Vaccines for women for preventing neonatal tetanus

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RHL summary

Key Findings

This review assessing the effectiveness of tetanus toxoid in preventing neonatal tetanus cases and deaths following its administration to women of reproductive age or pregnant women. The review found:

- Statistically significantly reduction in neonatal tetanus cases associated with administration of at least a single dose of tetanus toxoid injection
- Administration of two or more tetanus toxoid dose course, but not a single dose, was associated with statistically significant protection against neonatal tetanus deaths and all cause neonatal mortality
- No significant systemic side effect was associated with tetanus toxoid injections although there higher incidence of pain at injection site

Evidence included in this review

Three randomized controlled trials were included in the review. Two trials assessed effectiveness of tetanus toxoid vaccination (9823 infants); one comparing effects of tetanus-diphtheria toxoid against cholera toxoid administered to healthy women at reproductive age and children from 1 to 14 years; and the second comparing tetanus toxoid with influenza vaccine administered to women at reproductive age; One trial evaluated safety (48 mothers), comparing tetanus diphtheria acellular pertussis vaccine with saline placebo administered to pregnant women.

Quality assessment

The included trials had low to moderate quality with considerable variability regarding the risk of bias. Two of the trials included had moderate quality methodology with moderate risk of bias while the remaining trial was not adequately powered to test specific hypothesis.

Clinical implications

Although the findings of this review supports the implementation of immunization with tetanus toxoid in communities of high risk of neonatal tetanus, there is considerable heterogeneity in the quality of included trials.

The review demonstrated significant benefit associated with tetanus toxoid immunization in pregnancy in terms of preventing neonatal tetanus cases and mortality. There is not enough evidence to discourage current
practices of tetanus toxoid vaccination in high-risk populations, until results of further trials of adequate power and size are available to inform policy.

Further research

There is the need for large and high quality trials with adequate power to better understand the effectiveness of tetanus toxoid vaccination in reducing neonatal tetanus cases and deaths, focusing on interventions to improve community coverage and untoward effects of the vaccine.

Cochrane review


Abstract

Tetanus is an acute, often fatal, disease caused by an exotoxin produced by Clostridium tetani. It occurs in newborn infants born to mothers who do not have sufficient circulating antibodies to protect the infant passively, by transplacental transfer. Prevention may be possible by the vaccination of pregnant or non-pregnant women, or both, with tetanus toxoid, and the provision of clean delivery services. Tetanus toxoid consists of a formaldehyde-treated toxin that stimulates the production of antitoxin.

To assess the effectiveness of tetanus toxoid, administered to women of reproductive age or pregnant women, to prevent cases of, and deaths from, neonatal tetanus.


Randomised or quasi-randomised trials evaluating the effects of tetanus toxoid in pregnant women or women of reproductive age on numbers of neonatal tetanus cases and deaths.

Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy.

Two effectiveness trials (9823 infants) and one safety trial (48 mothers) were included. The main outcomes were measured on infants born to a subset of those randomised women who became pregnant during the course of the studies. For our primary outcomes, there was no high-quality evidence according to GRADE assessments.
One study (1182 infants) assessed the effectiveness of tetanus toxoid in comparison with influenza vaccine in preventing neonatal tetanus deaths. A single dose did not provide significant protection against neonatal tetanus deaths, (risk ratio (RR) 0.57, 95% confidence interval (CI) 0.26 to 1.24; 494 infants; GRADE: *low-quality evidence*). However, a two- or three-dose course did provide protection against neonatal deaths, (RR 0.02, 95% CI 0.00 to 0.30; 688 infants; GRADE: *moderate-quality evidence*). Administration of a two- or three-dose course resulted in significant protection when all causes of death are considered as an outcome (RR 0.31, 95% CI 0.17 to 0.55; 688 infants; GRADE: *moderate-quality evidence*). No effect was detected on causes of death other than tetanus. Cases of neonatal tetanus after at least one dose of tetanus toxoid were reduced in the tetanus toxoid group, (RR 0.20, 95% CI 0.10 to 0.40; 1182 infants; GRADE: *moderate-quality evidence*).

Another study, involving 8641 children, assessed the effectiveness of tetanus-diphtheria toxoid in comparison with cholera toxoid in preventing neonatal mortality after one or two doses. Neonatal mortality was reduced in the tetanus-diphtheria toxoid group (RR 0.68, 95% CI 0.56 to 0.82). In preventing deaths at four to 14 days, neonatal mortality was reduced again in the tetanus-diphtheria toxoid group (RR 0.38, 95% CI 0.27 to 0.55). The quality of evidence as assessed using GRADE was found to be low.

The third small trial assessed that pain at injection site was reported more frequently among pregnant women who received tetanus diphtheria acellular pertussis than placebo (RR 5.68, 95% CI 1.54 to 20.94; GRADE: *moderate-quality evidence*).

Available evidence supports the implementation of immunisation practices on women of reproductive age or pregnant women in communities with similar, or higher, levels of risk of neonatal tetanus, to the two study sites.

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