General Section

Evaluation of the feasibility of a new method for performing chorion villus sampling

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Summary

Objective: This study aimed to evaluate the usefulness and safety of a new method for taking a placental biopsy. *Methods:* The procedures were performed using the traditional single needle technique (group 1) or the new method (group 2). In group 2, the piston was fixed in a simple metallic clip and the negative pressure was maintained in a continuous manner which was controlled with a three-way stopcock. *Results:* Multiple uterine insertion was necessary in 14 cases (32.6%) in group 1 and five (11.9%) in group 2 ($p < 0.05$). The amount of chorionic tissue obtained was significantly higher in group 2 (19.1 ± 15.0 mg vs 33.9 ± 17.4 mg $p < 0.05$). The abortion rates did not differ in either group. *Conclusion:* While using this technique, the operator is capable of performing the procedure without any assistance and of applying constant negative pressure only in the placenta. The advantageous outcomes are probably related to the size as well as the incessant fashion of the vacuum force.

Key words: Chorionic villus sampling; Prenatal diagnosis; Ultrasound; Invasive prenatal procedure; Aspiration; New technique.

Introduction

Prenatal diagnosis of fetal genetic abnormalities as early as possible is quite important. While the pregnancy progresses the psychological linkage gets stronger, termination becomes dangerous and may be restricted in some countries or by religions. Although theoretically early amniocentesis and chorion villus sampling (CVS) are the techniques for assessment of the fetal karyotype in the first trimester, the former is no longer proposed because of its high rate of abortion and talipes equinovarus [1]. However, recent studies have demonstrated that CVS at ten weeks or later had similar abortion rates with second trimester amniocentesis which was estimated at 1% and did not increase the risk of limb abnormalities [2, 3].

Recently Danish data on CVS and amniocentesis over the last 11 years has been published. The authors demonstrated that the number of invasive procedures is decreasing, but the percentage of CVS is continuously increasing [4]. However, the technique has not developed since the first applications and the procedure is performed heterogeneously between operators and institutions. Carlin and Alfirevic conducted a questionnaire on a group of subspecialists to evaluate their attitude on invasive prenatal diagnoses. It revealed that while they usually performed CVS transabdominally, there were some nuances regarding the diameter of the needle and technique (single or double needle) [5]. Recently, we published an upgraded technique of CVS in which we tried to render the assistance redundant [6]. In this study, we aimed to evaluate the feasibility and safety of this technique.

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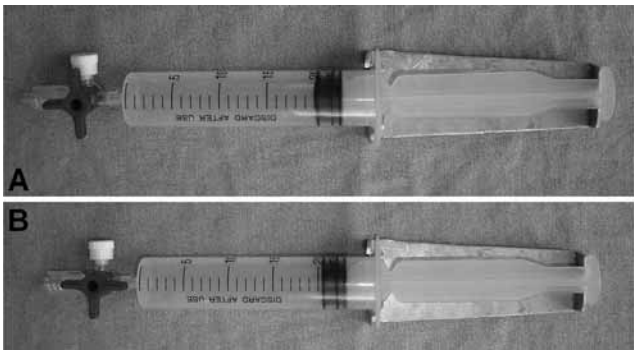
Methods

This was a randomized study which was conducted in the prenatal diagnosis unit of Cukurova University from April 2009 to September 2009. Inclusion criteria of the study were viable singleton pregnancies between week 11^{+0} and week 13^{+6} of gestation. The patients were placed into two groups according to the last number of their national identification number. If the last number was odd they were entered in group 1 and if it was even in group 2. In group 1 women had CVS with the traditional single needle technique and in group 2 they had the invasive procedure according to the technique that we have proposed [6]. Before the procedure, women were counseled about the disease which necessitated invasive testing and complications of the test. Women were also informed that some would undergo the procedure with a new technique. The women in each group gave written consent to participate in this trial.

The invasive tests were performed by one operator. Localization of the placenta was recorded and gestational age was also determined by measuring the crown-rump length in the saggital plan. Skin disinfection was performed with 10% povidone-iodine solution. Before the procedure, a 20-gauge needle was washed out with heparin and a quarter of the 20 ml syringe was filled with culture medium. The use of the biopsy line tool or biopsy needle guide was left to operator choice, and was necessary in a minority of cases.

In group 1 the procedure was performed traditionally with the help of an assistant. The procedure is carried out as follows: when the operator determines that the tip of the needle is in the chorion, the assistant removes the mandrin and attaches the syringe to the needle. While he/she holds the transducer, the operator handles the syringe. The operator moves the needle back ward and forward while pulling back the piston of the syringe to create negative pressure. The procedure in group 2 was performed with a simple metallic clip, designed in our institution, which takes over the assignment of creating negative pressure. The system is fixed to the needle when the operator detects that the tip of the needle is in the placenta. The three-



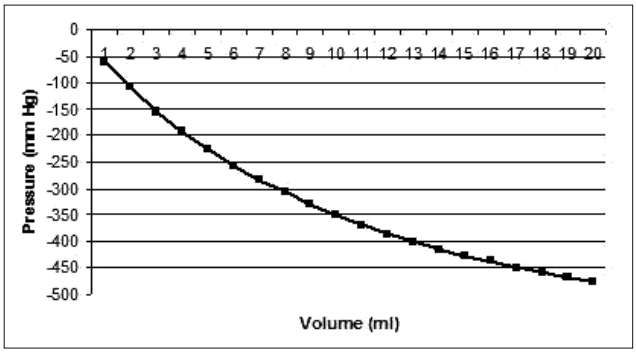


Figure 1. — To create negative pressure in the syringe, the piston is pulled and installed in the metallic clip while the three-way stopcock is turned off (A). When the system is fastened to the needle the three-way stopcock is turned on for aspiration (B).
Figure 2. — Relation between the negative pressure and syringe volume.

way stopcock, which is the control point of the negative pressure, is turned on and the needle is thrust into the chorionic tissue consecutively. This device assures the continuity of the negative pressure, allowing the operator to hold the transducer with one hand and the other is used to control the needle without needing any assistance (Figure 1). The three-way stopcock should be turned off before pulling back the needle to prevent any maternal tissue contamination.

The adequacy of the collected tissue quantity for both groups was visually evaluated in the operating room by the laboratory technician. Precise measurement was done in the laboratory with a microbalance enabling measurement of 0.001 mg. The women were followed for four weeks after the CVS for procedure-related complications.

Data were analyzed using the Statistical Package for the Social Sciences (version 11, SPSS Inc., Chicago, Ill., USA). Normality of each continuous variable was checked. The Student's t-test was used to compare the normally distributed variables and Mann Whitney U test was used to compare the non normal (skewed) distributed variables between the groups. The chi square test was used for categorical data analyses. Data are expressed as mean ± SD and median (min-max). A p-value less than 0.05 was considered statistically significant. This study was approved by the ethical committee of the Medical School of Cukurova University.

Results

The relationship between the negative pressure and volume obtained in the syringe was evaluated with a sensitive electronic calibrator. While the piston was pulled back step by step the amount of negative pressure was recorded every 0.1 ml (Figure 2).

Eighty-five women were eligible and agreed to participate in the study in which 43 (50.5%) were in group 1 and 42 (49.5%) in group 2. In the majority of cases the placenta was located anteriorly. Distribution of the placental localization was the same in each group. There was not any statistical difference between the groups regarding maternal age and gestational age (Table 1). Indications of CVS were advanced maternal age in 46 (54.12%), positive first trimester screening test in 13 (15.29%), and jeopardy of hemoglobinopathy in 26 (30.59%).

Table 1. — *Descriptive data of the patients in each group*.

	Group 1	Group 2	*p*
Placental localization			
• Anterior (n = 55)	28 (65.1%)	27 (64.3%)	0.936
• Posterior (n = 30)	15 (34.9%)	15 (35.7%)	
Gestational age*	12.5 ± 1.1	12.3 ± 0.9	0.298
	12.1 (11.0-13.7)	12.2 (11.0-13.9)	
Age*	33.7 ± 4.5	34.0 ± 5.0	0.726
	32.0 (27-44)	33.0 (27-44)	

*: Data expressed as Mean ± SD in the first line and Median (min-max) in the second line.

Table 2. — *Comparison of procedural results for both groups*.

	Group 1 (n = 43)	Group 2 (n = 42)	*p*
Attempt of uterine insertion			
• 1: n (%)	29 (67.4%)	37 (88.1%)	
• ≥ 2: n (%)	14 (32.6%)	5 (11.9%)	0.022
Tissue weight (mg)			
• Mean ± SD	19.1 ± 15.0	33.9 ± 17.4	
• Median (min-max)	13.1 (5.8-60.6)	33.5 (6.6-62.2)	0.001

The number of the women who needed more than one uterine needle insertion was higher in group 1. The amount of the chorionic tissue was particularly low in group 1 compared to group 2. Comparisons of the procedural results of the both techniques are shown in Table 2. Cytogenetic evaluation of chorionic tissue was successful in all cases and did not reveal inadequate material or failed culture in any case.

Two of the women from group 1 and one from group 2 elected termination of the pregnancy due to the pathological results which were sickle cell anemia and β-thalassemia for group 1 and β-thalassemia for group 2. Only one pregnancy loss was detected following CVS in group 1 and there was not any abortion in group 2 ($p = 0.314$).

Discussion

Invasive procedures during prenatal diagnosis have been performed all over the world since ultrasound became an essential part of obstetric units. Amniocentesis

is still the most performed invasive prenatal diagnostic procedure. However the rate of CVS has been increasing since the introduction of the first trimester trisomy screening test. The method that we are proposing provides a new way to retrieve placental tissue with no need for an assistant and with the of aim facilitating the procedure.

It is a well known fact that the number of insertions and the experience of the operator are the most important factors influencing the procedure-dependant abortion rates [7]. The rates of multiple insertions have been quite heterogeneously reported in previous publications. Mujezinovic and Alfirevic published in a review that multiple insertion rates in CVS range from 1.4% to 26.6%. They calculated the pooled risk to be 7.8 (95% CI 3.1-14.2) [8]. When compared to many previous publications the multiple insertion rate is higher in our study. This may be attributed to the small size of groups or the experience of the operator. All procedures were performed by a single operator which permits us to uniquely evaluate the performance of this technique.

Traditional methods constitute the negative pressure in a discontinuous fashion. The continuous aspiration of chorionic tissue was previously reported in two studies [9, 10]. The authors used a commercial blood collection tube, which is available in all wards. The ability to control the negative pressure is the main difference between these techniques and ours. The three-way stopcock permits negative pressure to be created only in the chorionic plate, thereby protecting the maternal tissue from contamination. There are also some differences in the setting of these studies. Calda and Brestak used an 18-gauge needle with a 10 ml vacutainer [10], whereas Battagliarin *et al*. used a 20-gauge needle with a 4 ml vacutainer [9]. According to our in vitro experiment, the corresponding pressures for each one were approximately 190 and 350 mm Hg consecutively. However the model that we have proposed offers nearly 475 mm Hg. Battagliarin *et al*. reported an increased second needle insertion rate while Calda and Brestak we found that the need of multiple needle insertion diminishes when negative pressure is sufficiently strong [9, 10]. We suppose that the continuous manner of the negative pressure is as important as the force created by the aspiration systems.

This device design was inspired by the widely used pregnancy termination tool: Karman cannula. We found that it apparently diminishes the risk of multiple insertions and assures that a sufficient amount of tissue can be collected. Subcuticular adipose tissue thickness and placental localization may additionally affect the performance of CVS. Larger studies are needed to evaluate and confirm the effect of these factors.

References

[1] Nikkilä A., Valentin L., Thelin A., Jörgensen C.: "Early amniocentesis and congenital foot deformities". *Fetal Diagn. Ther.*, 2002, *17,* 129.
[2] Brambati B., Tului L.: "Chorionic villus sampling and amniocentesis". *Curr. Opin. Obstet. Gynecol*., 2005, *17,* 197.
[3] Evans M.I., Wapner R.J.: "Invasive prenatal diagnostic procedures". *Semin. Perinatol*., 2005, *29,* 215.
[4] Tabor A., Vestergaard C.H.F., Lidegaard Ø.: "Fetal loss rate after chorionic villus sampling and amniocentesis: an 11-year national registry study". *Ultrasound Obstet. Gynecol.,* 2009, *34*, 19.
[5] Carlin A.J., Alfirevic Z.: "Techniques for chorionic villus sampling and amniocentesis: a survey of practice in specialist UK centres". *Prenat. Diagn*., 2008, *28,* 914.
[6] Buyukkurt S., Evruke C., Demir C., Ozgunen F.T., Kadayifci O.: "A new device to facilitate the chorion villus sampling". *J. Perinat. Med*., 2009, *37*, 425.
[7] Brambati B., Terzian E., Tognoni G.: "Randomized clinical trial of transabdominal versus transcervical chorionic villus sampling methods". *Prenat. Diagn*., 1991, *11,* 285.
[8] Mujezinovic F., Alfirevic Z.: "Procedure-related complications of amniocentesis and chorionic villous sampling: a systematic review". *Obstet. Gynecol*., 2007, *110,* 687.
[9] Battagliarin G., Lanna M., Coviello D., Tassis B., Quarenghi A., Nicolini U.: "A randomized study to assess two different techniques of aspiration while performing transabdominal chorionic villus sampling". *Ultrasound Obstet. Gynecol*., 2009, *33,* 169.
[10] Calda P., Brestak M.: "Chorionic villus vacu-sampling in 377 consecutive cases". *Prenat. Diagn*., 2009, *29,* 1075.

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