



SHORT COMMUNICATION

Is The Use of Antibiotics Useful in Patients with Term Premature Rupture of Membranes?

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Abstract

Term premature rupture of membranes (TPROM) is associated with an increased risk of infection of the mother and newborn. The current treatment of TPROM does not include prophylactic antibiotics, because systematic reviews conclude that its use does not modify maternal or neonatal outcomes. However, in the group of patients with latency at delivery greater than 12 hours, the rates of maternal infection, like chorioamnionitis and endometritis, are significantly lower with the use of antibiotics.

One of the studies with latency greater than 12 hours concludes that the determinant risk factor of maternal infection is the presence of cervicovaginal infection (CVI) and / or microbial invasion of the amniotic cavity (MIAC), and not other traditional risk factors. This study reports that MIAC and maternal infection occur only in patients with CVI and that the significant reduction in maternal infection is probably due to the effect of antibiotics on CVI and on amniotic fluid infections.

In agreement the known association between chorioamnionitis and perinatal infection/ cerebral palsy in the preterm rupture of membranes (PROM) of pregnancies less than < 34 weeks, it could be possible to affirm a reduction of the perinatal infection and the long-term neurological sequelae with the use of antibiotics in the TPROM.

Additional studies are needed to clarify the benefit of antibiotics in patients with TPROM without labor and latency at delivery > 12 h.

Keywords: Rupture of membranes, Intraamniotic infection, Chorioamnionitis, Puerperal endometritis, Antibiotics.

Term premature rupture of membranes occurs before the onset of labor [1] and is present in approximately 8% of term pregnancies. It has been associated with an increased risk of infection for both the mother (chorioamnionitis, endometritis) and the newborn (sepsis) [2]. Nevertheless these infectious risks, the current treatment of the TPROM does not include prophylactic antibiotics [2]. There is little information on the efficacy of antibiotics in TPROM, despite their infectious risks and the evidence of benefits with antibiotics prophylaxis in PROM < 34 weeks [3].

The most important reviews published on antibiotics in the TPROM, Cochrane [4] and Saccone [5], conclude that antibiotic prophylaxis in patients with TPROM or near-term PROM is not associated with any benefit in maternal or neonatal outcomes. They also recommend that the routine use of antibiotics in TPROM should be avoided in the absence of a confirmed maternal infection, due to the possible development of resistant organisms and the low risk of maternal infection in the control group [4].

However, Saccone reports that prophylactic antibiotics are associated with significantly lower rates of chorioamnionitis (RR, 0.49, 95% CI, 0.27-0.91) and endometritis (RR, 0.12, 95% CI, 0.02-0.62) in the subgroup of women with latency at delivery longer than 12 hours compared with the control group [5]. In this review only three of ten manuscripts mentioned

latency hours. Ovalle et al, (included in this review) [6] in series of patients with TPROM without labor, found latency > at 12 hours in all groups: antibiotic group mean (28.1h), placebo group mean (23.5h); group with maternal infection mean (27.6h), group without maternal infection mean (25.8h) [7]. Furthermore, it was the only study that had a low risk of bias in all the items according to the Cochrane risk of bias tool [6, 7].

According to the results of the second part of this serie, Ovalle finds that the determinant risk factor of maternal infection (chorioamnionitis, endometritis) in TPROM is the presence of CVI (prevalence of 61%) and / or MIAC) (prevalence of 41%) at the time of rupture of membranes, instead of other traditional risk factors, such as active or expectant management of labor, unfavorable or favorable cervical (condition (Bishop < 4 or > of 4), vaginal delivery vs cesarean section and primiparous vs multiparous [7]. This finding supports the participation of microorganisms of the lower genital tract in the pathogenesis of intraamniotic infection. It is reasonable to think that the increase in latency hours at birth favors bacterial growth in these compartments, raising the risk of maternal / neonatal

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infection.

Ovalle concludes that, according to the results found, the benefit of prophylactic antibiotics (reduction of maternal infection) is probably due to the effect of antibiotics on CVI (bacterial vaginosis and aerobic vaginitis) and subclinical infections of the amniotic fluid [6].

It is also possible to reduce perinatal infection (sepsis, pneumonia) and cerebral palsy, with the use of antibiotics. In this series, no neonatal infection was found in the placebo group probably because the mother or the newborn of cases that developed chorioamnionitis or had a positive culture of *S. agalactiae* in the cervix or amniotic fluid received antibiotics [6]. In addition, there are known the associations between chorioamnionitis and perinatal infection [8] and chorioamnionitis and long-term neurological sequelae [9] in the PROM of pregnancy <34 weeks, so the use of antibiotics in TPROM could reduce these results [5, 9], especially if there is evidence that antibiotics reduce the incidence of histological chorioamnionitis [10, 11].

What antibiotics to use? And why associated? The use of a certain antibiotic association is based on the microbiota found in the patients of these studies with TPROM. In summary, the isolated bacteria are correlated with microorganisms in bacterial vaginosis and aerobic vaginitis that are associated in 78% in the CVI and 48% in the MIAC [6, 7].

Recommended Antibiotic Associations

1. Clindamycin-Gentamicin [9]. Benefits: the best association by efficacy in the treatment of existing microorganisms in bacterial vaginosis and aerobic vaginitis, safety and low costs. Objection: increases the possibility of microbial resistance to clindamycin.
2. Clindamycin-Cefazolin or Cefuroxime [5, 6]: second best association. Efficacy in the treatment of existing microorganisms in bacterial vaginosis and aerobic vaginitis, safety and prudent costs. Objection: increases the possibility of microbial resistance to clindamycin and cefazolin / cefuroxime.
3. Penicillin-Gentamicin [11]-Metronidazole: third best association. Minimum increase in microbial resistance to gentamicin.

We recommend the use of the Penicillin-Metronidazole-Gentamicin association for efficacy in the treatment of existing microorganisms in bacterial vaginosis and aerobic vaginitis, with very low costs and low microbial resistance.

According to the evidence presented above, in our opinion, the following questions need to be investigated in order

to demonstrate the benefits with the use of antibiotics in these cases: a) investigations focused on the detection of cervicovaginal and intraamniotic infections in patients with TPROM without labor, with latency 12 hours or more and its relationship with maternal / neonatal outcomes; b) double-blind, randomized clinical trial comparing antibiotic use vs placebo in patients with these characteristics to evaluate the effects of antibiotic prophylaxis; and c) research that evaluates new modalities of antibiotic therapy.

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