ORIGINAL ARTICLE

TRANSABDOMINAL CHORIONIC VILLUS SAMPLING (CVS) FOR PRENATAL DIAGNOSIS OF GENETIC DISORDERS

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ABSTRACT

Objective: To determine the safety and outcome of transabdominal Chorionic Villus Sampling (CVS) for prenatal diagnosis of genetic disorders.

Design: Descriptive study.

Place and Duration of Study: Department of Pathology, PNS Shifa, Karachi, from January 2003 to December 2004.

Patients and Methods: A total of 143 couples with request for prenatal diagnosis of various genetic disorders were studied. Transabdominal CVS was done under local anesthesia and ultrasound guidance. A Co-axial Chorion Biopsy needle set with an outer guide and an inner aspiration needle was used. The needle was introduced into the placenta in its longitudinal direction. Once the needle was adequately placed, the chorionic villi were aspirated with a to and fro jiggling movement of the aspiration needle and a suction force was applied through a syringe. Results were recorded and analyzed for descriptive statistics.

Results: A total of 144 CVSs were done in the outdoor on 143 couples including one with a twin pregnancy. The most common indication was β-thalassaemia (97%). Most procedures (76%) were done between 12 and 14 weeks (range 10-21 weeks). All placental positions including 52% anterior and 48% posterior were approachable through the trans-abdominal route. Most aspirations were easy, however, in 28% the aspiration was difficult due to a variety of factors. The overall success rate was 100%. In 85% of the cases sample yield was >25mg while in the remaining cases 10-25mg of sample was obtained that allowed a comfortable diagnosis. The procedure related abortion occurred in 1/144 (0.7%).

Conclusion: Transabdominal CVS is a useful outdoor procedure for prenatal diagnosis. Placentae in almost any position can be approached without significant risk to the mother and the fetus.

KEY WORDS: *Chorionic villus sampling. Prenatal diagnosis. Pakistan. Transabdominal.*

INTRODUCTION

Genetic disorders are a fairly common cause of morbidity and mortality in Pakistan. Most such disorders are either not treatable or the cost of treatment, if available, is out of the reach of the population at large.[1] Early prenatal diagnosis and selective termination of the affected pregnancies have become an important component of the management of genetic disorders. The sample can be obtained by Chorionic Villus Sampling (CVS) through the transabdominal or the trans-cervical route. The transabdominal route is considered safer as well as convenient for the patient than the transcervical route.[2]

A clinical service for the prenatal diagnosis of genetic disorders was introduced in Pakistan in 1994.[3] Since then a large number of affected families have benefited from this facility.[4,5] The objective of this study was to determine the safety and outcome of transabdominal CVS for the prenatal diagnosis of common genetic disorders.

PATIENTS AND METHODS

Between January 2003 and December 2004, a total of 143 couples (including four couples who used the test twice and one with a twin pregnancy) requested prenatal diagnosis for various genetic disorders at the Department of Pathology, PNS Shifa, Karachi. At the time of booking the couples were counseled about the genetic risks, the procedure and complications of fetal sampling, errors in diagnosis and the termination of pregnancy and its religious implications. Before the procedure, a written consent was obtained from all couples.

A preliminary ultrasound scan was done to determine the fetal viability, gestational age, number and placental position. When the gestational age was 10 weeks or more, CVS was carried out immediately. Otherwise, the procedure was deferred till a date corresponding to about 12 weeks gestation.

The ultrasound scanning (USG) was done either on Sonica C scanner and Aloka SSD 900 scanner, using a 3.5MHz convex probe. The size and position of placenta was ascertained and a suitable site for introducing the needle on the anterior abdominal wall was selected. The abdominal skin in a radius of about 10 cm was cleaned with Pyodine. Approximately 5-10 ml of 2% xylocain was injected with a 23 gauge spinal needle. The whole tract of the CVS needle from the skin to the uterine serosa was infiltrated with the local anesthetic.

A co-axial chorion biopsy needle set (Luer Lock) 18G x 165 mm outer needle and 20G x 200 mm inner needle (Rocket, UK) was used (Figure 1). The inner needle can be passed freely through the outer needle when the stillet of the latter is removed leaving about 30mm of the inner needle to protrude

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beyond the outer needle. The needle sets were re-used after sterilization and sealing in a sterile pack.

While standing on the left side of the patient, the CVS outer needle was introduced from the puncture site of the local anesthetic. Thereafter, the USG probe was held in the left hand and the CVS needle was maneuvered with the right hand. An important step in the procedure was to keep the needle tip visible at all times. After piercing the uterine wall, the needle was pushed with a jerky movement to enter the placenta in its longitudinal plane. The jerky forward push was helpful in avoiding any placental separation at the site of the needle entry. For an anterior placenta, the needle was kept in a horizontal direction while for a posterior placenta, the needle was kept vertically placed. While approaching a posterior placenta special care was required to avoid intestinal loops. The point of entry into the uterine wall was particularly sensitive to pain and its adequate anesthesia was essential.

Figure 1: Co-axial chorion biopsy needle set (Luer Lock, Rocket, UK). From left to right are the assembled needle set, 200mm 20G aspiration (inner) needle, 165mm 18G outer needle, stillet, and the 30 ml syringe.

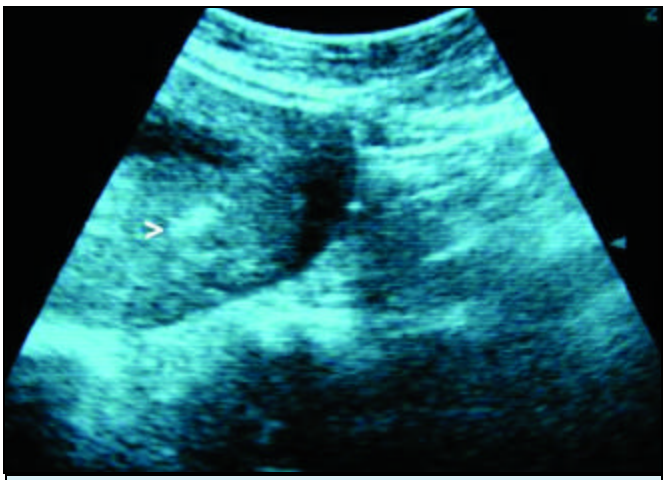

Figure 2: An ultrasound image showing the tip of the CVS needle (>) in a posterior placenta.

The entry of needle into the placenta was marked by a loss of resistance. Once the needle was in the placenta (Figure 2), it was sufficiently advanced to leave at least 2cm of the placental tissue ahead of the needle tip. A 30 ml disposable syringe was attached to the CVS inner needle and it was rinsed with about 1 ml sterile normal saline. The stillet was removed and the inner needle was introduced through the outer needle. Lack of resistance for the tip of the inner needle was another indication that the needle was in the placenta and not in the uterine wall. Once the inner needle was in place, the plunger of the syringe was pulled back to about 25 ml mark to create a suction force. The position was maintained by locking the plunger with the four fingers of the right hand. The aspiration syringe and the inner needle in the locked position were jiggled to and fro about 10-12 times. This caused localized damage to the placenta and with the simultaneous suction force the disrupted villi were sucked into the needle. The aspiration needle was removed and the outer needle was left as such. The sample was flushed into a sterile Patri dish containing normal saline. Adequate amount of grayish white placental villi confirmed a successful aspiration. In case of a poor yield of the sample, a second or rarely a third aspiration attempt was made through the same outer needle left in place. Finally, the outer needle was also removed and the puncture mark was sealed with a sterile elastic bandage.

A post-aspiration USG scan was done to see the fetal well-being, any haematoma formation, or placental separation. The patients were allowed home 30 minutes to one hour after the procedure with an advice to take bed rest for 24 hours. Two tablets paracetamol were advised for pain relief, if required. No prophylactic antibiotics were used. Follow-up regarding any complication was done after 1 week at the time of report collection.

The ethical issues related to prenatal diagnosis, and a possible termination of pregnancy to follow, were discussed with the couples in the light of a religious verdict (fatwa).[6]

Descriptive statistics were applied to the data using Sigmastat version 2.0.

RESULTS

A total of 144 CVSs were done on 139 couples (including one with a twin pregnancy and four who requested the test twice during the study period). The indications in 144 CVSs included β-thalassaemia (140), Down syndrome (03) and Becker muscular dystrophy (01).

The gestation at CVS ranged from 10-21 weeks. Most procedures (76%) were done between 12 and 14 weeks. Only 6/144 (4%) were done after the 16th week. There were 75 (52%) anterior and 69 (48%) posterior placed placentae. In 7 patients, the placenta was posterior and very low-lying. In 3 such cases the uterus was also retroverted. All low- lying placentae were approached either through the right or the left iliac fossa. Most aspirations were easy, however, in 40/144 (28%), the aspiration was difficult. The factors associated with a difficult aspiration were obesity, previous cesarean section (mostly in anterior placentae), fibroids, retroverted uterus and thin placentae. In 123/144 (85%) cases, the sample yield was very good (>25 mg). However, in the remaining cases, the sample was adequate enough (10-25 mg) to allow a comfortable lab diagnosis. In the vast majority (90%), aspiration was successful in the first attempt. In the remaining cases, a second or rarely a third attempt from the same outer needle, left in place, was required. There were only 3 patients in whom the aspiration was unsuccessful and all 3 were called for a repeat CVS one week later which was successful. The overall success rate was 100%. The time for one aspiration, from introduction of outer needle to its removal, ranged from 5-15 minutes (average 10 minutes).

Most patients felt pain and discomfort lasting upto 36 hours after the procedure that was relieved by simple analgesics. Haematoma formation within the placental tissue at the site of aspiration was seen in 7/144 (4.9%). Three patients developed spotting shortly after the procedure. Two recovered by rest for 3-6 hours in the hospital while the third patient aborted spontaneously six hours after the procedure. No case of post-procedure infection was observed. On the whole the procedure related abortion occurred in 1/144 (0.7%).

Discussion

Prenatal diagnosis through early fetal sampling has played a pivotal role in the prevention of genetic disorders.[7] Ultrasound guidance adds to the safety for the fetus as well as the mother. Nevertheless, an elaborate learning process to master the technique remains indispensable.[8] The choice is between amniocentesis and chorionic villus sampling. The main disadvantage of amniocentesis is the increased risk of pregnancy loss and higher incidence of talipes, if done earlier than 15 weeks.[9]

Chorionic villus sampling was introduced in the early 80s and since then it has given a new dimension to prenatal diagnosis.[10] The procedure can be done as early as 9 weeks of gestation. However, attempts to do it earlier than 9 weeks have resulted in an increased risk of fetal limb reduction defects.[11,12] In this study majority of the procedure were done between 12-14 weeks. At this stage, the placenta is of adequate size that can be sampled without much difficulty. The best time for CVS appears to be around 12-13 weeks. There is no upper time limit for doing the procedure. Due to anatomical reasons, it was easier to aspirate a placenta of an earlier stage than late. Another very important reason for doing the procedure early is that if it is to be followed by termination of pregnancy then it should be done within a reasonable time-frame defined by consensus. Most Islamic scholars in Pakistan have a consensus on legal termination of a pregnancy before 120 days (17 weeks) of gestation if the fetus is found to have a serious abnormality.[6] The response of the Pakistani couples to prenatal diagnosis and termination of pregnancy has shown that over 90% of the couples are willing to accept the test and terminate the pregnancy before 17 weeks.[5]

The CVS is done either transabdominally or through the transcervical route.[2] In Pakistan, at least five different centers are involved in doing the procedure using the transcervical as well as transabdominal routes. A disadvantage of the trans-cervical route is the possibility of transmitting infection from the contaminated cervical canal.[4] The transcervical CVS is more technically demanding than the transabdominal CVS with more failures to obtain sample and more multiple insertions.[9] Its main advantage is the ease with which the low-lying posterior placentae may be sampled.[13] The trans-abdominal route has an obvious advantage of mechanical similarity to amniocentesis that makes CVS easier and familiar to perform.[4] In this study, practically all positions of placenta were sampled through the transabdominal route without much difficulty that makes it the most feasible choice for use in routine practice. The transcervical route may be used as a complementary procedure to improve the results in posterior placentae.[2,13]

The choice of needle for CVS may vary from a simple 18-20G spinal needle to the co-axial chorion biopsy needles.[2,13] The latter have several advantages including greater length, better visibility under ultrasound, special design to disrupt placental villi, and the option of multiple sampling attempts through the same outer needle left in place.[14] Whichever needle is chosen, a larger syringe and needle size yields a larger quantity of chorionic villi.[15]

CVS is a safe procedure in experienced hands. Mild and transient postprocedure pain due to uterine cramps, not more than that felt after amniocentesis, is common.[16] Bleeding and spotting are uncommon and may result due to direct damage to the placental edge.[2] Transfixation of the large intestine and bacterial contamination is a rare but serious complication that is best avoided by taking utmost care in avoiding the intestinal loops.[2] Pregnancy loss is the most serious complication after CVS. The overall rate of fetal loss is 0.5-1.0%.[11] The results of this study also conform to the internationally accepted data. One reason for the low rate of miscarriage after an invasive procedure may be the low reactivity of the myometrium to transfixation during first trimester.[17]

Late obstetric complications could not be followed up in this study. But the incidence of complications like preterm delivery, premature rupture of membranes, placental disorders, perinatal mortality, such as low birth weight, and congenital defects compare favourably well in the general population not exposed to CVS.[18]

Prenatal diagnosis is an essential recommendation for all couples with recessive genetic disorders like thalassaemia with upto 25% recurrence risk. Prenatal diagnosis is also offered to women aged 35 years or above, or who are found by screening to be at a higher risk of having an infant with Down's syndrome or another chromosomal abnormality. A recent cost utility analysis of chorionic villus sampling and amniocentesis versus no invasive testing, using data from randomized trials, case registries, and a utility assessment of pregnant women, aged 16-47 years, have shown that prenatal diagnosis is cost-effective at any age or risk level.[19] Chorionic villus sampling has the great advantage over mid-trimester amniocentesis of producing early results. Moreover, rapid analytic techniques have significantly reduced the waiting time between sampling and diagnosis, whereas progress in recombinant DNA technology and human gene mapping has led to an increase in the range of conditions it can detect.[20]

Conclusion

Ultrasound guided transabdominal CVS is a useful outdoor procedure for fetal sampling and prenatal diagnosis. It can play an important role in the prevention of genetic disorders that are otherwise incurable. A placenta in almost any position can be approached without much difficulty. The procedure is also safe for the mother as well as the fetus.

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