MANAGEMENT OF PREGNANCY WITH PREMATURE RUPTURE OF MEMBRANES (PROM)

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Abstract
Amniotic fluid fulfills a lot of significant functions in pregnancy and birth. The membrane sac together with the amniotic fluid protect the foetus particularly against external insults and against penetration of infection into the ovum. The membrane sac usually bursts during birth, most often in the 1st birth stage, which appears in form of discharge of amniotic fluid.

Premature rupture of membranes (PROM) occurs, according to different literature sources, in 4-14% of pregnancies. In dependence on the pregnancy stage, this is considered the beginning of birth or miscarriage. The sooner in the pregnancy course the PROM occurs, the more serious are its consequences. About 30-40% of premature births start by premature rupture of membranes that has therefore substantial share on perinatal and infant morbidity and mortality. The article describes the approach to PROM pregnancy in the Czech Republic.

Key words: PROM – pPROM – premature birth - management

Introduction
Premature rupture of membranes (PROM) is an important topic in perinatology and proper management can affect pregnancy outcome. Incidence of premature rupture of membranes varies from 4% to 14%. In about 30% to 40% of cases it is a cause of preterm delivery, and therefore it contributes substantially to perinatal and infant mortality and morbidity. This article provides overview of theoretical knowledge and recommended procedures in pregnancy complicated by PROM and its management in Czech Republic.

Premature rupture membranes (PROM)

Definition
We call premature rupture of membranes the condition when the amniotic fluid drains away spontaneously before the birth starts, i.e. without presence of uterus contractions. The premature rupture of membranes is often termed with the abbreviation PROM. This term is used by some authors only for the discharge of amniotic fluid after the 37th pregnancy week finished. When the amniotic fluid drains away before the 37th pregnancy week, this condition is often called pPROM (Preterm Premature Rupture of the Membranes).

Epidemiology
The incidence of PROM stated in literature oscillated between 4-14% of pregnancies. As for pPROM in the concrete, i.e. premature rupture of membranes before 37th pregnancy week, the pPROM incidence is stated between 2-3%. 30-40% of premature births start with premature rupture of membranes. The different data are caused primarily by different methods used to diagnose the PROM, by demographic characteristics of the population researched or by the type of studies.

Clinical picture
Premature rupture of membranes usually shows in form of continuous light aqueous discharge from the vagina, that can but need not be very abundant. Sometimes blood ribbons
can be present in the amniotic fluid draining away. Uterus contractions are not present. When the amniotic fluid is turbid, rank or bloody, it can signalize a serious associated complication.

After the amniotic fluid is drained away, a differently long latent stage comes on, lasting until the start of active birth stage. Contact of the adjacent part of the foetus and the area of the os uteri internal originates. This leads to increase of secretion of endogenous prostaglandins and, by activation of Frankenhauser ganglion, to Fergusson reflex that provokes increased secretion of oxytocin from hypophysis, and so to uterus contractions.

Risk factors
Risk factors of premature rupture of membranes include:
- Infection of the woman’s genital tract (nonspecific vaginosis, Trichomonas vaginalis, Mycoplasma hominis, Chlamydia trachomatis, Neisseria gonnorhoe, streptococci of group B (GBS), other sexually transmittable diseases (STD)
- Premature uterus activity
- Multiple pregnancies
- Vaginal bleeding in current gravidity
- Premature birth in anamnesis
- PROM in past gravidity
- Spontaneous miscarriage in 2nd trimester in anamnesis
- Incompetence of cervix
- Placenta praevia and placentation disorders
- Polyhydramnion
- Inborn development defects of uterus
- Condition after interventions on the cervix (conization, cerclage)
- Coitus
- Low socio-economic status related to bad nutrition
- Cigarette smoking

Risk for mother and foetus
The highest risk for the mother following from premature rupture of membranes is possible infection, although serious mother consequences are not frequent.

Risks of premature rupture of membranes for the foetus include primarily infectious complications, prematurity related to risks of RDS (respiratory distress syndrome), intraventricular bleeding, nectorizing enterocolitis etc. Another possible complication is compression of umbilical cord, in oligo- to anhydramnion possible origin of extremities or face deformation or origin of pulmonary hypoplasia. PROM can lead to endouterine death of the foetus as well.

Diagnostic possibilities
Correct and timely detection of premature rupture of membranes has absolutely essential significance for further fate of pregnancy. Late diagnose can mean wasted opportunity of appropriate intervention. In most cases, the diagnostics does not cause bigger problems, but in some situation it may not be easy to make the right diagnosis.

Basic diagnostic methods of PROM detection
Clinical examination – we visualize the amniotic fluid draining away. In vaginal examination in mirrors, its accumulation in the rear arch can be seen.

Temesvary exam – is based on the change of acid pH of the vagina to alkaline pH at amniotic fluid discharge. The agent – bromthymol – changes colour to blue-green. Sometimes this exam must be carried out repeatedly. In case of uncertainty, some authors suggest introducing a swab into the rear arch and repeating the exam after some time. The result can sometimes influence also the type of the sanitary pad used.

Falsely positive result can occur in case of presence of blood, sperm, in case of use of alcaline antiseptics or in case of bacterial (non-specific) vaginosis.
Falsely negative result can occur on the contrary in case of anhydramnion.

**Ultrasound examination** - this is an orientation examination to determine the amniotic fluid quantity. The detection of oligo or anhydramnion has higher value of notice. This examination is carried out repeatedly in some cases.

**Less frequent or non-used PROM detection methods**

**PROM test** – this is a very sensitive and specific method with the use of detection strip. The test is based on determination of *insulin like growth factor binding protein – 1* (IGFBP-1), the concentration of which in amniotic fluid is 100-1000x higher than in the mother’s serum and which is not present in the vagina under normal circumstances. But its high price constitutes a disadvantage. Therefore it is used primarily in case of diagnostic uncertainty before an essential decision primarily in case of premature births.

**Determination of pH with the help of indication paper** - the pH of the vagina is 4,5-6,0, while the pH of the amniotic fluid oscillates between 7,1-7,3. But the method is not commonly used because it is burdened by low specificity.

**Kittrich test** (microscopic examination with the help of Nile blue), **crystallization test** on slide (using arborization phenomenon) and **prove of lanugo** in native coat are not used any more because of time demandingness or low sensitivity.

**Differential diagnostics**

In case of the pregnant woman’s subjective suspicion of amniotic fluid discharge we must also think of other alternatives as e.g. excessive vaginal discharge (fluor), escape of urine, sperm or bleeding.

**Suggested examinations at premature outflow of amniotic fluid**

The basic measure in case of premature rupture of membranes is hospitalization. Further examinations take place in its course.

- Complex gynecologic reception examination with verification of premature rupture of membranes
- In case of presence of cerclage stitch, the stitch must removed
- Ultrasound examination where determine the position of the foetus (foetuses), biometry, quantity of amniotic fluid are determined and flowmetric examination carried out
- Cardiotocographic record (CTG) to exclude foetus distress
- Laboratory determination of infection markers (leucocytes, C-reactive protein (CRP), sometimes, but not usually cytokines (IL-6, TNF-alpha). When birth does not occur, these examinations are repeated in 12-hour intervals.
- Microbiologic examination with cultivation taking from cervix and from vagina (aerobic and anaerobic when possible). In case of premature births or in case of infection marker positivity we take it always.
- Repeated check of general condition of the mother including measurement of values of vital functions, particularly pulse and body temperature
- Repeated check of the foetus condition.

**Procedure in case of proved premature rupture of membranes**

In deciding of further procedure, primarily the gestation age of the foetus, its position, the intrauterine foetus condition and last but not least the mother’s condition must be taken in consideration. The principle applies that the vaginal examinations are limited in order to reduce the infection risk to the lowest level possible.

The clinical signs of infection include temperature increase over 38°C, mother tachycardia, foetus tachycardia (but this must be evaluated with regard to the gestation age of the foetus), non-reactive cardiotocogram (here, the CTG
must be also evaluated with regard to the gestation age of the foetus, because extremely immature foetuses before 28th week of pregnancy often have non-reactive records physiologically), rarely palpation pain of the uterus.

The approach to pregnancies with proved premature rupture of membranes can be divided into active and expectation one. Active approach is used primarily in case of infection sign or in case of mother colonization by streptococci of B group (GBS). In these cases, it is necessary to guide the birth actively at once, while the birth induction at PROM is called provocation. Expectation approach is chosen in cases of premature births before 34th week, under the condition that no infection signs or other condition requiring immediate termination of pregnancy are present. The aim is to gain time for corticoid application (induction of pulmonary maturity of the foetus) and to try to reduce the risk of newborn mortality and morbidity in that way.

We carry out strict individualization in choosing the way of birth guiding. In case of contraindication to vaginal birth guiding, termination of pregnancy by elective caesarean section is indicated.

We will outline very shortly the basic procedures at PROM in dependence on the gestation week of the foetus in subsequent text.

PROM at gravidity >37 weeks
- Monitoring of foetus
- Monitoring of infection markers 12 hours from PROM each 12 hours
- In case of their negativity provocation of birth after 24 hours from PROM
- In case of their positivity or GBS positivity provocation of birth immediately
- Application of antibiotics after 12 hours from PROM

PROM at gravidity 34-36 weeks
- Monitoring of foetus
- Monitoring of infection markers each 12 hours
- In case of their negativity provocation of birth after 24 hours from PROM
- In case of their positivity or GBS positivity provocation of birth immediately
- Application of antibiotics as prophylaxis immediately

PROM at gravidity 32+0 to 33+6 weeks
- Transfer of foetus in utero to centre
- Monitoring of foetus
- Monitoring of infection markers each 12 hours
- In case of their negativity provocation of birth after 48 hours from PROM
- In case of their positivity or GBS positivity provocation of birth, neonatologist consultation should precede
- Application of antibiotics as prophylaxis immediately
- Application of corticosteroids (induction of pulmonary maturity of foetus)
- Application of preventive tocolysis during pulmonary maturation

PROM at gravidity 28+0 to 31+6 weeks
- Transfer of foetus in utero to centre
- Monitoring of foetus
- Monitoring of infection markers each 12 hours
- In case of their negativity termination of gravidity after 72 hours from PROM (24 hours after termination of maturation)
- In case of their positivity or GBS positivity, provocation of birth is considered, neonatologist consultation should precede
- Application of antibiotics as prophylaxis immediately
- Application of corticosteroids (induction of pulmonary maturity of foetus)
- Application of preventive tocolysis during pulmonary maturation
PROM at gravidity <28 weeks
- Transfer of foetus in utero to centre
- Expectation approach is chosen
- Always individual procedure after neonatologists consultation
- Monitoring of foetus
- Monitoring of infection markers each 12 hours
- In case of their negativity termination of gravidity after 72 hours from PROM (24 hours after termination of maturation)
- In case of their positivity or GBS positivity, provocation of birth is considered, neonatologist consultation should precede
  - Application of antibiotics as prophylaxis immediately
  - Application of corticosteroids (induction of pulmonary maturity of foetus)
  - Application of preventive tocolysis during pulmonary maturation
  - Theoretically, amnioinfusion can be considered

Application of antibiotics
We apply antibiotics intravenously as prophylaxis of prepartum and intrapartum infection. We administer them usually according to one of the suggested schedules; the preparations are usually changed in regular intervals after consultation of antibiotic centre because of risk of selection pressure in relation to microorganisms. It depends in certain measure also on the usages of the department.

Basic schedules are:
- amoxicillin with clavulane acid 1,2 g in infusion each 8 hours
- cefuroxim 1,5 g in inf. and further 750 mg in infusion or i.m. each 8 hours
- ampicillinum 1,0 g in infusion each 6 hours
- erythromycinum 15-20 mg/kg/day in infusion divided in 4 partial doses each 6 hours
- ampicillinum 1,0 g in infusion each 6 hours + erythromycinum (effect on Mycoplasma hominis) 15-20 mg/kg/day in infusion divided in 4 partial doses each 6 hours
- in indicated cases, e.g. combination of three antibiotics can be used: ampicillin 1,0 g each 6 hours, clindamycin 300-600 mg each 8 hours and ornidazol 500 mg each 12 hours. But the need of this combination requires at the same time immediate termination of pregnancy.

Application of corticoids
We apply corticoids only in case of negative infection markers. After their administration, reduced incidence of RDS, intraventricular bleeding, necrotizing enterocolitis and neonatal deaths is proved. We administer one cure before 32nd or 34th week of gravidity (the maximal recommended application of two cures can be considered only in case of pregnancies with expectation approach at extremely immature foetuses).

Long-term-effect corticoids are administered, and the schedule of one cure is as follows:
- betametazon - 2 amp. i.m., after 24 hours other 2 amp. i.m., 2 doses in total
- dexametazon - 8 mg i.m. after 12 hours, 4 doses in total

After application of corticoids, the number of leucocytes can be temporarily increased, therefore it is also necessary to monitor CRP. Narrowing of oscillations on CTG can occur as well, lasting 48 to 72 hours. Ultrasound flowmetry can help to distinguish it from imminent hypoxia of foetus.

Conclusion
Premature rupture of membranes is a significant problem in perinatology. Right and primarily timely diagnosis can influence the pregnancy result essentially. The midwife is often the first person whom the pregnant woman with suspicion of premature
rupture of membranes meets. Her incorrect decision can have fatal consequences for all participants. When the suspicion of premature rupture of membranes is not disproved unequivocally during examination, it is completely inadmissible that such situation is further solved by ambulatory methods or that it is not solved at all. In case of uncertainty whether the premature rupture of membranes occurred or not, we urgently suggest supposing the worse variant. It is much easier to explain the pregnant woman that sometimes short-term hospitalization is necessary to confirm or to disprove this diagnosis, than explain her that she lost the child or has a permanently seriously handicapped child because of our incorrect decision and attempt for “heroism”.

References:

ОСЕБЕННОСТИ ВЕДЕНИЯ БЕРЕМЕННОСТИ, СОПРОВОЖДАЮЩЕЙСЯ РАЗРЫВОМ МЕМБРАНЫ

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Преждевременный разрыв мембраны и истечение амниотической жидкости представляет существенную опасность как для матери, так и для плода. Согласно различным данным преждевременный разрыв мембраны происходит в 4-14% случаев беременности и часто, в зависимости от стадии беременности и готовности организма женщины к началу родов нередко обусловливается ошибочной тактикой акушера. Очевидно, что серьезность последствий напрямую зависит от срока разрыва мембраны. По наблюдению авторов статьи приблизительно 30-40% преждевременных родов сопровождаются преждевременным разрывом мембраны, что во многом обусловливает как перинатальную так и младенческую заболеваемость и смертность. В статье обсуждаются наиболее оптимальные подходы в тактике ведения беременных с преждевременным излиянием амниотической жидкости.