Transabdominal Chorionic Villus Sampling: Experience at Maharaj Nakorn Chiang Mai Hospital

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Objective: *To describe the experience of transabdominal chorionic villus sampling (CVS) at Maharaj Nakorn Chiang Mai Hospital.*

Material and Method: *Between January 2004 and July 2006, 185 pregnant women chose to have CVS for prenatal diagnosis after counseling. Transabdominal CVS under ultrasound guidance was performed in all cases under local anesthesia using spinal needle 20-gauge with back and forth movement technique. The sample was immediately examined under a microscope to determine if the villi were obtained and to remove the decidua (maternal cells) from the villi.*

Results: *The mean gestational age was 12.25 $\pm$ 1.05 weeks (range 10-20 weeks). The procedure was successful in all cases, 168 cases (90.9%) with one attempt. The indications for prenatal diagnosis included fetal risk for chromosomal abnormalities (110 cases; 59.46%), severe thalassemia syndrome (57 cases; 30.81%), both of them (17 cases; 9.19%) and for HLA typing in one case. The results could not be obtained in 11 cases (5.95%) due to laboratory failure. In the present study, abnormal chromosomes were detected in chorionic villi from 12 fetuses, including 45,X (3), trisomy 18 (3), trisomy 21 (2), trisomy 7 (1) and mosaicism (3). Additionally, 18 fetuses with severe thalassemia syndrome were identified; five homozygous beta-thalassemia, 11 beta-thalassemia/Hb E disease, and two homozygous alpha-thalassemia (Hb Bart's). The complications found in the present study included one case (0.54%) of fetal loss following the procedure and one case (0.54%) of vaginal bleeding. No case with limb reduction defect, infection, or rupture of membranes following the procedure was seen.*

Conclusions: *Transabdominal CVS is a rather safe and reliable prenatal diagnostic technique. The fetal loss rate following the procedure in the present study was 0.54%. However, operator's experience and skill in ultrasound-directed needle guidance procedure are essential.*

Keywords: *Chorionic villi sampling, Prenatal diagnosis, Fetal loss*

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Chorionic villi sampling (CVS) has been introduced as a first trimester prenatal diagnostic procedure since the early 1980s[1-3]. In the earlier period, the procedure was not widely accepted due to concern about the complications such as fetal limb reduction defects and higher fetal loss rate compared to mid-trimester amniocentesis[4,5]. However, data from later studies confirmed that CVS did not increase the risk of limb reduction defect when performed after 9 weeks gestation and carried comparable fetal loss rate to that of amniocentesis[6,7]. From the supported data, CVS has been accepted as a relatively safe method of prenatal diagnosis in the first trimester since early 1990s. The procedure can be done either transvaginal or transabdominal approach between 10-14 weeks of gestation. Chorionic villi obtained from the procedure can be used for karyotyping or DNA analysis for various genetic disorders.

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The introduction of Down syndrome screening in the past decade using biochemical markers and measurement of nuchal translucency (NT) leads to increasing demand for prenatal diagnosis in first trimester. Thus, CVS has gained more acceptance and there are more centers performing this procedure. The aim of the present study was to describe the authors' experience of transabdominal CVS at Maharaj Nakorn Chiang Mai Hospital, including indication, safety, and complications from the procedure.

Material and Method

This is a retrospective descriptive study designed to include all women undergoing CVS for prenatal diagnosis at Maharaj Nakorn Chiang Mai Hospital. The present study was approved by the Institutional Research Ethic Committee. Those women who had vaginal bleeding prior to the procedure or contraindications for CVS were counseled to have other prenatal diagnostic procedures. Between January 2004 and July 2006, 185 pregnant women chose to have CVS after counseling. With informed consent, transabdominal CVS under ultrasound guidance was performed in all cases under local anesthesia using 20-gauge spinal needle with back and forth movement technique. The sample was immediately examined under a microscope to determine if the villi were adequately obtained and to remove the decidua (maternal cells) from the villi. Then the tissues were sent to laboratories for processing. For karyotyping, the chorionic villi were cultured and analyzed. For DNA analysis, extraction of DNA was performed and PCR-base technique was used for mutation detection. The pregnancy outcomes were subsequently assessed. Data were summarized with frequency and percentage, mean $\pm$ standard deviation (SD) and range were used to describe data characteristics.

Results

The mean gestational age was 12.25 $\pm$ 1.05 weeks (range 10-20 weeks) as shown in Table 1. The procedure was successful in all cases, 168 cases (90.9%) with one puncture and 17 cases (9.1%) with two or more punctures. The indications for prenatal diagnosis included fetal risk for chromosomal abnormalities (110 cases; 59.46%), severe thalassemia syndrome (57 cases; 30.81%), both of them (17 cases; 9.19%) and for HLA typing in one case (Table 2).

The results could not be obtained in 11 cases (5.95%) due to laboratory failure; mutation could not be identified in three risk couples for thalassemia, the remainders were due to inadequate metaphase for karyotyping from the villi culture. In the present study, abnormal chromosomes were detected in chorionic villi from 12 fetuses, including 45,X (3), trisomy 18 (3), trisomy 21(2), trisomy 7 (1) and mosaicism (3). Two fetuses with 45,X had cystic hygroma appearance prior to the procedures while another fetus appeared normal in first trimester ultrasound scan and the confirmation test by cordocentesis at midpregnancy showed normal karyotype (46,XX). All fetuses with trisomy 18 and trisomy 21 showed increased nuchal translucency (NT) prior to CVS. The fetus with trisomy 7 revealed normal ultrasound scan and had normal karyotype on the confirmatory test as well. Two cases of mosaicism were confirmed and showed normal karyotype, while the other (46,XX/47,XX,+7) already had cystic hygroma prior to CVS (Table 3).

Additionally, 18 fetuses with severe thalassemia syndrome were identified; five homozygous beta-thalassemia, 11 beta-thalassemia/Hb E disease, and two homozygous alpha-thalassemia (Hb Bart's).

The complications found in the present study included one case (0.54%) of fetal loss before 28 weeks and one case (0.54%) of vaginal bleeding. No case with limb reduction defect, infection, or leakage of amniotic fluid following the procedures was encountered in this series. Pregnancy outcomes were comparable to those

Table 1. Gestational age at the time of CVS (n = 185)

GA (weeks)	Number (%)
10	4 (2.2)
11	25 (13.5)
12	96 (51.9)
13	42 (22.7)
14	11 (5.9)
15	2 (1.1)
20	1 (0.5)
No record	4 (2.2)

Mean $\pm$ SD 12.25 $\pm$ 1.05 weeks

Table 2. Indications for prenatal diagnosis (n = 185)

Indications	Number (%)
Chromosome study	110 (59.46)
Thalassemia	57 (30.81)
Chromosome study + Thalassemia	17 (9.19)
HLA typing	1 (0.54)

Table 3. Results of CVS

Results	No.	Detail		
Chromosome	127		Lab failed 8 cases	
Normal	107			
45,X	3	Thick NT in 2 cases	Normal US 1 case : Repeat = 46,XX	
Trisomy 18	3	Thick NT all		
Trisomy 21	2	Thick NT all		
Trisomy 7	1	Normal US : Repeat = 46,XX		
Mosaic	3	46,XY/47,XXY (Repeat = 46,XY)	46,XY/47,XY,+13 (Repeat = 46,XY)	46,XX/47,XX,+7 (cystic hygroma)
Thalassemia	74		mutation were not identified in 3 cases	
Normal	20			
Trait	33			
Affected	18			

of pregnant women who did not have CVS at Maharaj Nakorn Chiang Mai Hospital. The incidence of low birth weight (less than 2,500 grams), preterm birth, and premature rupture of membrane were 13.8%, 10.3%, and 2.3% respectively.

Discussion

CVS has been widely accepted as a prenatal diagnostic technique in the first trimester since 1990s. Its safety and reliability have been documented in many publications[6-9]. Fetal loss rate was reported from 1.3-3.0%[7,8,10,11] and confined placental mosaicism was 1-2%[10].

In the present study, the authors found fetal loss after the procedure in one case, giving the loss rate of 0.54%, which was rather low compared to other studies. This may be due to too small sample size in the present series to show a real fetal loss rate. However, operators' skills and experience may be associated with low fetal loss rate in the present report. Although our institute started to offer CVS as an alternative method of prenatal diagnosis in 2004, the authors had performed cordocentesis for over 15 years. The authors reported a 1.4% procedure-related fetal loss rate from cordocentesis[12]. The five authors were familiar with ultrasound guided prenatal diagnostic procedures such as amniocentesis and cordocentesis. In fact, all of them had performed over 100 cases of cordocentesis before performing CVS.

All procedures in the present study were transabdominal CVS. The authors chose to perform transabdominal approach because the supported data from a Chochrane review concluded that transabdominal CVS is preferable to transcervical CVS[9]. Transcervical CVS is more technically demanding and associated with more failures to obtain sample[9]. In the authors' study CVS was performed between 10-14 weeks in majority of the cases (96.2%). The CVS was done at 20 weeks gestation in one case after failure to obtain fetal blood from cordocentesis due to the patient's thickness of abdominal wall. The anteriorly located placenta enabled the authors to perform transabdominal CVS instead. The success rate of CVS after one puncture was 90.9%. Most cases that required more than one puncture were confined to the beginning period of the operators' experience.

The rate of abnormal chromosomes in the present study was 9.45% (12 out of 127 cases). In cases where the ultrasound scan did not find any abnormality, either amniocentesis or cordocentesis was offered for repeat chromosome testing. After excluding four cases of normal chromosome after repeat testing, the rate of true abnormal chromosome in the present study was 6.3%. The observed high rate of abnormal chromosome in the present study was the result of the Down syndrome screening program (NT and first trimester serum markers). The implementation of this program enable the authors to detect high-risk fetuses (thickened NT or positive serum markers) who had a higher rate of chromosomal abnormality.

Among the four cases of abnormal chromosome in chorionic villi and normal chromosome in the repeat testing, there were two mosaicism (46,XY/47,XXY and 46,XY/47,XY,+13), one trisomy 7, and one 45,X. Abnormal chromosome found only in the placenta but not in the fetuses were the result of confined placental

mosaicism (CPM) or chromosome abnormalities confined to the placenta (CACP)[8,10].

The main indications of CVS in the present study were karyotyping and mutation analysis for severe thalassemia syndrome. There were three cases in which the mutation of beta-thalassemia gene could not be identified and cordocentesis was offered for prenatal diagnosis. Failure to obtain the result in the present study was 5.95%, mainly due to laboratory technique. In the present study, the authors did not find any case with limb reduction defect, infection, or leakage of the fluid after the procedure.

In conclusion, the present study suggests that transabdominal CVS is a safe and reliable method of prenatal diagnosis. With the skilled and experienced operators, the complications and fetal loss rate are relatively low.

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การตรวจวินิจฉัยก่อนคลอดโดยการเจาะชิ้นเนื้อรกผ่านทางหน้าท้อง: ประสบการณ์ของโรงพยาบาลมหาราชนครเชียงใหม่

สุพัตรา ศิริโชติยะกุล, วีรวิทย์ ปิยะมงคล, เฟื่องลดา ทองประเสริฐ, เกษมศรี ศรีสุพรรณดิฐ, สุชยา ลือวรรณ

วัตถุประสงค์: *เพื่อบรรยายประสบการณ์การตรวจวินิจฉัยก่อนคลอดโดยการเจาะชิ้นเนื้อรกผ่านทางหน้าท้องของโรงพยาบาลมหาราชนครเชียงใหม่*

วัสดุและวิธีการ: *ศึกษาสตรีตั้งครรภ์ 185 รายที่เลือกรับการตรวจวินิจฉัยก่อนคลอด โดยการเจาะชิ้นเนื้อรกผ่านทางหน้าท้องที่โรงพยาบาลมหาราชนครเชียงใหม่ ระหว่างเดือนมกราคม พ.ศ. 2547 ถึง เดือนกรกฎาคม พ.ศ. 2549 ทุกรายได้รับการเจาะชิ้นเนื้อรกโดยใช้คลื่นเสียงความถี่สูงชี้นำ ได้รับยาชาเฉพาะที่ ใช้เข็มเจาะไขสันหลังเบอร์ 20 เจาะดูดชิ้นเนื้อรกโดยเทคนิค to and fro ชิ้นเนื้อรกที่ดูดออกมาได้รับการดูด้วยกล้องจุลทรรศน์ทันที เพื่อตรวจว่ามีปริมาณเพียงพอหรือไม่ และเพื่อขจัดเซลล์ของมารดา (decidua) ที่อาจปนเปื้อนอยู่*

ผลการศึกษา: *อายุครรภ์เฉลี่ย 12.25 $\pm$ 1.05 สัปดาห์ (พิสัย 10-20 สัปดาห์) สามารถเจาะชิ้นเนื้อรกได้สำเร็จทุกรายโดยเจาะสำเร็จในครั้งเดียว 168 ราย (ร้อยละ 90.9) ข้อบ่งชี้ในการตรวจวินิจฉัยก่อนคลอด มีดังนี้ ทารกเสี่ยงต่อโครโมโซมผิดปกติ (110 ราย; ร้อยละ 59.46) ทารกเสี่ยงต่อโรคธาลัสซีเมียชนิดรุนแรง (57 ราย; ร้อยละ 30.81) ข้อบ่งชี้ทั้งสองอย่าง (17 ราย; ร้อยละ 9.19) และเพื่อตรวจชนิดของ HLA 1 ราย มีอยู่ 11 ราย (ร้อยละ 5.95) ไม่ได้ผลการตรวจเนื่องจากความล้มเหลวทางห้องปฏิบัติการ ในการศึกษานี้พบโครโมโซมผิดปกติจากการตรวจชิ้นเนื้อรก 12 ราย ได้แก่ 45,X (3 ราย), trisomy 18 (3 ราย), trisomy 21 (2 ราย), trisomy 7 (1 ราย) และ mosaicism (3 ราย) นอกจากนี้พบทารกเป็นโรคธาลัสซีเมียชนิดรุนแรง 18 ราย ได้แก่ homozygous beta-thalassemia 5 ราย, beta-thalassemia/Hb E disease 11 ราย และ homozygous alpha-thalassemia (Hb Bart's) 2 ราย ภาวะแทรกซ้อนที่พบในการศึกษานี้ได้แก่ แท้งบุตร 1 ราย (ร้อยละ 0.54) และมีเลือดออกทางช่องคลอด 1 ราย (ร้อยละ 0.54) ไม่พบภาวะ limb reduction defect, การติดเชื้อ หรือถุงน้ำคร่ำแตกภายหลังการทำหัตถการในการศึกษานี้*

สรุป: *การเจาะชิ้นเนื้อรกผ่านทางหน้าท้องเป็นวิธีตรวจวินิจฉัยก่อนคลอดที่ค่อนข้างปลอดภัยและเชื่อถือได้ ในการศึกษานี้พบการแท้งบุตรจากการทำหัตถการร้อยละ 0.54 อย่างไรก็ดี ประสบการณ์ และความชำนาญของผู้ทำในการทำหัตถการโดยใช้คลื่นเสียงความถี่สูงชี้นำเป็นสิ่งจำเป็น*