EVALUATION OF THE RESULTS OF CORDOCENTESIS

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SUMMARY

Objective: To evaluate the results of cordocentesis carried out in our clinic at Meram Medicine Faculty of Selcuk University in Konya, Turkey.

Materials and Methods: Cytogenetic results and complication data were obtained by cordocentesis from 250 pregnancies performed in our clinic.

Results: Adequate amount of cord blood was taken 98% of the time, the successful culture rate was 92.8%, and none of the 18 cases in which no proliferation was detected in the culture accepted a new intervention. Cordocentesis was performed in 14 cases (5.6%), because no results were obtained from amniocentesis carried out for various indications. According to cytogenetic evaluation, chromosomal abnormality was detected in 12 cases (5.17%), including four cases of trisomy 21, four cases of trisomy 18, one case of trisomy 13, one case of triploidy (69,XXX) and two cases of chromosomal inversion. Of the 250 cordocentesis cases, there were 12 (4.8%) cases of fetal loss, including four cases of rupture of membranes, four cases of abdominal pain and vaginal bleeding and four cases of a spontaneous abortus. In 53 (21.2%) cases, cordocentesis was performed because of hydrops fetalis; and of the total 12 losses, six were in this group. The fetal loss rate was 11.32% in the hydrops fetalis group.

Conclusion: If cordocentesis is carried out by highly skilled physicians and optimal culture conditions are available, cordocentesis is an invasive prenatal diagnostic and therapeutic procedure that is performed secondary to amniocentesis with high accuracy and safety. In cases of hydrops fetalis in which cordocentesis is carried out, fetal loss is more likely to occur. [*Taiwan J Obstet Gynecol* 2007;46(4):405–409]

Key Words: cordocentesis, fetal abnormality, hydrops fetalis

Introduction

As the maternal age increases to middle age, the frequency of chromosomal anomalies increases; thus, prenatal diagnostic methods are used more often in order to diagnose such cases effectively.

When identifying cases at risk of having a baby with chromosomal anomaly and suggesting the use of invasive prenatal diagnosis methods, besides an advanced maternal age and a previous history of fetal chromosomal anomaly, abnormal ultrasonography (USG) results and results from the triple test and first-trimester screening test (nuchal translucency, human chorionic gonadotropin, pregnancy-associated plasma protein-A) can be effective in the determination [1,2].

In order to have a definite diagnosis of pregnancies having a risk of fetal chromosomal anomaly, prenatal diagnosis methods, such as chorionic villus sampling and early amniocentesis in the first trimester and amniocentesis or cordocentesis in the second trimester, can be applied. Among the methods mentioned above, amniocentesis is still the most used invasive prenatal diagnosis method, because (1) chorionic villus sampling requires more experience, and the fetal loss and complication rates are high; (2) there are no controlled studies on the safety of early amniocentesis, and current reports present a high rate of fetal loss and some deformities in some fetuses; and (3) cordocentesis requires more experience and fetal loss rate is high [2,3]. However, when quick results are required, cordocentesis can

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be performed, since it is highly safe with reasonable complication frequency.

Materials and Methods

This study consisted of 250 cases in which cordocentesis was carried out in the Department of Obstetrics and Gynecology at Meram Medicine Faculty of Selcuk University in Konya, Turkey from June 2001 to June 2006. Cordocentesis was performed for various indications. A second cordocentesis was offered to 18 patients, because amniotic cells could not be cultured. None of these patients accepted a second intervention.

In this study, the cytogenetic results and complication data of the cordocentesis procedure performed on 250 pregnant women were examined and analyzed. These women were admitted to our clinic because of advanced maternal age, a history of amniocentesis due to high risk of carrying a chromosomally abnormal fetus in whom no karyotype result could be obtained by amniocentesis, and a previous history of having a chromosomally abnormal fetus.

Prior to cordocentesis, a detailed interview with the family was conducted. A detailed history was obtained after determining the career position, educational background and economical status. The complications and risks of cordocentesis were explained to the family in detail. The risk of abortion (1–3%) due to the procedure was explained to the families, and the signatures of the couples for their informed consent were obtained.

Cordocentesis was performed between the 17th and 28th gestational weeks in 250 cases that accepted the procedure. All cordocentesis procedures were carried out by the same perinatologist. Before the attempt, each fetus was examined in detail using USG and the anomaly type detected was recorded. The localization of the placenta, amniotic fluid quantity, needle insertion site, the distance of the fetus to the needle insertion site, and fetal position were assessed. Before starting the procedure of cordocentesis, essential preparations were made. After preparing the abdominal region with povidone-iodine, cordocentesis was performed, which was accompanied by USG using a sterile spinal needle with the freehand technique transabdominally. For cytogenetic analysis, 0.5–1 mL fetal blood was taken using a heparinized syringe. Anti-Rh IgG (300 μg) was administered to cases at risk of Rh alloimmunization.

The blood obtained from cordocentesis was sent to the Meram Medicine Faculty Genetic Laboratory of Selcuk University. Following laboratory processing and by using standard methods, chromosomal preparations were prepared from the cells taken from cell cultures. Quantitative and structural chromosome disorders observed in the cases were examined and assessed in accordance with the International System for Human Cytogenetic Nomenclature (ISCN, 1995). The patients who had normal results were called for routine prenatal visits until delivery. Pregnancies with chromosomal anomalies incompatible with life and with multiple anomalies detected on USG were terminated at the request of the family.

For statistical evaluation of the results, SPSS 10.0 for Windows was used. Data are expressed as mean ± standard deviation. Chi-squared test was used to compare the data obtained. Statistical significance was accepted at $p < 0.05$.

Results

The average maternal age was 27.85 ± 6.66 years (range, 17–43 years). Thirty-five (14%) patients were ≥ 35 years of age, 18 (7.2%) were below the age of 20, and 197 (78.8%) were between 20 and 35 years. Eighty-eight (35.2%) were nulliparous, and 162 (64.8%) were multiparous. While eight (3.2%) of the cases had chronic disorder, only two had a genetic disorder (beta-thalassemia minor). There was consanguinity between the women and their husbands in 64 cases (25.6%).

Eight (3.2%) patients had a history of giving birth to an infant with anomaly. No relationship between the history of an infant with anomaly and chromosomal abnormality could be established.

Cordocentesis was performed in 124 (49.6%) patients before or during the 24th week of pregnancy and in 126 (50.4%) patients between the 24th and 28th week of pregnancy.

Most of the cases that underwent the cordocentesis procedure comprised patients who showed signs of fetal anomalies on USG and patients who were referred to our clinic with suspicion of chromosomal abnormality because of fetal anomaly detected on USG. The major indication for cordocentesis was abnormal USG results, which accounted for 194 (77.6%) cases. In the cases for which cordocentesis was performed, 14 (5.6%) had failed cell culture in amniocentesis, 15 (6%) had advanced maternal age, 15 (5%) had a poor obstetric history (e.g. having an infant with anomaly), 10 (4%) had high risk of chromosomal abnormality on triple test, and two (0.8%) had mosaicism on amniocentesis.

Table 1 shows the fetal anomalies and their frequencies in 194 cases that underwent cordocentesis, based on anomaly assessed on USG.

According to the USG results, hydrops fetalis was the most frequent anomaly in 53 (27.31%) cases. Next, 41 (21.13%) cases had multiple fetal anomalies and 34 (17.52%) had central nervous system anomalies. Among the central nervous system anomalies, the most frequent pathology was hydrocephaly. In addition to this group of anomalies, microcephaly, choroid plexus cysts and meningomyelocele were among the other frequent anomalies. In the cases with multiple fetal anomalies, two or more anomalies existed together on USG.

A second attempt at puncture was required in only 18 cases, so the failure rate at first puncture was 7.2%; only two attempts could be made in each examination.

Fetal blood samples taken from five out of 250 cases were found to be insufficient by the laboratory. Thus, the rate of obtaining sufficient cord blood was 98%. In 18 (7.2%) of the 250 fetal blood samples, there was a failed cell culture; thus, the successful cord blood culture rate was 92.8%. Insufficient fetal blood in the five (2%) samples and contamination in the 13 (5.2%) samples were deemed to be the cause of culture failure. None of the 18 cases with a failed culture accepted a second intervention.

Out of the 232 cases with successful cell culture, 220 (94.82%) revealed normal results of chromosomal analysis and 12 (4.8%) had a chromosomal anomaly. The chromosomal anomalies were: trisomy 18 (four cases), trisomy 21 (four cases), trisomy 13 (one case), inversion (two cases), and triploidy (69,XXX; one case) (Table 2).

Of the cases with chromosomal anomalies, eight patients were aged 35 years or younger, and four patients were over 35 years of age. Seven patients were multiparous and five were primiparous. In nine of the patients, the procedure was conducted in the 24th week of pregnancy and later. The procedure was performed, because eight patients had abnormal USG results, three were of advanced maternal age, and one was of advanced maternal age and had abnormal USG results.

Ten of the pregnancies with quantitative chromosomal anomaly were terminated according to the request of the family. Two cases in which structural chromosomal abnormality was detected had a delivery in our clinic on time, and no abnormality was detected in the babies.

The results obtained from the patients who underwent cordocentesis are shown in Table 3.

Of the 250 patients who underwent cordocentesis, 12 (4.8%) had fetal loss due to the procedure, including four with rupture of the membranes, four with abdominal cramps and vaginal bleeding, and four in which spontaneous abortion was detected. In 53 (21.2%) of the cases, cordocentesis was performed because of hydrops fetalis, and six of the total fetal losses occurred in this group. Thus, the fetal loss rate

Table 1. Abnormal ultrasonographic findings in 194 cordocentesis cases

Ultrasonographic findings	*n* (%)
Hydrops fetalis	53 (27.31)
Multiple fetal anomalies	41 (21.13)
Central nervous system anomalies	34 (17.52)
Oligohydramnios	23 (11.85)
Intrauterine retardation	15 (7.73)
Polyhydramnios	13 (6.70)
Renal anomaly	5 (2.57)
Omphalocele	5 (2.57)
Extremity anomaly	5 (2.57)

Table 2. Chromosomal anomalies in 12 cordocentesis (CS) cases

Maternal age (yr)	Gestational weeks at CS	Indications for CS	Karyotype
21	26	Anomaly on USG	47,XY,+21
23	18	Anomaly on USG	47,XX,+18
23	25	Anomaly on USG	47,XY,+18
24	25	Anomaly on USG	69,XXX
25	19	Anomaly on USG	47,XY,+13
26	25	Anomaly on USG	47,XY,+18
27	26	Anomaly on USG	46,XX inv(9)
32	23	Anomaly on USG	47,XX,+21
36	24	Anomaly on USG + late maternal age	47,XX,+18
39	22	Late maternal age	47,XY,+21
39	27	Late maternal age	46,XY inv(9qh)
40	20	Late maternal age	47,XX,+21

USG = ultrasonography; inv = inversion.

Table 3. Findings from the cordocentesis cases ($n = 250$)

Findings	*n* (%)
Sufficient cord blood	245 (98.00)
Insufficient cord blood	5 (2.00)
Successful cell culture	232 (92.80)
Cell culture failure	18 (7.20)
Normal chromosomal result	220 (94.82)
Chromosomal anomaly	12 (5.17)
Abortus	12 (4.80)

was 11.32% in this group. In the non-hydrops fetalis group, the fetal loss rate was 3.04%. The fetuses lost in the non-hydrops fetalis group all had normal USG findings.

Discussion

Cordocentesis seems to be a widely accepted method for prenatal diagnosis. The rate of complications due to the procedure is one of the most crucial factor as to whether or not the patients accept this method of diagnosis, and the most important complication is fetal loss. Today, there seems to be a major transformation regarding the management and timing of cordocentesis, and procedures performed during midgestation are now performed earlier.

Because there is no alternative method that can be used for the patient population concerned, controlled studies cannot be conducted; and because of a lack of a proper controlled group, only cohort studies can be performed. The procedure can only be applied, owing to ethical reasons, to patient population with abnormal fetus. Therefore, it seems difficult to determine that fetal loss was associated purely to the procedure, as these fetuses were already at high risk for intrauterine death. Results of studies conducted previously reflected that the fetal loss rates were due to both procedure and underlying fetal pathologies.

Studies conducted have shown that the determinants of fetal loss rate are: age at cordocentesis, experience of the operator, indication for cordocentesis, and cordocentesis site.

A comprehensive and safe study that examined real fetal loss due to the procedure was conducted by Ghidini et al [4]. Ghidini et al grouped the patients who underwent cordocentesis into those having high or low risk. The low-risk group did not include the patients with chromosomal anomaly, intrauterine retardation, fetal infection or nonimmune hydrops fetalis. In this group, the fetal loss rate was 3% using the free-hand technique. In another study [5], the group of 1,020 women who had cordocentesis and the controlled group of 1,020 women who did not have cordocentesis were compared, and it was shown that fetal loss was associated with midgestational cordocentesis. When compared with the 1.8% basal fetal loss rate observed during midgestational period in the controlled group patients, an increased fetal loss rate of about 3.2% were found in the patients who underwent midgestational cordocentesis. It was reported that the calculated rate of 1.4% is the real fetal loss rate due to cordocentesis [5]. In the other studies, the rates of fetal loss due to the procedure varied from 1.9% to 3.1% [6,7]. This rate increases with pregnancies having high risks, such as those with nonimmune hydrops fetalis.

In our study, fetal loss due to the procedure was found in 12 (4.8%) out of a total of 250 cases of cordocentesis. In this study, the possible reasons for the high fetal loss rate were, for the majority in the study population, the fetal anomalies detected on USG for the high-risk pregnancies and the high likelihood of having a high-risk pregnancy. Fifty-three (21.2%) of our cases had cordocentesis because of hydrops fetalis, and six of the total fetal losses occurred in this group. The fetal loss rate was 11.32% in this group and 3.04% in the other group.

The rate of obtaining sufficient cord blood in our study was 98%, and the successful culture rate with cord blood was 92.8%. These results are consistent with those of previous studies [8]. None of the 18 patients with a failed cell culture accepted a second intervention.

According to the results of our cytogenetic examination, 12 (5.17%) cases had chromosomal anomalies. Although this rate was significantly lower than the rates reported in many studies [9], a similar rate of chromosomal anomaly was reported by Kabra et al [10]. Our results revealed that four had trisomy 18, four had trisomy 21, one had trisomy 13, one had triploidy (69,XXX), and two had chromosomal inversion. In our study, numerical chromosomal anomalies were found more often, as in the study by den Hollander et al [11]. The rate of patients with chromosomal anomalies found with multiple fetal anomalies on USG was high. Of the 12 fetuses with chromosomal anomalies, we detected multiple fetal anomalies on USG in eight of them.

During the procedure, almost every case had bleeding at the site of fetal blood sampling. However, the bleeding was not severe enough to cause hematoma formation or affect the fetal loss rate. Moreover, fetal bradycardia due to the procedure was found to be of high incidence. However, it was not high enough to warrant an intervention or cause fetal loss. None of

the patients developed chorioamnionitis. The results obtained in our study are consistent with those reported by Tongsong et al [12].

In conclusion, our results show that cordocentesis is safe and effective if conducted by experienced physicians under proper laboratory conditions. In addition, cordocentesis is an important invasive prenatal diagnosis and treatment method but is secondary to amniocentesis since there are less complications associated with amniocentesis. The fact that the results of cordocentesis can be obtained earlier than those of amniocentesis can be regarded as an advantage, particularly for patients who are after the 20th week of pregnancy. It should also be noted that with cases in which cordocentesis is performed, the risk of fetal loss may be greater because of multiple fetal anomalies, chiefly hydrops fetalis.

References

1. American College of Obstetricians and Gynecologists. *Down Syndrome Screening*. ACOG Committee Opinion No. 141. Washington, DC: ACOG, 1994.
2. Lynch L, Berkowitz RL. Amniocentesis, skin biopsy, umbilical cord blood sampling in the prenatal diagnosis of genetic disorders. In: Reece EA, Hobbins JC, Mahoney MJ, eds. *Medicine of the Fetus and Mother*. Philadelphia: JB Lippincott, 1992;641–652.
3. Lippman A, Tomkins DJ, Shime J, Hamerton JL. Canadian multicentre randomized clinical trial of chorion villus sampling and amniocentesis. Final report. *Prenat Diagn* 1992;12:385–408.
4. Ghidini A, Sepulveda W, Lockwood CJ, Romero R. Complications of fetal blood sampling. *Am J Obstet Gynecol* 1993;168:1339–44.
5. Tongsong T, Wanapirak C, Kunavikatikul C, Sirirchotiyakul S, Piyamongkol W, Chanprapaph P. Fetal loss rate associated with cordocentesis at midgestation. *Am J Obstet Gynecol* 2001;184:719–23.
6. Daffos F, Capella-Pavlovsky M, Forestier F. Fetal blood sampling during pregnancy with use of a needle guided by ultrasound: a study of 606 consecutive cases. *Am J Obstet Gynecol* 1985;153:655–60.
7. Boulot P, Deschamps F, Lefort G, et al. Pure fetal blood samples obtained by cordocentesis: technical aspects of 322 cases. *Prenat Diagn* 1990;10:93–100.
8. Hickok DE, Mills M. Percutaneous umbilical blood sampling: results from a multicenter collaborative registry. The Western Collaborative Perinatal Group. *Am J Obstet Gynecol* 1992;166:1614–7.
9. Nicolaides KH, Rodeck CH, Gosden CM. Rapid karyotyping in non-lethal fetal malformations. *Lancet* 1986;1:283–7.
10. Kabra M, Saxena R, Chinnappan D, Sanders V, Deka D, Buckshee K, Verma IC. Karyotyping of at risk fetuses by cordocentesis in advanced gestation. *Indian J Med Res* 1996; 104:288–91.
11. den Hollander NS, Cohen-Overbeek TE, Heydanus R, et al. Cordocentesis for rapid karyotyping in fetuses with congenital anomalies or severe IUGR. *Eur J Obstet Gynecol Reprod Biol* 1994;53:183–7.
12. Tongsong T, Wanapirak C, Kunavikatikul C, Sirirchotiyakul S, Piyamongkol W, Chanprapaph P. Cordocentesis at 16–24 weeks of gestation: experience of 1,320 cases. *Prenat Diagn* 2000;20:224–8.