CORDOCENTESIS IN PRENATAL DIAGNOSIS
– CASE REPORT

SUMMARY:
The continuously increase in resolution of transducers allows a precise introduction of a needle in the amniotic cavity and the ultrasound guided techniques are diagnostic and therapeutic safe procedures. Usually this method – cordocentesis (PUBS) – has become a large used technique in order to obtain fetal blood and to perform fetal intrauterine transfusion. The technique of cordocentesis can be performed by one operator (“freehand” technique or with a guide attached to the transducer) or with the help of an assistant. The complications of cordocentesis are similar to the complications of amniocentesis and in addition we mention fetal bradycardia with an incidence of 10% of cases (the risk is increased when the artery is punctured: 17%, compared to the puncture of the vein - 2%), fetal-maternal haemorrhage, cord hematoma (17%), overall fetal demise: 1.4-2%, prematurity. We describe the first cordocentesis performed in the University Clinic of Obstetrics-Gynecology “Bega”, Timisoara, at a patient with pregnancy of 27 WG + 2 days, in order to obtain fetal blood for karyotyping in a very short time (ultrasound suspicion of trisomy 21). We wish to underline the utility in current obstetrical practice of this method in order to obtain in a short time fetal karyotype, when this is needed.

Keywords: prenatal diagnosis, cordocentesis, rapid karyotyping

INTRODUCTION
Ultrasound is the essential method for diagnosis in obstetrics and gynecology. The continuously increase in resolution of transducers allows a precise introduction of a needle in the amniotic cavity and the ultrasound guided techniques are diagnostic and therapeutic safe procedures (1). In this category is included cordocentesis (per cutaneous umbilical blood sampling - PUBS), that allows
the access to the fetal blood vessels and the replacement of the initial fetoscopic monitoring (2, 3).

Daffos et al have described the technique of PUBS through ultrasound-guidance, using a needle of 20G and they have opened a new field of fetal medicine (3). Usually this method – cordocentesis (PUBS) – has become a large used technique in order to obtain fetal blood and to perform fetal intrauterine transfusion (4).

The most important indications of cordocentesis are: prenatal diagnosis of inherited metabolic and hematological diseases; detection of fetal infections (rubella, toxoplasmosis, varicella-zoster, Parvovirus 19); determination of fetal karyotype in fetuses with abnormalities; rapid determination of fetal karyotype; detection of fetal acid-base equilibrium in fetal growth restriction; evaluation and treatment of pregnancies with Rh-immunization and thrombocytopenia (4, 5).

The technique of cordocentesis can be performed by one operator or with the help of an assistant (when one introduces the needle and the other one has to hold the transducer).

The patient can be hospitalized or the procedure can be performed in an outpatient manner. Sedation, antibiotics, tocolysis or paralyzing medication for the fetus is not necessary (6).

Ultrasound transducers can have a needle guide; the needles have 8-15 cm in length and are of 20-27 G size.

The patient must sign an informed consent about the risks and the limits of this procedure. Usually fetal biometry by ultrasound is performed in order to detect eventual fetal abnormalities and to establish the place for insertion of the needle into the umbilical cord. When the placenta is localized on the anterior and lateral uterine wall, the needle passes the placenta and enters into the umbilical cord. If the placenta is localized on the posterior uterine wall – the needle passes the amniotic fluid and enters into a free loop of umbilical cord or near the placental insertion of the umbilical cord (~ 1 cm), where the umbilical cord has a lesser motility. Umbilical vein has a larger diameter and is frequently punctioned. To determine the origin of fetal blood – arterial or venous blood – one may inject 1 ml isotonic saline solution (NaCl 9%). If the turbidity goes to the placenta, it means that the needle is in the artery.

Usually we aspirate first 20 ml amniotic fluid before the puncture of umbilical cord, the reason for that is not to contaminate the fetal blood (karyotype from amniotic fluid). The amount of fetal blood sample in a heparinized test tube depends on gestational age and on the indication of cordocentesis. Usually we aspirate 1-4 ml blood; initially 0.5 ml blood are thrown away, in order to avoid contamination with maternal blood, if the needle passes the placenta.

Cordocentesis can be performed after 18 weeks of gestation (WG) until term.

The patient lies in a supine position and the abdominal skin is prepared like in amniocentesis (aseptic technique).

We aspirate fetal blood and the quality of the sample is very important, because the miscibility with maternal blood or amniotic fluid can impair the diagnostic value of the sample (7).

The purity of fetal blood is tested by determining the mean corpuscular volume (MCV) from the fetal sample and from maternal blood, collected before cordocentesis. It is known that fetal MCV > maternal MCV and the difference decreases with the increase in gestational weeks.

The site of puncture is monitored by ultrasound at the end of the procedure, to identify a possible bleeding in the umbilical cord and fetal heart rate is monitored for 1-2 hours.

The complications of cordocentesis are similar to the complications of amniocentesis and in addition we mention fetal bradycardia with an incidence of 10% of cases (the risk is increased when the artery is punctioned: 17% compared to the puncture of the vein -2%) (8), fetal-maternal haemorrhage, cord hematoma (17%), overall fetal demise: 1.4-2%, prematurity (11).

Factors like a prolonged duration of the procedure > 14 min or the anterior localization of the placenta can have a negative influence. Another complication is bleeding at the site of puncture, in 10-40% of cases and lasts for less than 90 sec (9, 10).

We describe the first cordocentesis performed in the University Clinic of Obstetrics-Gynecology “Bega”, Timisoara, at a patient with pregnancy of 27 WG + 2 days, in order to obtain fetal blood for karyotyping in a very short time (ultrasound suspicion of trisomy 21).

**CASE REPORT**

The patient P.M., age: 37 years, G1I0Ab1, 27 WG + 2 days, monofetal pregnancy, Rh negative without immunization, is hospitalized in the University Clinic of Obstetrics-Gynecology “Bega”, Timisoara, in 17.03.2008 - for a suspicion of trisomy 21 at ultrasound at the beginning of the second trimester.

For personal reasons the patient didn’t follow the diagnostic procedures to elucidate this problem and at this gestational age she developed new interest to make clear the fetal karyotype.
The pregnancy had no remarkable events. Before the hospitalization the patient underwent a new ultrasound 3D/4D and the suspicion of trisomy 21 still remains, reason for which she decided to make clear the correct diagnosis.

The maternal age (37 years) is in the range of risk for chromosomal abnormalities. During the hospitalization a 2D ultrasound was performed and no fetal abnormalities or ultrasound markers for trisomy 21 have been detected.

Fetal biometry is according to the gestational age of 27 WG +2 days. The placenta has a posterior position, the amniotic fluid is normal; the fetus is in cephalic lie. To certify the diagnosis of aneuploidy – a fetal karyotype is necessary and cordocentesis must be performed. Karyotype can be determined from fetal lymphocytes and the result is obtained in 2-5 days. This short interval to the diagnosis can allow a decision in case of a pathologic result. Cordocentesis was performed at this patient in 19.03.2008 and before that she signed an informed consent.

The patient lies in a supine position, with the abdominal skin prepared like in amniocentesis (aseptic technique). The patient didn’t wish local anesthesia and no sedation. The operator decides not to administer medication in order to paralyze the fetus.

The operator (Gh. Budau) used an ultrasound machine “Esaote”, with a convex multifrequency transducer (3.5 – 5 MHz) and a 22G needle.

The procedure was that of the “free-hand” technique and the “2 operators” technique. The assistant has to monitor by ultrasound permanently the procedure.

The posterior placental position makes the decision to puncture a free loop of umbilical cord in the superior part of the uterine cavity, after a transamniotic passage of the needle. During the intervention the fetus changes the position and the free loop of the umbilical cord is no longer available, so that the needle is extracted. During this puncture a sample of amniotic fluid is collected (for fetal karyotype from amniotic fluid). The patient agrees for another puncture and again the needle enters a free loop of umbilical cord, with a sudden movement. The free loop was “pressed” against the uterine wall. We could aspirate 3 ml fetal blood in a heparinized test tube, in order to determine fetal karyotype and 1 ml fetal blood was collected to evaluate MCV and to determine hemoglobin.

After withdrawal of the needle we observed a transient fetal bradycardia (63 beats/min) and the fetus recovered spontaneously in a few seconds (< 1 min) (Fig 1).

We consider to prescribe antibiotics for 5 days, regarding the 2 attempts of puncture and the prolonged time of procedure. MCV from fetal blood was 100 fl and MCV from maternal blood (tested before punction) was 87 fl (this demonstrates the fetal origin of the blood sample).

In 26.03.2008 the fetal karyotype was communicated to the patient (46 XX) and patient was released from the hospital. A week after cordocentesis the pregnancy was ongoing, without any complications (fig.1).

![Image](image_url)

**Fig 1:** Recovery of the fetal heart rate after a short time of bradycardia. Control after 15 min – normal fetal heart rate
DISCUSSIONS

Fetoscopy has allowed for the first time the access to the umbilical cord and placental vessels and was suddenly replaced in the years of the ’80th with transcutaneous puncture of the umbilical cord, named also cordocentesis. One indication in performing cordocentesis is the rapid obtaining of fetal karyotype (2-5 days) in order to diagnose late in pregnancy fetal pathology. This is also the reason for the first cordocentesis performed in our clinic.

The importance of fetal karyotype obtained from lymphocytes and its result in a short time is as greater as pregnancy is at a gestational age close to the limit of fetal viability (like in our case).

Fetal blood sample can be obtained through a puncture of the umbilical cord, near the placental insertion; from the puncture of the umbilical vein in the fetal liver, in a free loop of the umbilical cord (site chosen also by the operator in our case) or in the fetal heart (12).

The procedure can be applied starting from pregnancies > 18 weeks of gestation till term. The gestational age of our patient was in this interval of gestational weeks.

A sedation of the patient and paralyzing medication for the fetus (in order to avoid sudden movements that can lead to the failure of the puncture) is not always necessary (pancuronium 0.1-0.3 mg/kg i.v. or D-tubocurraminium 1.2-2.5 mg/kg fetal weight estimated by ultrasound). We have not used these types of medication in our case.

Local anesthesia, antibiotics and tocolysis (betamimetic agents) are used only if the operator considers this necessary (13). If there is any estimation of a prolonged procedure, local anesthesia and antibiotics are useful. We have used antibiotics for 5 days, regarding the prolonged time of the procedure, because there were 2 serial punctures for obtaining the fetal blood sample. Furthermore some authors consider useful the administration of antibiotics because 40% of fetal demise after cordocentesis is caused by chorioamnionitis (13).

Regarding the technique – the operator has chosen a convex transducer; the “free-hand technique” and the technique of “2 operators” because he is familiarized with them from other obstetrical ultrasound guided interventions like amniocentesis; embryoreduction and placental sampling (CVS).

After an evaluation of the distance to the umbilical loop chosen for the puncture, we used the needle of 15 cm length (as recommended by Ghidini et al) (7).

The size of the 22G needle (usually 8-9 cm length) used by many operators (we have used also a 22G needle) is small in order to avoid morbidity and the needle is stiff, in order to move it once it passes the uterine wall (14).

We had also a complication of cordocentesis – fetal bradycardia, spontaneously recovered in a time shorter than 60 sec.

Although fetal platelets are below 100.000/ mm3 (in our case 96.000), we have not noticed any bleeding at the site of puncture. Weiner et al have noticed there is no relation between the incidence and the duration of haemorrhage from the umbilical cord at the site of puncture (it is the most frequent complication and benign for the most of the time) and the number of retal thrombocytes (15). It appears in 41-53% of cases, with an average time of 35 sec (13, 16).

An essential step is the evaluation of quality of our blood sample, because its contamination with maternal blood or amniotic fluid can influence his diagnostic value.

In this sense it is useful to evaluate MCV that has a greater value at the fetus compared to maternal blood. Fetal erythrocyte is larger than maternal erythrocyte. The count of fetal lymphocytes is also useful, because they are of larger amount in fetal blood, compared to neutrophil granulocytes, which are more in maternal blood.

In our case fetal lymphocytes are 82.4% and maternal neutrophil granulocytes are 81.9%.

Fetal MCV: 100 fl > maternal MCV: 87 fl.

From technical point of view there were 2 punctures necessary. The attempt is one passage of the needle through uterine wall (1).

At the first attempt the fetus (without any paralyzing medication) had sudden movements; the free loop of umbilical cord was not anymore accessible for the needle. The second attempt during the same intervention was successful. Some authors (Santolaya) recommend a delay for 2-7 days, because a new and immediate punction can increase the risk of pregnancy loss. Our needle enters the second time into the umbilical vein, the blood was intensely red and the aspiration was easier compared to the blood from the artery. This particularity was mentioned by U. Nicolini and Ch. Rodeck (17).

The patient was Rh negative, without immunization and she received 300 iqd immunoglobulin anti-D (1 amp. Rhogam).

After the procedure and the transient bradycardia, the evolution was without any other events.

The patient was released and the fetal karyotype was normal (46 XX).
CONCLUSION

In conclusion, we described this case to underline the utility in current obstetrical practice of this method in order to obtain a short time fetal karyotype (compared to fetal karyotype from amniotic fluid). These are tools of prenatal diagnosis. Cordocentesis is a method that has lost in importance in the last years, but for our clinic and for the operator it was for the first time.

REFERENCES

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