Fetomaternal Hemorrhage After Midtrimester Genetic Amniocentesis at King Chulalongkorn Memorial Hospital

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Abstract

Midtrimester genetic amniocentesis has become an accepted part of modern obstetric care. Although its accuracy is well established, the risk of fetomaternal hemorrhage remains controversial. This prospective study was conducted to determine how effective continuous ultrasound guided amniocentesis is in preventing fetomaternal hemorrhage. The authors investigated 30 patients undergoing midtrimester genetic amniocentesis at our institution. Amniocentesis was performed under continuous real-time ultrasound guidance using a 21-gauge, 3.5-inch long spinal needle. Maternal serum alpha-fetoprotein (AFP) levels were determined before, at 5 minutes and at 1 hour after amniocentesis. There were no significant changes in maternal serum AFP levels either at 5 minutes or at 1 hour after amniocentesis.

Midtrimester genetic amniocentesis performed by a trained and experienced operator under continuous ultrasound guidance does not significantly increase the risk of fetomaternal hemorrhage after the procedure.

Key word : Fetomaternal Hemorrhage, Amniocentesis

Midtrimester amniocentesis is being used increasingly for the diagnosis of genetic diseases. Large collaborative studies have been reported regarding the safety and accuracy of midtrimester genetic amniocentesis[1-3]. It seems probable that genetic amniocentesis may cause a fetomaternal hemorrhage. The incidence of fetomaternal hemorrhage following amniocentesis varies from study-to-study[4-6], due to the methods for detection of fetomaternal hemorrhage. The most sensitive method to diagnose fetomaternal hemorrhage in the second trimester is the demonstration of changes in the level of maternal serum alpha-fetoprotein (AFP)[6,7]. The significant increase in maternal serum AFP levels in association of genetic amniocentesis has been reported to be between 4.9 per

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cent and 21 per cent[8,9]. Therefore, it seems that triple tests (AFP, unconjugated estriol and human chorionic gonadotropin) for screening of fetal Down syndrome should not be performed immediately after amniocentesis. However, the technique of genetic amniocentesis has been changed, it is now performed in our institution under continuous real-time ultrasound guidance[10,11]. This technique allows visualization of the path of the needle during insertion and documents with certainty whether the placenta and the fetus have been traversed[10,11].

This prospective study was performed to determine how effective continuous ultrasound guided amniocentesis is in preventing fetomaternal hemorrhage.

MATERIAL AND METHOD

Subjects for this study were recruited from women undergoing genetic amniocentesis at the Division of Maternal-Fetal Medicine, Faculty of Medicine, King Chulalongkorn Memorial Hospital, Chulalongkorn University. Each woman had genetic counseling and informed consent before the study. Detailed ultrasound was performed before the procedure to measure fetal biometry (biparietal diameter, head circumference, abdominal circumference, and femur length), placental location and fetal malformations. Gestational age was determined by the last normal menstrual period combined with estimation of fetal biometry.

Amniocentesis

Amniocentesis was performed by one very experienced doctor (YT). The procedure was performed under continuous real-time ultrasound guidance using a 21-gauge, 3.5-inch long spinal needle with stylet without local anesthesia and under sterile conditions, as previously described in detail elsewhere[10,11]. Transplacental puncture was avoided, if possible. In cases of an anterior placenta if a window could not be identified, cord insertion was identified and the area was avoided. Amniocentesis was performed through the thinnest portion of the placenta. Twenty milliliters of amniotic fluid were withdrawn and sent for fetal karyotyping.

Blood samples for maternal serum AFP determination

These were obtained immediately before, at 5 minutes and at 1 hour after amniocentesis. Complete mixing of AFP in the maternal circulation has been shown to occur in the first 5 and 15 minutes [7,12] and the half life of AFP is approximately 5 days[13]. The samples from each patient were marked as number 1 (before), number 2 (at 5 minutes after) and number 3 (at 1 hour after), and analyzed 'blind' in the central laboratory in the same run. Serum AFP level was determined using the enzyme-linked immunosorbent assay (ELISA) technique. The within assay coefficient of variation was less than 10 per cent. A fetomaternal hemorrhage was estimated to have occurred on the basis of increases in maternal serum AFP levels[5,7].

Statistics

Descriptive statistics were analyzed with the SPSS program. Changes in maternal serum AFP levels in each patient were tested for significance with paired *t* test.

RESULTS

Thirty patients were included in the study. Mean age of subjects in the study was 37.2 years ± 3.9 standard deviation (SD) (Range = 25-45); mean gestational age at the time of amniocentesis was 18.2 weeks ± 1.8 SD (Range = 15-24). The indications for amniocentesis were advanced maternal age in 27 cases and previous aneuploidy baby in 3 cases. All patients had 1 needle insertion. Clear amniotic fluid was obtained in all cases. No fetal abnormalities were detected. The results of the chromosomes were all normal. Fig. 1 shows maternal serum AFP levels in individual patients before, at 5 minutes and at 1 hour after amniocentesis. Means and standard deviation of maternal serum AFP levels before, at 5 minutes and at 1 hour after amniocentesis were 55.4 ± 23.6 IU/ml (95% confidence interval (CI) 46.6 - 64.2), 54.5 ± 26.5 IU/ml (95% CI 44.6 - 64.4), and 54.4 ± 23.4 (95% CI 45.7 - 63.2), respectively. There were no significant changes in maternal serum AFP levels (Δ AFP) either at 5 minutes (mean Δ AFP ± SD = 0.88 ± 12.51 IU/ml, 95% CI = -3.8 - 5.6) or at 1 hour (mean Δ AFP ± SD = 0.94 ± 13.69 IU/ml, 95% CI = -4.2 - 6.1) after amniocentesis. The placentas were traversed during the procedure in 7 cases. However, there were no significant changes in maternal serum AFP levels (Δ AFP) after the procedure (at 5 minutes, mean Δ AFP ± SD = 6.9 ± 11.7 IU/ml, 95% CI = -3.98 - 17.7; at 1 hour, mean Δ AFP ± SD = 5.2 ± 18.0 IU/ml, 95% CI = -11.5 - 21.8).

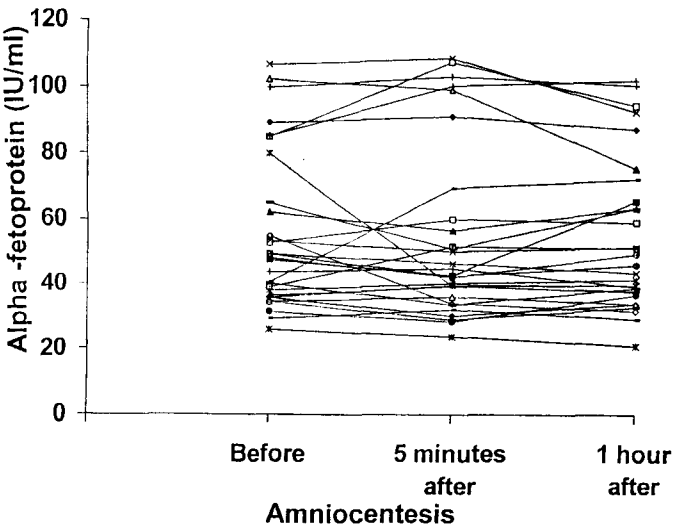

Fig. 1. Maternal serum AFP levels immediately before, at 5 minutes, and at 1 hour after amniocentesis in each case (N = 30).

DISCUSSION

Modern developments in prenatal diagnosis of genetic disease, widespread publicity of the accuracy and safety of amniocentesis have resulted in an appreciable increase in the number of amniocenteses done in referral centers such as the authors' (1-3,14). The presence of fetal trauma or bleeding has been recognized as a complication of amniocentesis(10,11). The prevalence of fetomaternal hemorrhage depends on the skilled perinatal obstetricians, the technique, number of puncture and placental trauma(6,8,15-17). Diagnosis of fetomaternal hemorrhage has been difficult because of 1) the relatively complicated techniques used, e.g., estimation of fetal hemoglobin by electrophoresis, immunologic techniques, or the Kleihauer-Betke staining method (6), and 2) the possibility of early entrapment of fetal red blood cells by the maternal reticuloendothelial system in cases of ABO blood incompatibilty(6). It has been reported that the most sensitive method to diagnose fetomaternal hemorrhage in the second trimester is the demonstration of changes in the level of maternal serum AFP(6,7). Therefore, we measured the changes in the level of maternal serum AFP for the detection of fetomaternal hemorrhage following midtrimester amniocentesis. At present there are 2 commonly used techniques for amniocentesis. The first technique is to locate the site of puncture by ultrasound immediately before amniocentesis(6, 10,11). The second technique is to perform amniocentesis under continuous ultrasound guidance(10, 11). The incidence of fetomaternal bleeding after amniocentesis without ultrasound monitoring was found to be 15 per cent(7). In the report of Lele et al (6) who performed amniocentesis immediately after the scan without moving the patient, they found that fetomaternal bleeding was detected in 2 of 107 (1.8%) patients by the Kleihauer-Betke staining technique and in 8 of 107 (7.02%) patients by AFP technique. In their report 18 of 107 (16.8%) had more than 1 needle insertion. Tabor et al(5) reported the rate of amniocentesis induced fetomaternal hemorrhage to be 17 per cent, which was performed under real-time ultrasound guidance. Such fetomaternal hemorrhage was seen significantly more often after transplacental amniocentesis or after amniocentesis performed by less experienced operators(5). However, no association was detected between birth weight and fetomaternal hemorrhage attributable to amniocentesis(5). In the present study, we performed amniocentesis under continuous real-time ultrasound guidance by a highly experienced operator who obtained amniotic fluid on the first attempt with 1 needle insertion in all cases. With the use of changes in maternal serum AFP levels after amniocentesis as an estimate of

the magnitude of fetomaternal hemorrhage, we observed that maternal serum AFP levels does not significantly increase in all subjects after amniocentesis either at 5 minutes or at 1 hour after the procedure. However, if we had used Lachman et al 's criterion who reported that a fetomaternal hemorrhage had occurred if the Δ AFP was 40 per cent or more, we found only one case (3.3%). In our study, clear amniotic fluid was obtained in all cases. However, it has been reported that fetomaternal bleeding was not restricted to patients with presence of blood in the amniotic fluid[6]. In addition it has been found that fetal death related to amniocentesis occurred in a patient who underwent uncomplicated amniocentesis[18]. Recovery of clear amniotic fluid did not rule out fetal trauma and danger of fetal death[6]. We found no correlation between placental location and fetomaternal hemorrhage as evidence by evaluation of the changes in maternal serum AFP levels. In the study of Lenke et al[15], simultaneous ultrasound was used to determine if there was a correlation between visualized intraamniotic bleeding, placental location, and fetomaternal hemorrhage. They found that visualized intraamniotic bleeding showed no correlation to fetomaternal hemorrhage[15]. Intraamniotic bleeding was commonly associated with needle insertion through an anterior placenta, but also occurred regardless of placental location and in the absence of placental needle traversal[15]. They also found no correlation between placental location and fetomaternal hemorrhage[15].

In conclusion, midtrimester genetic amniocentesis performed by a trained and experienced operator under continuous ultrasound guidance with only one puncture using a 21-gauge spinal needle does not significantly increase the risk of fetomaternal hemorrhage after the procedure.

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ภาวะเลือดออกจากทารกในครรภ์สู่มารดาภายหลังการเจาะดูดน้ำคร่ำ เพื่อตรวจหาโรคทางพันธุกรรมในระยะกึ่งกลางของการตั้งครรภ์ ที่โรงพยาบาลจุฬาลงกรณ์

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การเจาะดูดน้ำคร่ำเพื่อตรวจโรคทางพันธุกรรม ในช่วงกึ่งกลางของการตั้งครรภ์ เป็นหัตถการที่ยอมรับในสูติศาสตร์ร่วมสมัย แม้ว่าความแม่นยำจะเป็นที่ยอมรับกัน แต่อัตราเสี่ยงของภาวะเลือดออกจากทารกในครรภ์สู่มารดายังเป็นที่ถกเถียงกัน การศึกษานี้ได้ทำการศึกษาแบบไปข้างหน้า เพื่อหาว่าการใช้คลื่นเสียงความถี่สูงร่วมกับการเจาะดูดน้ำคร่ำตลอดเวลา จะป้องกันภาวะเลือดออกจากทารกในครรภ์สู่มารดา ผู้วิจัยได้ทำการศึกษาสตรีตั้งครรภ์ 30 ราย ที่มารับการเจาะดูดน้ำคร่ำเพื่อตรวจหาโรคทางพันธุกรรมในช่วงกึ่งกลางของการตั้งครรภ์ การเจาะดูดน้ำคร่ำทำโดยอาศัยการตรวจคลื่นเสียงความถี่สูงตลอดเวลาที่ทำการเจาะ โดยใช้เข็มเจาะช่องไขสันหลังขนาดเบอร์ 21 ยาว 3.5 นิ้ว ได้ทำการเจาะเลือดมารดาตรวจหาระดับ แอลฟา ฟีโตโปรตีน ก่อนทำการเจาะที่ 5 นาที และที่ 1 ชั่วโมง หลังการเจาะ พบว่าไม่มีการเปลี่ยนแปลงของค่า แอลฟา ฟีโตโปรตีนในเลือดของมารดาที่ 5 นาที หรือที่ 1 ชั่วโมงภายหลังการเจาะดูดน้ำคร่ำ

การเจาะดูดน้ำคร่ำเพื่อตรวจหาโรคทางพันธุกรรมในระยะกึ่งกลางของการตั้งครรภ์ ทำโดยแพทย์ที่ชำนาญและผ่านการฝึกอบรมโดยใช้การตรวจคลื่นเสียงความถี่สูงร่วมกับการเจาะ จะไม่เพิ่มอัตราเสี่ยงต่อการเกิดภาวะเลือดออกจากทารกในครรภ์สู่มารดาภายหลังการทำหัตถการ

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