WHO recommendation against routine antibiotic prophylaxis during the second or third trimester to all women with the aim of reducing infectious morbidity

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Recommendation

Routine antibiotic prophylaxis during the second or third trimester to all women with the aim of reducing infectious morbidity is not recommended.

(Very low-quality evidence, strong recommendation)

Publication history

First published: September 2015

Updated: no update planned

Assessed as up-to-date: September 2015

Remarks

- This recommendation applies to an unselected population of pregnant women in the second or third trimester of pregnancy.
- The GDG noted that prophylactic antibiotic use may be necessitated in a clearly defined group of women with high-risk pregnancy, but the description in the systematic review is inadequate to identify such a group.
- The GDG identified the evaluation of the effects of routine antibiotics in specific groups of women with high-risk pregnancy as a research priority.

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.(1, 2) 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.(3) 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.(3, 4)

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.(5, 6) 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.(7) Outcomes used for this recommendation were aligned with the prioritized outcomes from the WHO recommendations on prevention and treatment of maternal peripartum infections (2015).(8)

A Cochrane systematic review was conducted on the administration of prophylactic antibiotics to pregnant women during the second or third trimester for the prevention of infectious morbidities.(9) 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 women in the second or third trimester of pregnancy (P), does routine antibiotic prophylaxis (I), compared with no antibiotic prophylaxis (C), prevent infectious morbidities and improve outcomes (O)?

**Evidence Summary**

Evidence on the administration of prophylactic antibiotics to pregnant women during the second or third trimester for the prevention of infectious morbidities was extracted from a Cochrane systematic review of eight trials involving approximately 4300 women (3663 included in the analysis).(9)

One trial each was conducted in Belgium, the Netherlands and Malawi, and two trials each in India and the USA. In addition, one single-country and one multicountry trial also included data from Kenya.

Women in their second or third trimester of pregnancy (between 14 and 34 weeks of gestation) who were not in labour were eligible for inclusion in the trials. In three trials, women with high-risk pregnancies (defined variously as a history of preterm birth, low birthweight, stillbirth or early perinatal death, pre-pregnancy weight < 50 kg or previous preterm birth who had bacterial vaginosis diagnosis in current pregnancy). Women receiving antibiotics due to infection were excluded.

Trials used a range of antibiotics and administration routes: oral cefetamet-pivoxil, cephalexin, metronidazole, azithromycin or erythromycin, intramuscular (IM) ceftriaxone or clindamycin vaginal cream.

Subgroup analyses were performed on women who might be at higher risk of presenting with adverse outcomes. Authors defined high-risk women as those who had a previous spontaneous preterm delivery, history of low birthweight, a diagnosis of bacterial vaginosis in the current pregnancy (BV identified after enrolment and antibiotics used only for prophylaxis before knowing if the participant had BV or not) or a
pregnancy weight less than 50 kg.

There were no data reported on side-effects of antibiotics, antimicrobial resistance or cost of care.

**Prophylactic antibiotics versus placebo (EB Table 5)**

- There was a significant reduction in postpartum endometritis (RR 0.53, 95% CI 0.35 to 0.82; 3 trials, 627 women) in the group receiving antibiotics compared to the placebo group, but no significant difference between groups regarding chorioamnionitis (RR 0.62, 95% CI 0.10 to 3.62; 1 trial, 229 women). A reduction was observed for prelabour rupture of membranes (RR 0.34 95% CI 0.15, 0.78; 1 trial, 229 women), but not for preterm prelabour rupture of membranes (RR 0.31 95% CI 0.06, 1.49; 1 trial, 229 women).
- There was no significant difference between groups for perinatal mortality (RR 0.83, 95% CI 0.57 to 1.20; 4 trials, 2710 infants).
- There was no significant difference between groups for preterm birth (RR 0.88 95% CI 0.72, 1.09; 6 trials, 3663 women), low birthweight (RR 0.86 95% CI 0.53, 1.39; 4 trials, 978 women) or mean birthweight (RR 41.60, 95% CI -78.20 to 161.40; 4 trials, 978 women).
- The included trials did not report any serious adverse effects of antibiotic prophylaxis.

**Prophylactic antibiotics versus placebo: unselected pregnant women**

- There were no significant reductions in the incidence of postpartum endometritis (RR 0.51 95% CI 0.24 to 1.08; 2 trials, 431 women) or chorioamnionitis (RR 0.62 95% CI 0.10 to 3.62; 1 trial, 229 women) among unselected women.
- There was no significant difference between groups on perinatal mortality (RR 0.84, 95% CI 0.57 to 1.23; 2 trials, 2315 infants) among unselected women.
- There were no differences in the risk of low birthweight (RR 1.07; 95% CI 0.71 to 1.63; three trials, 725 women), small for gestational age (RR 1.29 95% CI 0.42 to 3.96; one trial, 229 women) or congenital anomalies (RR 1.49 95% CI 0.20 to 11.14; two trials, 463 women).

**Prophylactic antibiotics versus placebo: high-risk women**

- There was a significant reduction in postpartum endometritis in high-risk pregnant women (women with a history of preterm birth, low birthweight, stillbirth or early perinatal death) (RR 0.55; 95% CI 0.33 to 0.92; 1 trial, 196 women) and postpartum detected gonococcal infection (RR 0.35, 95% CI 0.13 to 0.94; 1 trial, 204 women) in the group receiving antibiotics compared to the placebo group.
- There were no differences between subgroups of high-risk pregnant women on preterm delivery, except in the subgroup of pregnant women with a previous preterm birth who had bacterial vaginosis during the current pregnancy (RR 0.64, 95% CI 0.47 to 0.88; 1 trial, 258 women, subgroup differences P = 0.08).
- There was no significant difference between groups on perinatal mortality among different high-risk groups (in women with a history of preterm birth, low birthweight, stillbirth or early perinatal death) (RR 0.53 95% CI 0.13 to 2.18; 1 trial, 253 infants) or in women with a history of preterm delivery alone (RR 3.08 95% CI 0.13 to 74.46; 1 trial, 142 women).
- The risk of low birthweight was reduced in the subgroup of high-risk women who received antibiotics compared to a placebo (RR 0.57; 95% CI 0.37 to 0.88; 1 trial, 253 women).
- There was no difference between control and intervention groups on neonatal sepsis (RR 11.31; 95% CI 0.64 to 200.79; 1 trial, 142 infants)

**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 are the effects of routine prophylactic antibiotics on preventing infection morbidity among women with normal (uncomplicated) vaginal birth?
- What are the effects of routine prophylactic antibiotics during the second and third trimester on women carrying high-risk pregnancies (e.g. history of preterm birth, low birthweight, previous preterm birth with bacterial vaginosis in the current pregnancy)?

Related Links


Supporting systematic review:


References


Citation

WHO recommendation against routine antibiotic prophylaxis during the second or third trimester to all women with the aim of reducing infectious morbidity (September 2015). The WHO Reproductive Health Library; Geneva: World Health Organization.

Source URL: https://extranet.who.int/rhl/topics/preconception-pregnancy-childbirth-and-postpartum-care/who-recommendation-against-routine-antibiotic-prophylaxis-during-second-or-third-trimester-all-women
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