“孕中期唐氏综合征在双胎妊娠孕妇的血清标志物筛查”点评

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1　原文摘要

Second-trimester Down syndrome maternal serum marker screening: a prospective study of 11 040 twin pregnancies

The general approach to prenatal screening for Down syndrome (DS) is to estimate a woman's risk of having a trisomy 21-affected pregnancy on the basis of factors such as maternal age, maternal serum markers (MSMs), and first-trimester nuchal translucency (NT) measurement. Maternal serum screening for DS in twin pregnancies is fraught with difficulties (Cuckle, 1998; Wald and Rish, 2005). Firstly, serum marker levels in unaffected twin pregnancies are considered to be double those observed in singleton pregnancies. In addition, the distributions of the serum markers in DS-affected twin pregnancies are not known with any degree of reliability. Secondly, MSM levels in twins are a reflection of both twins and may be confounded by the presence of an unaffected co-twin resulting in a lower detection rate than in a singleton pregnancy, while NT measurement is specific to each fetus. Thirdly, the patient-specific maternal age-related risk in twin pregnancies depends on zygosity and chorionicity. In monochorionic twin pregnancies, DS risk due to maternal age is the same as in singleton pregnancies (but both fetuses are DS-affected), whereas in dichorionic twin pregnancies, the risk of having at least one aneuploid fetus is doubled (each with an a priori risk of aneuploidy). Whatever the method, because of specific problems related to twin pregnancies (double amniocentesis, selective TOP), DS screening in twins must be performed in tandem with multidisciplinary centers and clear information must be given to patients by a geneticist and an obstetrician.

Learning Objectives: After completion of this article, the reader should be able to know about the value of Down Syndrome (DS) second-trimester maternal serum screening of twin pregnancies, choose the method for second-trimester DS screening to perform in twin pregnancies.

2　论文核心内容及点评

该论文发表在 TWIN RESEARCH AND HUMAN GENETICS, 2009, JUN 12(3): 237-245 上。该文对孕中期唐氏综合征的孕妇血清标志物筛查在双胎妊娠的应用价值进行了大样本的前瞻性研究,主要内容如下:

唐氏综合征(Down Syndrome, DS)又称 21-三体综合征,是 1 种由染色体异常导致的出生缺陷。患儿表现为智力障碍、生长发育迟缓、特殊面容、常伴有心脏、消化道等多系统畸形,是最常见的非致死性染色体疾病,因此也是产前筛查和诊断的焦点。通常唐氏综合征的产前筛查是结合某些因素及检查对孕妇怀有 21-三体综合征胎儿的风险进行评估,这些因素及检查包括产妇年龄,孕妇血清标志物和早孕期胎儿颈项透明层厚度(nuchal translucency, NT)的测量。在单胎妊娠中,这项筛查已经普遍运

用于临床,而在双胎妊娠中,母体血清唐氏筛查却困难重重。首先,目前认为正常双胎妊娠的孕妇的血清标志物水平是单胎妊娠中观察到的2倍,而从实际临床中的数据显示并非如此。此外,在有唐氏患儿的双胎妊娠的孕妇的血清标志物数值与唐氏综合征发病率预测的相关性并不可靠。其次,双胎妊娠的母体血清学指标是反映2个胎儿的情况,可能由于1名正常胎儿的存在使检出率低于单胎妊娠的检出率。第三,在双胎妊娠中,产妇的年龄相关性风险取决于妊娠的卵型和绒毛膜型。在单绒毛膜双胎妊娠中,唐氏综合征的年龄相关性风险与单胎妊娠相同(即2个胎儿均为唐氏综合征患儿);而在双绒毛膜双胎妊娠中,至少怀有1个非整倍体染色体异常胎儿的风险会增加1倍(每个胎儿均有非整倍体染色体异常的风险)。

本文对1998～2006年间收集的全法国11 040例双胎妊娠的孕中期孕妇血清标志物(包括甲胎蛋白AFP以及游离β-hCG)情况进行了前瞻性研究,比较了单胎妊娠与双胎妊娠中21-三体综合征的发病率、母体血清学标记物对应的患儿检出率及假阳性率。21-三体综合征在双胎妊娠中的发病率为1/649(27/11 040例),而在单胎妊娠中为1/754(86/64 815例),这一结果无显著差异。而在双胎妊娠中,DS患儿检出率为63%(2个胎儿均为DS患儿时检出率为71%,仅有1名DS患儿的检出率为60%);在单胎妊娠中,DS患儿检出率为74.4%。而假阳性率在双胎妊娠中为10.8%;在单胎妊娠中为10.3%,两者无明显差异。

同样,作者对于这些孕妇也开展了孕早期的相关唐氏综合征的筛查项目检测。在孕早期对于双胎妊娠的21-三体综合征患病风险的评估中,胎儿颈项透明层厚度(NT)筛查结果也是极具争议的。该项检测的敏感度与单胎妊娠检测相近,但其假阳性率较之明显升高。数据表明,在孕早期进行母体血清学标记物筛查(PAPP-A、游离β-hCG)结合胎儿NT筛查可以将唐氏患儿检出率由64.9%提高到86.5%,而假阳性率也由2.3%升至4.7%。

综上所述,作者认为可以在双胎妊娠开展孕中期唐氏综合征的孕妇血清学标志物筛查。但结合筛查方法的敏感性以及特异性,首先可以建议孕妇在早孕期间进行胎儿颈项透明层厚度(NT)检测,如有特殊情况或者孕妇拒绝此项筛查时,可于孕中期进行母体血清学标志物筛查。

点评:近年来,随着孕产妇年龄增长而随之开展了许多的辅助生殖技术,这也致使双胎及多胎妊娠发生率逐年增长,因此对于这部分孕妇胎儿的唐氏综合征筛查方法的选择引起越来越多临床医生的关注。与单胎妊娠比较,双胎及多胎妊娠的唐氏筛查的检出率及假阳性率受到更多因素的影响,诸如孕产妇的年龄、胎儿卵型等情况。因此,对双胎妊娠进行唐氏综合征进行筛查和诊断方法的选择至关重要。

本文作者进行了1项大样本的关于双胎妊娠的唐氏综合征孕妇孕中期血清标志物筛查的前瞻性研究,并将常用的早孕期筛查标志物(PAPP-A、游离β-hCG、胎儿颈项透明层厚度等)与孕中期孕妇血清标志物筛查的敏感性、检出率及假阳性率进行比较,指出在孕中期对双胎妊娠孕妇可以进行血清标志物的筛查,但其风险计算与单胎妊娠不同,需要进行调整。文章还提出无论选择何种筛查方法,都需要在明确孕妇情况后,由遗传学家联合产科医生对孕妇进行筛查结果的告知,这对于目前产前诊断及咨询方式有很好的指导意义。