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REVIEW ARTICLE

Cordocentesis

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Abstract Cordocentesis is an ultrasound-guided procedure to obtain fetal band from umbilical cord. It is indicated for rapid evaluation of fetal karyotype, fetal hematological disorders, and identification of fetal infection. Results are available in 48–72 h. If patient presents late and the results from amniocentesis would not be available within time for elective termination of pregnancy, it is the preferred procedure. Therapeutic indications include intravascular cord transfusion in Rh isoimmunization, fetal anemia, or drug administration. Procedure is performed from 18 weeks of gestation onward. Umbilical cord at placental attachment is the site of choice for puncture. We use 21–22 gauge spinal needle for this procedure. It needs expertise and is safe if performed by experienced surgeon. Single dose of antibiotic prior to procedure can be given. The rate of pregnancy loss varies and depends on the indication of procedure. Overall procedure related loss is <2 %.

Keywords Cordocentesis · Prenatal diagnosis · Thalassemia · Hemophilia · Infection · Chromosomal disease

Introduction

Fetal blood sampling was first carried out in 1974 by fetoscopy for the diagnosis of hemoglobinopathies using a rigid endoscope inserted through the mother's abdomen and uterus [1]. Later, transabdominal ultrasound-guided cordocentesis was performed by Daffos in Paris in 1983 [2]. This ultrasound-guided technique has replaced the fetoscopy method of fetal blood sampling. It is also called percutaneous umbilical blood sampling (PUBS).

Indications for Cordocentesis

a. For Diagnostic Purposes

1. Chromosomal analysis to obtain a rapid karyotype for
   i. Prenatal diagnosis in late gestation.
   ii. Presence of fetal structural malformations on ultrasound studies.
   iii. Severe fetal growth restriction of early onset or oligohydramnios.
   iv. Failed diagnosis by amniocentesis or chorionic villous sampling (CVS).
   v. Chromosomal mosaicism on amniotic fluid or chorionic villus sample.
2. Single gene defects such as thalassemia and hemophilia, when the patient seeks care in later gestation or the molecular defect has not been identified. High performance liquid chromatography (HPLC) and factor VII assay in cord blood are feasible alternatives for prenatal diagnosis (PND) in thalassemia and hemophilia, respectively. At AIIMS, New Delhi, cord blood sampling at 18–26 weeks of gestation rightly helped to detect these conditions [3].

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3. Other hematological disorders like thrombocytopenia.
4. Congenital infection due to rubella, Cytomegalovirus (CMV), toxoplasmosis, parvovirus, varicella by assay of specific genomic material by PCR, IgM, and white blood cell and platelet counts.
5. Hemoglobin and hematocrit estimation in fetal anemia due to Rh isoimmunization or nonimmune hydrops.
6. Fetal blood gas analysis for delayed labor.

b. For Therapeutic Purposes

1. Intrauterine blood transfusion in cases of fetal anemia due to isoimmunization or parvovirus infection.
2. Administration of drugs for fetal arrhythmias, or fetal paralysis to facilitate invasive procedures.
3. Administration of thyroxine in cases of fetal goiter for treating hypothyroidism.
4. Stem cell transfer and gene therapy [4].

The commonest therapeutic indication for cordocentesis is carrying out intrauterine transfusion in cases of hydrops due to Rh incompatibility, or less commonly, in cases of anemia due to other causes. In cases of fetal arrhythmia, anti-arrhythmic drugs are infused, or drugs may be administered to cause fetal paralysis to facilitate invasive procedures such as transfusions or fetal MRI.

Experience in India

In India, there are numerous reports on the use of cordocentesis. Kabra et al. [5] cultured fetal blood obtained by cordocentesis to obtain rapid karyotypes of 99 fetuses at risk during the late second trimester. The commonest indications for the procedure were abnormalities detected on ultrasonography (47.7 %), and previous child with Down syndrome. Analysis of the 67 successful cultures showed four (5.9 %) karyotypic abnormalities. Later, Mathur et al. [6] reported their experience with cordocentesis in 187 cases. The common indications were ultrasonographic abnormalities (47.6 %), history of Down syndrome in previous pregnancy (13.3 %), advanced maternal age (11.7 %), low maternal serum alpha fetoprotein levels (10.7 %), previous child with malformation (10.7 %), previous child with trisomy 13/18 (2.6 %), parent having a balanced translocation (1.6 %), and high maternal serum alpha fetoprotein levels (1.6 %). Of 137 successful cultures, eight (5.2 %) showed karyotype abnormalities. The remaining samples could not be reported due to the presence of maternal contamination of the sample (12.3 %), inadequate sample (6.4 %), or culture failure (9.8 %).

Ranjan et al. [7] used cordocentesis to make a PND of hemophilia A in eight families. The choice between CVS and cordocentesis depended upon the gestation at which the woman presented. Mota et al. [8] described two families with coagulation disorders, one with severe factor VII (FVII) deficiency and the other with severe factor X (FX) deficiency, where PND was provided after cordocentesis between 17 and 19 weeks using a battery of coagulation factor assays.

Shetty et al. [9] performed cord blood analysis between 17.4 and 20.6 weeks of gestation in 172 confirmed carriers belonging to families of hemophilia A, hemophilia B, von Willebrand disease (VWD), and factor VII and X deficiency. Carriers for hemophilia A were 133, for hemophilia B 30, for type 3 VWD six, FX deficiency two, and FVII deficiency one case. The approach to the cord was either transabdominal or transamniotic. The volume of blood collected varied between 1 and 2 mL. In case of hemophilias, the diagnosis was offered by factor VIII/IX:C activity and antigen assays, wherever required. In case of VWD, the diagnosis was based on VWB factor antigen assays, as detected by ELISA along with FVIII:C assay while in cases of FVII and FX deficiency, the diagnosis was based on FVII:C and FX:C, respectively.

Deka et al. [10] performed cordocentesis in 1342 cases of high-risk pregnancy—hemoglobin estimation in Rh isoimmunized pregnancies in 553 cases, chromosomal analysis in 427 cases, nonimmune hydrops/pleural effusion/ascites in 88 cases, congenital infections in 31 cases, intrauterine growth restriction in 51 cases, thalassemia in 53 cases, hemophilia in 36 cases, and thyroid function tests for fetal goiter in three cases.

Mishra et al. [11] used fetal blood obtained by cordocentesis to make PND of primary immune disorders (PIDs), as molecular studies were not available. Normal reference range of lymphocyte subsets, CD 18/CD11 integrins on leukocytes, MHC class II expression and oxidative burst activity of fetal neutrophils at 18 weeks of gestation were established on 30 cord blood samples. Prenatal diagnosis was performed in 13 families with PIDs. Maternal contamination was ruled out by variable number of tandem repeats (VNTR) analysis. Of 13 fetuses, nine were found to be unaffected [three cases with leukocyte adhesion deficiency (LAD-I), four cases with severe combined immunodeficiency diseases (SCID), one with X-linked agammaglobulinemia (XLA), and one with chronic granulomatous disease (CGD)]. Three fetuses were found to be affected (one with T−B+NK − SCID, one with MHC class II deficiency and one with LAD-I deficiency). Diagnosis was confirmed by testing the cord blood samples after delivery and further follow-up of the children.

Timing

Cordocentesis is generally performed after 18 weeks of gestation. Before that, the procedure is difficult due to a small cord size. As the period of gestation advances, cord vessel diameter increases and so the procedure becomes easier. However, most often the diagnosis is required earlier than 20 weeks so that termination can be offered if results come out to be abnormal. Mean gestation at time of cordocentesis is reported as 19.8 weeks [12].

Procedure

After preparation of the abdominal part, ultrasound evaluation is done for placental localization and placental origin of cord as this is the best site for cordocentesis. The umbilical cord is comparatively fixed at its origin and so the needle entry is most likely to be successful at this site. Color Doppler also facilitates the localization of cord insertion. Maternal blood contamination rate is higher when cord insertion is targeted [12]. If access to this site is not feasible then free loop of the cord can be selected for puncture. Fetal side of the cord should be avoided as there is increased risk of inducing fetal bradycardia. Needle size is decided on the basis of distance from skin to site of puncture. Spinal or Chiba needle is used depending on the length of the needle required. Needle size of 20–21 G can be used. Under continuous ultrasound guidance, the needle is inserted into the abdomen. Prior confirmation of the site of abdomen is carried out by dipping the back of the needle and assessing the tract, if needle-guide facility is not there. Needle tip is advanced towards the puncture site avoiding injury to the fetal structures. Pancuronium 0.1 mg can be given intramuscularly to the fetus if there are excessive fetal movements. It is required when the needle has to be kept in position for a longer time, like in intrauterine transfusion.

When the needle tip is near the cord, sharp and quick puncture is made over the wall to achieve penetration into the vessel. The umbilical vein is punctured 1 cm away from insertion to avoid maternal contamination. Arterial puncture is avoided as it may result in bradycardia. The tip of the needle can be visualized inside the lumen of the vessel. Two to 4 mL of fetal blood is collected. After obtaining blood, the needle is withdrawn with the stylet in position and fetal heart activity is checked afterwards. Figure 1 shows the needle tip in the lumen of vessel during cordocentesis.

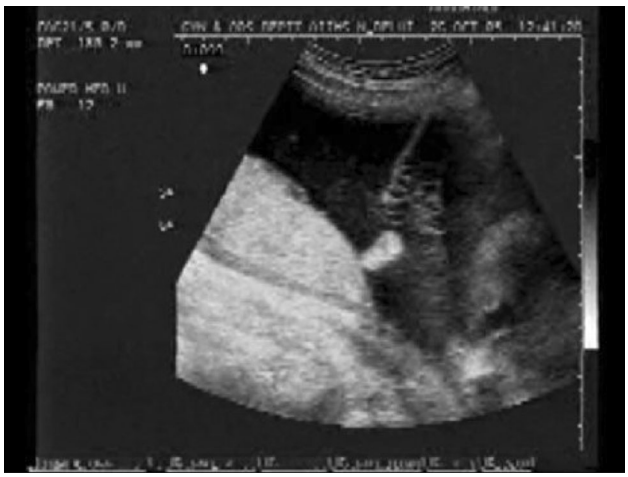

Fig. 1 Needle tip in the lumen of the vessel

Problems

Cordocentesis requires high expertise. Mean duration of the procedure is reported as 10–15 min in expert hands, but significantly longer time is required in the initial 50 cases or so [12]. For diagnostic purposes, quite often, the procedure is carried out at <20 weeks of gestation, and the procedure is more difficult as the umbilical vein is thin.

Localized uterine contractions may occur immediately on insertion of the needle. Such contractions alter the course or decrease the visualization of the needle. It is unavoidable. The operator should wait for contraction to pass away or remove the needle and readjust its direction

Fetal parts may obstruct the route where the needle has to be passed. In such situations, one should wait for the fetus to change its position.

Post-procedure Observation

1. Observe for any bleeding from the puncture site, although such bleeding is usually self limiting. If it is prolonged, intrauterine transfusion may be required.
2. Post-cordocentesis, fetal bradycardia may develop, but it is usually transient. It is more commonly seen when the artery is punctured instead of the vein. Patient can be monitored for fetal heart rate monitoring.
3. Patient may not perceive fetal movement for 2 h if pancuronium has been given to the fetus.
4. Anti-D should be given if the patient is Rh negative, and has a nonimmunized pregnancy.
5. Prophylactic antibiotics may be administered. The authors' practice is to give single IV dose of cefazolin 1 g half an hour prior to the procedure.

Limitations

Occasionally, there may be inability to visualize the site of cord insertion. Fetal position or movement may interfere with optimal cord visualization and needle placement. Placental position influences the likelihood of success or occurrence of complications associated with the procedure. In the presence of anterior placenta, cordocentesis is easier but as the needle is traversing the placental villi, there is higher probability of maternal cell contamination in the specimen or it may worsen Rh immunization in an Rh negative women. If the placenta is posterior, attempting cordocentesis is likely to be difficult because the interposed fetus may obstruct the optimal pathway for the needle.

Complications

Complications of the procedure depend upon the indication for the procedure itself. There is higher fetal loss if it is performed for severe IUGR or for nonimmune hydrops, compared to structural anomalies or for diagnosis of genetic diseases. Overall procedure related complications are <2 % [12].

Fetal Complications

1. Bleeding from puncture site occurs in about 10–20 % of the cases and cord hematoma may form in 0.07 % of cases [3, 5]. Bleeding from puncture site may be transient or persistent (>60 s). Transient bleeding was reported in 23 % whereas persistent bleeding was observed in 2.3 % of the cases in a large study of more than 2000 cases [13].
2. Fetal bradycardia occurs in 4.3 % [11] to 4.9 % of cases [14].
3. Preterm premature rupture of membranes and chorioamnionitis occurs in about 0.15 % of the cases [12].
4. Risk of preterm birth was found to be 12.7 % as compared to 7.4 %, in control subjects, while the frequency of small for gestation babies was 6.9 % as compared to 4.6 % of controls [14].
5. Fetal loss is reported to be 1.9 % in cordocentesis versus 1 % in the control group [14]. In another study, fetal loss was observed in 3.2 % of the cases but procedure-related risk was found to be only 1 % [12]. Before 24 weeks of gestation, fetal loss within 2 weeks of the procedure was 2.7 % as compared to 1 %, while after 24 weeks, the total and procedure-related risk of loss was 1.9 and 0.8 %, respectively [15]. Of the patients who underwent cordocentesis in the presence of structural abnormalities, the presence of stillbirth has been observed in up to 24.6 % of cases [16]. Hence, fetal loss due to complications after cordocentesis is in the range of 1.3 % of the normal fetuses and up to 25 % in fetus with congenital abnormalities [17].

Maternal Complications after Cordocentesis

Chorioamnionitis
Bleeding
Risk of emergency lower segment cesarian section (LSCS)
Needle injury to maternal intra-abdominal organs

It is recommended that the procedure should be postponed if the condition is unfavorable as duration of the procedure is an important factor for outcome of cordocentesis [18]. Recently, four-dimensional ultrasonographic guidance for needle placement in PND procedures has been recommended to eliminate the errors in the techniques [19].

Cordocentesis in Multifetal Gestation

It should be performed after proper mapping of fetuses so that interpretation of results can be applied to correct fetus if selective termination is required. Total fetal loss is recorded higher in multiple gestation up to 10.5 % [20]

Detection of fetal cells or cell-free fetal DNA in maternal blood, and its analysis may provide a noninvasion technique for diagnosis and may obviate the need for this procedure in the future.

Compliance with Ethical Standards

Conflict of interest None.

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