WHO recommendation on antibiotic administration for women with preterm prelabour rupture of membranes for the prevention of peripartum infection

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Recommendation

Antibiotic administration is recommended for women with preterm prelabour rupture of membranes.

(Strong recommendation, moderate-quality evidence)

Publication history

First published: September 2015

Updated: no update planned

Assessed as up-to-date: September 2015

Remarks

- This recommendation is in keeping with the WHO guideline on interventions to improve preterm birth outcomes.(1)
- For near-term (i.e. ≥36 weeks) PPROM where the clinical policy of immediate or early labour induction (within 12 hours of rupture) is in place, antibiotic use does not confer any benefit and should not be used.
- Erythromycin is recommended as the antibiotic of choice for prophylaxis in women with preterm prelabour rupture of membranes according to the WHO recommendations on interventions to improve preterm birth outcomes.(1)
- To avoid inadvertent antibiotic administration to women with intact amniotic membranes, antibiotics should not be prescribed unless a definite diagnosis of PPROM has been made. Therefore, a policy to prescribe antibiotics for women with PPROM should be accompanied by a protocol to reliably diagnose PPROM.
- Long latent phase (interval between rupture of membranes and onset of preterm labour) could predispose to intrauterine infection. Therefore, women should be closely monitored for signs of clinical chorioamnionitis.
Background

Bacterial infections during labour and the puerperium are among the leading causes of maternal mortality worldwide, accounting for about one tenth of the global burden of maternal deaths.(2, 3) While the number of deaths arising from these infections has decreased considerably in high-income settings, the situation has not improved in resource-limited settings. Most of the estimated 75,000 maternal deaths occurring worldwide yearly as a result of infections are recorded in low-income countries.(4) Although the reported incidence in high-income countries is relatively low (between 0.1 and 0.6 per 1000 births), it is nonetheless an important direct cause of maternal mortality.(4, 5)

Apart from deaths and acute morbidities associated with infections during or following childbirth, long-term disabilities such as chronic pelvic pain, fallopian tube blockage and secondary infertility can also occur. Maternal infections around childbirth also have a considerable impact on newborn mortality, and an estimated 1 million newborn deaths are associated with such infections annually.(6, 7) In addition, infection-related morbidities and prolonged hospitalization can interfere with mother–infant bonding in the first days after birth.

Methods

The recommendation was developed using standardized operating procedures in accordance with the process described in the “WHO handbook for guideline development”, guided by the GRADE approach.(8) Outcomes used for this recommendation were aligned with the prioritized outcomes from the WHO recommendations on prevention and treatment of maternal peripartum infections (2015).(9)

A Cochrane systematic review was conducted on the routine administration of prophylactic antibiotics to women with PPROM.(10) In the review, randomized controlled trials relevant to the key question were screened by review authors, and data on relevant outcomes and comparisons were extracted. Evidence profiles (in the form of GRADE tables) were prepared for comparisons of interest, including the assessment and judgments for each outcome, and the estimated risks.

WHO convened a Guideline Development Group (GDG) meeting on recommendations on prevention and treatment of maternal peripartum infections in September 2015, where this recommendation was developed. The GDG comprised of a group of independent experts, who used the evidence profiles to assess evidence on effects on the pre-specified outcomes. GDG members discussed the balance between desirable and undesirable effects, overall quality of supporting evidence, values and preferences of stakeholders, resource requirements, cost-effectiveness, acceptability, feasibility and equity, to formulate the recommendation. Remarks were added to clarify the recommendation, and aid implementation.

Recommendation question

For this recommendation, we aimed to answer the following question:

- Among pregnant women with preterm prelabour rupture of membranes (PPROM) (P), does routine antibiotic prophylaxis (I), compared with no routine antibiotic prophylaxis (C), prevent infectious morbidities and improve outcomes (O)?
Evidence Summary

Evidence for routine administration of prophylactic antibiotics to women with PPROM was extracted from a Cochrane systematic review of 22 trials involving 6872 women.(10)

The majority of the trials included in the review were conducted in high-income countries: 14 in the USA, and one each in Finland, Germany and Spain. One trial was conducted in Turkey, one in Zimbabwe and one multi-country trial in Chile and the USA. Results on short- and long-term outcomes were dominated by one trial conducted in the UK. Trials were conducted in the 1990s and early 2000s.

Women were recruited between 20 and 37 weeks of gestation. Clinical definitions and methods for diagnosis of PPROM varied between trials. The majority of the women were not in active labour.

Included trials compared different antibiotic regimens with placebo, other antibiotic class or no treatment, using different routes of administration (oral alone, intravenous alone or a combination).

**Any prophylactic antibiotics versus placebo (all women and babies)**

- Sixteen trials compared any antibiotic with placebo and randomized 6300 women. These trials tested a broad spectrum of penicillins, beta-lactam, macrolide (erythromycin) and other antibiotics (clindamycin, gentamycin) either alone or in combination.
- There was a statistically significant reduction in chorioamnionitis (RR 0.66, 95% CI 0.46 to 0.96; 11 trials, 1559 women).
- There was no difference in perinatal deaths for all antibiotic comparisons (RR 0.93, 95% CI 0.76 to 1.14; 12 trials, 6301 infants), but there was a significant reduction in neonatal infections, including pneumonia, for all antibiotic comparisons (for any antibiotics (RR 0.67, 95% CI 0.52 to 0.85; 12 trials, 1680 infants), all penicillins, excluding co-amoxiclav (RR 0.81, 95% CI 0.68 to 0.98; five trials, 521 infants), and other antibiotics (RR 0.71, 95% CI 0.53 to 0.95; 3 trials, 763 infants)). There was a significant reduction in the number of positive neonatal blood culture (RR 0.79, 95% CI 0.63 to 0.99; 3 trials, 4961 infants).
- There was a significant reduction in the number of infants receiving surfactant (RR 0.83, 95% CI 0.72 to 0.96; 1 trial, 4809 infants), of infants requiring oxygen therapy (RR 0.88, 95% CI 0.81 to 0.96, 1 trial, 4809 infants) and of infants with abnormal cerebral ultrasound scans before discharge (RR 0.81, 95% CI 0.68 to 0.98; 12 trials, 6289 infants) in the treated group compared with placebo. The duration of NICU admission was shorter in the treated group than in the placebo group (mean difference (MD) - 5.05 days, 95% CI -9.77 to -0.33; 3 trials, 255 infants).
- No differences were observed for neonatal respiratory distress syndrome (RR 0.95, 95% CI 0.83 to 1.09, 12 studies, 6287 infants), the number of babies requiring ventilation (RR 0.90, 95% CI 0.80 to 1.02, 2 studies, 4924 infants), neonatal oxygenation > 28 days (RR 0.79, 95% CI 0.61 to 1.03, 3 studies, 5487 infants) or necrotizing enterocolitis (RR 1.09, 95% CI 0.65 to 1.83, 6229 infants). However, the incidence of necrotizing enterocolitis appeared to be increased only with the use of beta-lactam antibiotics (including coamoxiclav) (RR 4.72, 95% CI 1.57 to 14.23; 2 trials, 1880 infants).
- Regarding long-term outcomes, one trial showed that antibiotics seemed to have little effect on serious childhood disability at seven years (RR 1.01, 95% CI 0.91 to 1.12; 3171 children).
- Maternal deaths, serious maternal morbidities, puerperal sepsis, neonatal encephalopathy, major adverse drug reactions or antibiotic resistance were not reported.

Implementation considerations

- The successful introduction of this recommendation into national programmes and health-care services depends on well-planned and participatory consensus-driven processes of adaptation and implementation. The adaptation and implementation processes may include the development or
revision of existing national guidelines or protocols based on this recommendation.

- The recommendation should be adapted into a locally appropriate document that can meet the specific needs of each country and health service. Any changes should be made in an explicit and transparent manner.
- A set of interventions should be established to ensure that an enabling environment is created for the use of the recommendations, and that the behaviour of the healthcare practitioner changes towards the use of this evidence-based practice.
- In this process, the role of local professional societies is important and an all-inclusive and participatory process should be encouraged.

Research implications

The GDG identified that further research on the following high-priority questions is needed:

- What is the contribution of the duration of rupture of membranes and length of labour on maternal and neonatal infectious morbidity among women with PROM at term?
- What are the benefits of initiating prophylactic antibiotics after prolonged rupture of membranes at term?

Related Links


Supporting systematic review:


References

1. WHO recommendations on interventions to improve preterm birth outcomes. 2015.


Citation


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