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CONFERENCE REPORT

Prelabour rupture of the membranes: recent evidence

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Abstract. Premature rupture of the membranes (PROM) complicates 10% of all gestations and 2-4% of preterm pregnancy. Our success in preventing preterm PROM and preterm birth is hampered by our limited knowledge of its etiology. PROM remains the single most identifiable cause of preterm delivery and the major contributor to perinatal morbidity and mortality. Its clinical management continues to be controversial. The management dilemma associated with preterm PROM (PPROM) involves a balance between expectant management and intervention, taking into consideration the risks of infection with the increased duration of membrane rupture. Recent evidence on the use of antibiotics and amnioinfusion, together with advances in the prediction, diagnosis and estimation of risk based upon occupational factors and genetics have provided additional therapeutic tools in our approach to the problem of PPROM. While PPROM at very early gestation is a serious complication and a major management dilemma often associated with poor outcome, the prognosis is not without hope.

Key words: Preterm, prelabour rupture of the membranes, prematurity, management

Premature rupture of membranes represents to-date one of the most frequent and most controversial problem obstetricians are faced with. The amniotic membranes other than having a contenitive function for amniotic fluid, the latter fundamental for fetal growth, also needs to be considered as a barrier that protects the fetus and maintains the amniotic fluid sterile away from the vagina and prevents prolapse of its contents into the cervix.

Besides the membranes also function as a deposit for substances that are essential for many metabolic processes e.g. as precusors for prostaglandines.

Definition

Premature rupture of membranes (PROM) can also be defined as rupture of chorioamniotic membranes prior to labour regardless of the gestational age. When the membranes rupture before term, the correct term is preterm premature rupture of membranes (pPROM).

The incidence of PROM reported in literature rates from 3-18.5% (1). This range of variability is partly due to the different definitions used but also particularly due to the different incidences of PROM in the different populations studied.

About 9-10% of the patients at term present rupture of membranes before labour. pPROM accounts for about 25% of all PROM and is associated with 30% of all preterm deliveries (2). PPROM as a cause of preterm delivery seems to be more common in lower socioeconomic classes and in those presenting high incidences of sexually transmitted diseases.

Aetiology

The chorioamniotic membranes are extremely resistent in the early stages of pregnancy to the extent of resisting all forces except those that are acutely penetrating (3, 4). Gradually as term approaches, the amniotic membranes are subjected to forces of different nature which contribute to rendering them progressi-

vely less elastic (3-7). Forces associated with growth in uterine size together with those caused by normal uterine contractions and fetal movements contribute to the reduction in membrane resistence.

Moreover, as term approaches, significant modifications in the biochemical structures occur with reduction in the collagen quantities.

PROM at term can therefore be considered as a physiological variant rather than pathological.

Since the membranes are very resistent at the beginning of pregnancy, factors responsible for PPROM could be both due to intrinsic weakness of the membranes and to extrinsic factors.

Studies that examined patients with pPROM were unable to demonstrate differences in the membranes' strength except at the site of rupture (3). These differences at the site of rupture could therefore be due to extrinsic factors. In an appreciable number of cases, local infections ascending from the vagina seem to be responsible initially in weakening the membranes and thereafter in their rupture (8). Infact, carriers of one or more of these sexually transmitted microorganisms (Gonnorhea, Group B Streptococcus, Chlamydia, Trichomonas, Gardnerella vaginalis) have an increased risk of PPROM (9-12). Even though the data regarding these microorganisms remain however inconsistent, various studies have demonstrated that carriers of GBS, Gonnococcus, Gardnerella have an increased risk of pPROM. Furthermore finding of chorioamnionitis at histology is more frequent with PPROM than with PROM (13). Moreover studies that examined the amniotic fluid and checked for immunoglobulins in cord blood discovered that most patients with PPROM had infections prior to rupture of the membranes (14). Patients with pPROM more often have clinically manifested chorioamnionitis and endometritis (15, 16) even after correcting this incidence for other clinical variables. Other studies demonstrated that the bacteria that colonise the membranes produce substances such as proteases which weaken the membranes and thereafter probably leading to their rupture (17). Recent studies hypothesise that matrix metalloproteinases and in particular metalloproteinase 9 could contain some specific enzymatic properties involved in the rupture of membranes following infection (18, 19). Ascending bacterial infections are therefore responsible for the weakening of the membranes and consequently for their rupture.It however remains unclear why in some of the patients with the same microorganisms, these do not lead to rupture of their membranes. Other factors therefore such as individual immunological reactivity or immunological polimorfism typical of some individuals are probably involved.

Other causes of PROM include polyhydramnios, multifetal gestations and following obstetric procedures such as amniocentesis and cervical cerclage. Recent attention has focused on the possibility of persistent endometritis preceding pregnancy or in the interval between one pregnancy and the other being the cause of PROM. Other risk factors include cigarette smoke, drug abuse, Vit C and Vit E defficiency, strenous work, cervical injury or history of cervical conization could play a role in the pathogenesis of PROM (20, 21). Maternal age, parity and increase in maternal weight do not seem to cause PPROM.

Complications

PROM leads to a wide spectrum of risks and complications depending on the gestational age at which it occurs.Lack of univocity regarding the contribution of each of these complications in terms of perinatal mortality and morbility are the basis of the controversies which exist regarding clinical management.

The most common complications include:

- Maternal, fetal and neonatal infections
- Labour and preterm birth
- Hypoxia and asphyxia secondary to umbilical cord compression and/or following placental abruption
- Increase in the number of Cesarean sections
- Fetal deformity

Preterm labour

Once the membranes rupture, patients usually go into labour within a relatively brief interval. The latency period is inversely proportional to the gestational age. 90% of the patients at term enter labour within 24 hours (1).

When membranes rupture between the 28th and 34th week of gestational age, 50% of the patients go into labour within 24 hours and 80-90% within a week (22, 23) while if PPROM occurs before 26 weeks of gestational age, about 50% of the patients go into labor within a week (24).

Once PPROM occurs and consequently delivery, the complications are linked with prematurity and these are the most common causes of perinatal morbidity and mortality.

Concerning the mode of delivery following rupture of membranes, even though the results available seem contrasting, there seems to be an increase in the number of Cesarean sections in those patients who require induction compared to those in whom labour begins spontaneously (25, 26).

Infections

Following the rupture of membranes, both the mother and fetus have an increased risk of infection. Fetal infections can both be systemic and local. Generally, maternal infections (chorioamnionitis) precede fetal infections, however fetal infections can be manifested several days before overt clinical signs of infection in the mother are observed. The incidence of maternal infection following PROM differs depending on the population studied. On the basis of the overall number of pregnancies, this range from 0.5-1%. With prolonged PROM this incidence rises to range from 3-15% .

Maternal infection however seems to be more common in cases of PPROM with percentages ranging from 15-25% (27, 16, 28). The incidence of chorioamnionitis goes up to 40% when PROM occurs before 24 weeks. Neonatal sepsis at term has an incidence of about 1/500 newborns. On the other hand, after prolonged PROM this incidence increases significantly and in cases of chorioamnionitis, this reaches 3-5% (29). Following PPROM, perinatal infections are more frequent than at term. Neonatal infections occur in about 5% of the cases of PPROM and in 15-20 % of the cases where maternal infections had developed before term (16, 27, 30). Consequently mortality in these preterm newborns, due to infection, is higher compared to those born at term.

It is generally agreed that the incidence of infection following PROM increases with increase in the latency period. This can easily be explained by the fact that as the period from rupture of membranes increases, the probability of ascending infections proportionately increases. This however seems to be valid only for pregnancies at term. Infact in PPROM, the incidence of maternal and perinatal infections does not change with duration from rupture of membranes.

In cases of PPROM, the specific contribution of prematurity and infections in terms of perinatal mortality justifies the unresolved controversies, regarding treatment of these patients

In majority of the cases, perinatal mortality secondary to PPROM, are due to complications given by prematurity rather than duration of PROM (31). At 26 weeks the risks of perinatal mortality and morbidity due to prematurity are more feared as compared to those given by infection therefore efforts need to be made to reduce these complications. At 34 weeks perinatal mortality is comparable to that of the fetus at term, and with a relatively low morbility rate , hence the consequences of infection become more important. These assumptions however could lead to making easy conclusions. Various studies of Gatrite (16) and Morales (32), demonstrated that the risk of severe neonatal infections and of respiratory distress syndrome (RDS) remarkably increase in preterm pregnancies in the case of chorioamnionites. Long-term neurologial outcomes also increase in those born after maternal infection (33).

Yoon, Romero et al. (34, 35) introduced the term “Fetal Inflammatory Response Syndrome” to describe the phenomenon of fetal infection that precedes overt clinically evident chorioamnionitis, capable of damaging the fetal central nervous system (CNS). Lesions of the periventricular white matter (leucomalacia) are infact visible, and are given by the inflammatory response of the CNS, with release of cytochines responsible for the damage. These lesions and cerebral paralysis that develops at the age of 3 years were correlated to the high concentration of intramniotic leukocytes, of interleukin-6 and the finding of funisitis. These and other studies contributed in illustrating how most if not all cases of cerebral paralysis especially in preterm newborns are secondary to in-

traamniotic infection. Therefore the dilemma regarding to the expectant option when the risk of infection exceeds that given by prematurity is still far from resolution. Obviously, correct diagnosis of PROM is essential. Incase a patient notes loss of appreciable quantities of limpid liquid from the vagina, followed by continuous leakage of liquid, the diagnostic accuracy reaches upto 90% (36). Differential diagnosis needs to exclude urine loss or that of excessive vaginal discharge. Use of a sterile speculum to document the diagnostic suspect remains the most valid manoeuvre. The Valsava manoeuvre or pressure on the uterine fundus, could also be useful. Subsequently, the nitrazine paper test could be used. Vaginal pH during pregnancy usually lies between 4.5-6 while the amniotic fluid pH is between 7.1-7.3. Validity of this test could however be altered by presence of blood , semen or if alkaline antiseptics have been used. Finding of oligohydramnios established using ultrasound confirms diagnosis. Nevertheless if diagnosis remains uncertain, intra-amniotic instillation of a dye which successively leaks from the cervical canal is documentable using a sterile speculum.

Treatment

Even though a number of studies (including randomised prospectic trials) regarding the treatment options for patients with PROM at different stages of pregnancy have been carried out, this subject remains one of the most controversial and enigmatic problems obstetricians are faced with.

It is however evident that patients with history of PROM should be admitted to hospital on confirmation of diagnosis and remain hospitalised till delivery.

In some the membranes spontaneously reseal with re-accumulation of amniotic fluid monitorable using ultrasound. In these patients prognosis is comparable to those without rupture of membranes and could be discharged (37). Immediate delivery in those in advanced labour is necessary especially if signs of maternal or fetal infections are observed or if signs of irreversible fetal distress appear. Otherwise adoption of other treatment options such as (tocolysis , somministration of corticosteroids etc.) will depend the gestational age.

Premature rupture of membranes

After 36 weeks, delivery should be considered with the same modes of delivery as in term pregnancies. Since the risks of fetal infections increase proportionately to the latency period, many authors propose active management immediately after PROM. In the last decade, studies that compared immediate induction of labour to those managed expectantly often obtained discordant results. Some suggested that an active conduct (induction with oxytocin) led to an increase in the number of Ceasarean sections given by failure of induction and contemporarily were unable to reduce the number of infections (25, 38). In a study carried out by Hannah et al (26) where over 5000 patients were enrolled in a randomised study, comparison between patients induced using either prostaglandine E_2 gel or oxytocin immediately after rupture of membranes with those managed expectantly upto 4 days, no differences were found between the two groups both for the number of Ceasarean sections and neonatal sepsis, even though a slightly lower number of patients developed chorioamnionitis and fever in puerperium in those managed actively. It was interesting to note from this study that most patients prefered active management. Another controversy regards the establishment on how long should one wait once the expectant option has been chosen before induction of labour.

A randomised study of 200 patients (39) with PROM at term, attendance of 24 hours led to a reduction of the need for induction in over 30% of the patients with respect to those who waited for only 12 hours.No increase in the number of infections was observed.

Preterm premature rupture of membranes

The most feared risks are due to prematurity. Clinical behaviour should therefore aim in prolonging pregnancy for those patients who are not labour, without signs of infection and fetal distress. The treatment scheme proposed for those pregnancies below 36 weeks with PPROM proposes an expectant management with hospitalisation of the patients.

Various recent studies considered the option of immediate induction of patients between the 30th and

34th week of gestational age, and in these no differences in perinatal mortality and morbility were observed compared to those managed expectantly (40, 41).

Ramsey (42) recently published a metanalysis on 344 patients with PPROM comprised between the 30th and 36th week . Immediate induction when compared to expectant management did not whatsoever lead to an increase in perinatal mortality and morbility, associated to significant reduction in chorioamnionitis.

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