Preterm prelabour amniorrhexis: intrauterine infection and interval between membrane rupture and delivery

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Abstract

This study aimed to determine if fetal bacteraemia and amniotic fluid infection at the time of membrane rupture reduces the interval between membrane rupture and the onset of labour in pregnancies complicated by preterm prelabour amniorrhexis.

Sixty nine pregnancies with preterm prelabour amniorrhexis at 12–36 weeks' gestation that were managed expectantly had spontaneous onset of labour. In all cases cordocentesis and amniocentesis were performed and fetal blood and amniotic fluid were cultured for aerobic and anaerobic bacteria. In the group with negative fetal blood and amniotic fluid cultures (group 1) the median interval from amniorrhexis to delivery was 41 days (range 1–161) and there was an inverse correlation between gestational age at amniorrhexis and delivery interval. In the group with negative fetal blood but positive amniotic fluid cultures (group 2) the median amniorrhexis to delivery interval was nine days (range 1–37), and in the group with positive fetal blood cultures (group 3) the interval was two days (range 1–5).

These findings suggest that pregnancies complicated by preterm prelabour amniorrhexis and fetal bacteraemia undergo spontaneous labour within five days of membrane rupture, and if labour does not occur then infection is unlikely.

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Keywords: amniorrhexis, intrauterine infection, cordocentesis, amniocentesis.

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Prematurity is the leading cause of perinatal mortality and 30%–60% of preterm deliveries are associated with preterm prelabour amniorrhexis.[1 2] Because of the association between amniorrhexis and intrauterine infection, iatrogenic interruption of the pregnancy is common practice, in an effort to reduce maternal and neonatal infectious complications. However, this policy is questionable because the incidence of neonatal complications arising from preterm delivery is greater than the risk of neonatal sepsis.[3–5] Iatrogenic preterm delivery could be avoided if the interval between amniorrhexis and spontaneous onset of labour is shorter than when there is no intrauterine infection.

Methods

Sixty nine singleton pregnancies with preterm prelabour amniorrhexis at 12–36 weeks' gestation that were managed expectantly and had spontaneous onset of labour were studied. They comprised a subgroup of patients with amniorrhexis who were referred to our centre for further assessment which included cordocentesis. An additional 20 patients that had cordocentesis during the same period (June 1992 to February 1994) were excluded from this study because they had iatrogenic delivery. This was a prospective study of two groups of patients. One group was recruited from our own hospital with the aim of performing cordocentesis and amniocentesis within 48 hours of amniorrhexis. The second group was referred from other hospitals and included women with a long interval between amniorrhexis and referral.

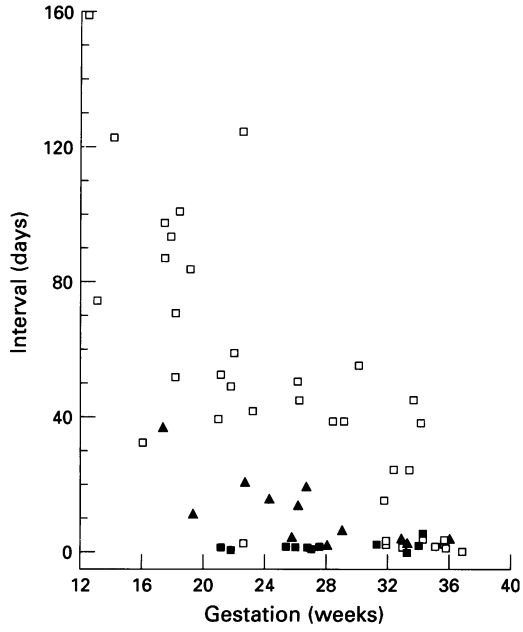
Gestation was determined from the menstrual history and was confirmed by an ultrasound scan in early pregnancy. Amniorrhexis was diagnosed by the ultrasonographic demonstration of decreased or absent amniotic fluid and the visualisation of nitrazine positive fluid in the vagina. In all cases written informed consent was obtained for cordocentesis and amniocentesis to determine fetal karyotype, measure fetal blood gases, and investigate possible intrauterine infection.

The study was approved by the hospital ethics committee.

Cordocentesis and amniocentesis were performed using a single uterine transabdominal entry of a 20 gauge needle under ultrasound guidance. In all cases umbilical venous blood was obtained and the Kleihauer-Betke test confirmed that all blood samples contained only fetal blood. None of the patients had received tocolytics or antibiotics before cordocentesis.

Fetal and maternal blood (obtained from the antecubital vein just before cordocentesis) were inoculated into aerobic and anaerobic blood culture bottles (Bactec, Becton-Dickinson).

The amniotic fluid was cultured using standard microbiological techniques and was also inoculated into Mycofast liquid cultures for *Ureaplasma urealyticum* and *Mycoplasma hominis* (International Mycoplasma, Toulon, France). The results of cultures were communicated to the clinicians managing the patients. Blood cultures were also performed in samples taken from the umbilical cord after



Time interval (days) between preterm prelabour amniorrhexis and spontaneous onset of labour in relation to gestation (weeks) at amniorrhexis: (□)=negative fetal blood and negative amniotic fluid cultures; (▲)=negative fetal blood but positive amniotic fluid cultures; (■)=positive fetal blood cultures.

delivery and from the neonates during the first day of life.

Rank Anova was used to assess the interval between amniorrhexis and delivery in the groups with and without evidence of intrauterine infection, and regression analysis was used to determine the significance of the association between interval and gestation at amniorrhexis.

Results

The median gestation at amniorrhexis in the 69 cases was 27 (range 12–36) weeks, the median interval from amniorrhexis to delivery was 13 (range 1–161) days, and the median interval between amniorrhexis and cordocentesis or amniocentesis was two (1–76) days.

Fetal blood cultures were positive in 11 and negative in 58 of the 69 cases. The organisms isolated were *Streptococcus agalactiae* and *Streptococcus milleri* in two cases each, and *Lactobacillus* sp, *Enterobacter* sp, *Candida albicans*, *Streptococcus viridans*, *Streptococcus sanguis*, *Haemophilus influenzae* and *Staphylococcus epidermidis* in one case each. Amniotic fluid was successfully obtained in 60 of the 69 cases and cultures were positive in 21. In nine of the 21 cases the fetal blood cultures were also positive and in seven of these the organisms were the same in the two compartments (*S milleri* in two cases and one case each of *Enterobacter*, *C albicans*, *S agalactiae*, *H influenzae* and *S epidermidis*). In one of the 11 cases with positive fetal blood cultures no fluid was obtained and in another the culture was negative. In the 12 cases of positive amniotic fluid and negative fetal blood cultures the organisms isolated in the amniotic fluid were *M hominis* and/or *U urealyticum* in seven cases, and one case each of *H influenzae*, *Gardnerella vaginalis*, *S milleri*, *Cryseomonas* and *S agalactiae*. Maternal blood cultures were negative in all cases.

In the fetal bacteraemia group (group 3) antibiotics (erythromycin or amoxycillin and clavulanic acid) were given, either antenatally or intrapartum, in six of the 11 cases. However, cultures of umbilical cord blood at delivery or neonatal blood, which were performed in all cases, were negative in only one case which had not been given antibiotics. In all 11 cases cordocentesis was performed within five days of amniorrhexis which occurred at 21–34 (median 27) weeks' gestation. The interval between amniorrhexis and delivery was one to five (median two) days and there was no significant association between gestation at amniorrhexis and the interval ($r=0{\cdot}56$).

In the 12 cases of negative fetal blood but positive amniotic fluid cultures (group 2) the median gestation at sampling was 26 (range 20–36) weeks, which was performed within five days of amniorrhexis in 11 cases. The interval between amniorrhexis and delivery was one to 37 (median nine) days and there was a significant association between gestation at amniorrhexis and this interval ($r=-0{\cdot}76$, $p<0{\cdot}05$). Cord blood at delivery or neonatal blood cultures were negative in all but one of the cases. Antibiotics had been given to seven of the patients including the one with positive postnatal blood cultures. Of these seven cases, five were infected with *M hominis*, *U urealyticum*, or both.

In the 38 patients with negative fetal blood and amniotic fluid cultures (group 1) the median gestation at amniorrhexis was 26 (range 12–36) weeks. In 22 of these patients the interval between amniorrhexis and sampling was less than five days, and in 16 the interval was 10–76 (median 29) days. The median interval between amniorrhexis and delivery (41 days, range 1–161) was significantly longer than in those with fetal bacteraemia ($p<0{\cdot}0001$) and those with positive amniotic fluid cultures ($p<0{\cdot}01$) (figure). There was an inverse correlation between gestation at amniorrhexis and delivery interval, when all cases were considered ($r=-0{\cdot}80$, $n=38$, $p<0{\cdot}0001$) and when the 16 with a long interval between amniorrhexis and sampling were excluded ($r=-0{\cdot}64$, $p<0{\cdot}01$). Neonatal or umbilical cord blood cultures following delivery were obtained in 36 of the 38 cases and all were negative.

In group 2 the median interval between amniorrhexis and delivery in the patients who received antibiotics (median 16, range 7–37 days) was significantly longer than in patients with no antibiotic treatment (median three, range one to five days, $p<0{\cdot}01$, $z=2{\cdot}84$). In group 3 the median interval between amniorrhexis and delivery in the patients who received antibiotics was one to five (median two) days and was not significantly different than the interval in patients without treatment (median two, range one to five days, $z=0{\cdot}19$).

In the group with negative fetal blood cultures there were four spontaneous abortions

and six neonatal deaths due to pulmonary hypoplasia or other complications of prematurity. In the group with fetal bacteraemia there were two spontaneous abortions and two neonatal deaths due to a combination of prematurity and sepsis.

Discussion

In this study intrauterine infection was diagnosed from the results of fetal blood and amniotic fluid cultures. Traditionally amnionitis is diagnosed on the basis of clinical features, such as maternal fever, leucocytosis, uterine tenderness or foul vaginal discharge. However, many authors have advocated the use of amniocentesis because these clinical signs are not specific and they develop late in the course of the disease.[6–8]

In postnatal studies most infants with positive cultures of skin swabs or gastric aspirates (the equivalent of positive amniotic fluid cultures) are not infected and do not have any morbidity, unlike those who are shown to have bacteraemia.[9] We assumed that the same may be true for the fetus, hence our protocol for the management of amniorrhexis included culture of fetal blood. We have extensive experience of using cordocentesis and this procedure in the presence of ruptured membranes does not seem to pose any additional risks to those found with amniocentesis. Both procedures are performed using a single uterine entry with the needle directed into a pool of amniotic fluid containing a loop of umbilical cord. Nevertheless, it is hoped that the need for amniocentesis or cordocentesis will be temporary. By defining specific criteria for intrauterine infection it would be possible to determine which non-invasive methods of assessment are sufficiently reliable to replace invasive tests.

The findings of this study suggest that:
(i) in some cases of preterm prelabour amniorrhexis there is evidence of intrauterine infection at the time of membrane rupture;
(ii) in the absence of positive cultures of fetal blood or amniotic fluid amniorrhexis is unlikely to predispose to intrauterine infection; and
(iii) in the presence of fetal bacteraemia the interval between amniorrhexis and spontaneous onset of labour is very short, whereas in the absence of infection this interval may extend to several weeks and depends largely on the gestation at amniorrhexis.

If these findings are confirmed in larger series there would be important clinical implications for the management of preterm prelabour amniorrhexis. When spontaneous labour occurs within five days of amniorrhexis there is a high risk of intrauterine infection and tocolytic treatment may be contraindicated. In contrast, when labour does not occur the pregnancies can be managed expectantly as infection is unlikely. This should also be taken into account when designing studies to examine the effectiveness of antibiotic treatment.

There are conflicting reports on the value of prophylactic antibiotics, both in prolonging the interval between membrane rupture and delivery and in reducing the incidence of neonatal sepsis in cases of preterm prelabour amniorrhexis.[10–12] In our study the latency interval in patients with positive amniotic fluid but negative fetal blood cultures was apparently prolonged by the use of antibiotics. However, this was not a prospective randomised study addressing the value of antibiotics and the number of patients examined was too small to draw definite conclusions.

Whether infection is the cause or effect of amniorrhexis is controversial,[13] but there is considerable evidence in favour of the former. In the combined data from three large series of patients with preterm prelabour amniorrhexis at 16–27 weeks' gestation that were managed expectantly, chorioamnionitis was diagnosed in 109 of 241 (45%) cases and in 67% of these the infection was diagnosed within five days of amniorrhexis. Thereafter the incidence of infection was low and was not related to the time interval from amniorrhexis.[14–16] If the amniotic membranes protected against ascending infection the incidence of chorioamnionitis would presumably increase with time after amniorrhexis.

The association between infection and onset of labour is compatible with the findings of previous studies, that in preterm prelabour amniorrhexis patients with clinical amnionitis or positive amniotic fluid cultures deliver earlier than those without infection.[14 15 17] Furthermore, in patients with preterm amniorrhexis the incidence of positive amniotic fluid cultures is much higher in those presenting in labour than in those not in labour. The suggested mechanism for the association between infection and labour is infection mediated release of cytokines which stimulate production of prostaglandins that induce uterine contractions.[19 20] In the non-infected group the finding of an inverse correlation between gestation at amniorrhexis and the latent period suggests that with advancing gestation there is an increase in uterine sensitivity to the trigger of labour which is not mediated by infection.

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