WHO recommendation on administration of prophylactic antibiotics prior to skin incision, rather than intraoperatively after umbilical cord clamping, for caesarean section

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Recommendation

For caesarean section, prophylactic antibiotics should be given prior to skin incision, rather than intraoperatively after umbilical cord clamping.

(Moderate - quality evidence, strong recommendation)

Publication history

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Remarks

- The GDG highlighted the importance of administering prophylactic antibiotics at least 15–60 minutes prior to skin incision in optimizing tissue and blood antibiotic concentrations. Based on the pharmacokinetics of common intravenous antibiotics, maximal benefit can be expected when administered between 30 and 60 minutes before skin incision.
- The GDG acknowledged that evidence also supports the effectiveness of prophylactic antibiotics after umbilical cord clamping for the prevention of post-caesarean infectious morbidities. Therefore, antibiotics are still beneficial when used outside the suggested timeframe (i.e. 15–60 minutes before incision) and should be applied as circumstances demand. This is particularly important in cases of emergency caesarean section where the available time to administer a prophylactic antibiotic might be limited.
- There are no data on the effects of preoperative administration on possible longer-term effects of antibiotic exposure on the baby, and women should be counselled as appropriate. The GDG considers this question a research priority and suggested that opportunities for longer-term follow-up of babies from previous trials should be explored.

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.\(^1\) 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 review was conducted on appropriate timing (preoperative versus intraoperative) for the administration of prophylactic antibiotics for preventing infectious morbidities following caesarean.(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 receiving antibiotic prophylaxis for caesarean section (P), is preoperative administration of antibiotics (I), compared with intraoperative administration of antibiotics (after umbilical cord clamping) (C), more effective in preventing maternal and neonatal infectious morbidities (O)?

Evidence Summary

Evidence on appropriate timing (preoperative versus intraoperative) for the administration of prophylactic antibiotics for preventing infectious morbidities following caesarean section was extracted from a Cochrane systematic review of 10 trials involving 5589 women (5041 analysed).(9)

Trials were conducted in low-, middle- and high-income countries: five in the USA, two in India and one each in Austria, Egypt and Turkey. The target population was women undergoing caesarean section, predominantly elective and non-emergency procedures. All but two trials excluded emergency caesarean section. Most of the trials excluded women with chorioamnionitis or other signs of infection, those who had received antibiotics prior to delivery, with ruptured membranes or who delivered preterm. Two trials excluded multiple pregnancies.
Antibiotics for prophylaxis were given intravenously either before the incision or after clamping of the neonatal umbilical cord. Studies administering antibiotics before incision used different timeframes, with the majority ranging from 15 to 60 minutes. The antibiotics used were different regimens of cephalosporins: seven trials used first-generation cephalosporin (cefaizolin 1 g or 2 g), while the other three trials used third-generation cephalosporin (ceftriaxone 1 g or 2 g). Clindamycin was typically the agent of choice for women who had known allergy to cephalosporins.

Prophylactic antibiotics before skin incision versus after umbilical cord clamping (EB Table 17)

- Compared with administration after umbilical cord clamping, preoperative antibiotic administration was associated with a 43% reduction in the incidence of endomyometritis (RR 0.54, 95% CI 0.36 to 0.79; 10 trials, 5041 women) and a 41% reduction in the incidence of wound infection (RR 0.59, 95% CI 0.44 to 0.81; 10 trials, 5041 women). These findings were consistent between trials testing first- and second-generation cephalosporins.
- There were no significant differences between the group receiving antibiotics before incision versus after umbilical cord clamping in the incidence of urinary tract infection (RR 1.02, 95% CI 0.65 to 1.59; 8 trials, 4001 women), pelvic abscesses (RR 1.00, 95% CI 0.06 to 15.97; 1 trial, 741 women), respiratory infections (e.g. pneumonia) (RR 2.30, 95% CI 0.34 to 15.45; 4 trials, 1849 women) or febrile illness (RR 0.93, 95% CI 0.63 to 1.35; 4 trials, 2650 women).
- Two trials (1274 women) collected information on septic pelvic thrombophlebitis, and one trial (874 women) on septic shock and maternal death, but reported no events.
- There was evidence of a significant reduction in maternal hospital stay among women receiving antibiotics preoperatively compared with women receiving it during caesarean section (MD -0.17, 95% CI -0.30 to -0.04; 2 trials, 1342 women).
- For the neonate, there was no statistically significant difference between the group receiving antibiotics before incision versus after umbilical cord clamping regarding the incidence of neonatal sepsis (RR 0.76, 95% CI 0.51 to 1.13; 5 trials, 2907 neonates), neonatal sepsis workup (RR 0.92, 95% CI 0.69 to 1.23; 4 trials, 1170 neonates), infection with a resistant organism (RR 0.70, 95% CI 0.12 to 4.14; 1 trial, 379 neonates)’ febrile illness (RR 0.67, 95% CI 0.28 to 1.62, 1 trial, 953 neonates), ICU admission (RR 0.91, 95% CI 0.74 to 1.13; 6 trials, 3708 neonates) or duration of ICU stay (MD -0.07 days, 95% CI -2.60 to 2.46; 3 trials, 1731 neonates). Neonatal mortality was not reported by any of the trials.
- Other critical outcomes 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 effect of administration of antibiotics prior to initiation of caesarean section on antibiotic resistance patterns in the neonates and longer-term infant health?

**Related Links**


**Supporting systematic review:**


**References**


**Citation**