠显著增加^[5],常伴有3胎及以上多胎妊娠,使患者面临的风险进一步增加^[6],为减少妊娠风险和患儿并发症,减胎术被认为是一种有效的补救方法^[7],本文对比了减单绒毛膜双胎孕囊组和保留单绒毛膜双胎孕囊组妊娠结局的差异,认为在单绒毛膜双胎合并的多胎妊娠

中,选择单绒毛膜双胎孕囊为减胎对象且保留单胎更为合适。这可能是由于单绒毛膜双胎的两个胚胎在同一个孕囊中,同时减去两个胚胎,操作时间短,术后组织残留少,炎症反应轻,对其他的胚胎影响有限所致。

3.2 减胎术的安全性及时机 本研究结果显示术后各减胎组与对照组围产儿严重并发症、出生缺陷、男女出生性别百分率无显著差异,可见减胎术本身并不造成胎儿出生缺陷及严重并发症的增加。早孕期胚胎抽吸减胎时,由于不能确定保留胚胎的染色体是否正常及保留胎儿在发育过程中是否会发生结构的异常,为此,部分学者^[8]认为可以在妊娠中期行选择性减胎术,但是孕中期减胎其流产率明显高于孕早期。而孕早期经阴道负压抽吸减胎术,因其操作简单,易于成功,术后并发症少且安全有效,仍是目前生殖医学工作者选择的主要减胎方法^[9]。

综上所述,孕早期经阴道负压抽吸减胎术可安全、有效的改善多胎及多胎合并单绒毛膜双胎的妊娠结局,选择单绒毛膜双胎孕囊做为减胎对象,减为单胎可获得更好的妊娠结局。减胎可改善妊娠结局,但减胎术对于患者来说只是一种补救措施,在ART过程中如何在保证妊娠成功率的同时降低多胎妊娠发生率,仍需进一步探讨。

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Analysis of pregnancy outcomes of multifetal reduction in the first trimester for multi-pregnancy and multi-pregnancy accompany monochorionic twins

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Abstract Objective To study the safety and the effect of pregnancy outcomes of negative pressure suction through the vagina for multifetal reduction in the first trimester for multi-pregnancy and multi-pregnancy accompanied monochorionic twins. **Methods** The clinical data of 350 patients who received multifetal reduction and 297 patients at the same period without such operations during early pregnancy were collected to analyze the differences of the pregnancy outcomes. **Results** After fetal reduction, there were no statistically significant differences in complete abortion rate, severe complication rate for perinatal infants, birth defects, and gender ratio at birth ($P > 0.05$). In the non-monochorionic polyembryony group, the sub-group that was reduced to singleton had lower rate for premature delivery and low birth weight than the sub-group that was reduced to twins, the differences were statistically significant ($P < 0.05$); compared with the control group, the fetal reduction group had no significant differences in early delivery rate, and the rate of infants with low birth weight ($P > 0.05$). The group that reduced gestational sacs of monochorionic twins had lower early delivery rate, lower birth rate of low-weight infants, and higher average birth weight, compared with the group that kept them, the differences were statistically significant ($P < 0.05$). **Conclusion** Transvaginal multifetal pregnancy reduction can safely and efficiently improve pregnancy outcomes of multi-pregnancy and multi-pregnancy accompanied monochorionic twins in the first trimester; it will achieve better pregnancy outcomes that choose gestational sacs of monochorionic twins as the target for multifetal reduction and to reduce to singleton.

Key words monochorionic characteristic; multiple gestation; negative pressure suction pregnancy reduction; pregnancy outcomes