Preventing group B streptococcal and other bacterial infections in early infancy

Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses

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Executive summary

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Executive summary

Background

Prenatal screening for maternal colonisation with group B streptococcus (GBS) is well established in many western industrialised countries but is not currently recommended in the UK because evidence is lacking about its effectiveness.

Aims

The aims were to determine the cost-effectiveness of prenatal strategies for preventing GBS and other serious bacterial infections in early infancy and to establish the expected value of further information.

Methods

Twelve mutually exclusive maternal risk groups were defined at presentation in labour (see below) and the consequences considered of early-onset GBS and non-GBS bacterial infections and late onset GBS infection, measured in terms of lifetime NHS costs and quality-adjusted life-years (QALYs).

The maternal risk groups were (in hierarchical order from 1 to 6 and from 7 to 12):

Preterm delivery (<37 weeks):

1. planned Caesarean section
2. previous baby with GBS disease
3. positive urine or vaginal swab for GBS in current pregnancy
4. fever ⩾38°C during labour
5. membrane rupture ⩾2 hours before labour onset
6. membrane rupture <2 hours before labour onset.

Term delivery (⩾37 weeks):

7. planned Caesarean section
8. previous baby with GBS disease
9. positive urine or vaginal swab for GBS in current pregnancy
10. fever ⩾38°C during labour
11. membrane rupture ⩾18 hours
12. none of the above risk factors.

Fourteen intervention strategies were applied to each maternal risk group: doing nothing; culture of a vaginal and rectal swab at 35–37 weeks and treating women with at least one positive result at onset of labour with oral erythromycin or intravenous penicillin; polymerase chain reaction (PCR) testing of vaginal and rectal swabs at presentation in labour and treating one or more positive results; oral or intravenous treatment without testing; and vaccination alone or in addition to each of the six interventions. Data inputs were obtained from systematic reviews, primary data and expert opinion. The model parameters were simultaneously estimated from the data inputs using Bayesian evidence synthesis.

The expected net benefit relative to no intervention was calculated for each intervention within each risk group for two scenarios, with and without vaccination. Interventions with more than a 1% probability of being cost-effective (i.e. maximising net benefit at a threshold of £25,000 per QALY gained) in a specific risk group were combined to form strategies. To limit antibiotic exposure, women who were low risk at presentation (groups 11 and 12) could not be treated without a positive culture or PCR result.

Results

Current best practice, comprising intravenous treatment for pyrexia, previous GBS baby and previous GBS swab or urine culture, and oral treatment for preterm pre-labour membrane rupture (groups 2–5 and 8–10) was not cost-effective. All cost-effective options involved treatment of all preterm groups and high-risk term groups (groups 8–10). Testing high-risk women for maternal GBS colonisation would not be cost-effective, as even those with negative results would be better off treated to reduce the risk of early-onset non-GBS infection. In the absence of vaccination, culture-based testing of women in groups 11 and 12, combined with treatment for the rest, would be the most cost-effective strategy. If vaccination was available, vaccination for all and treatment for groups 1–10 would be marginally more cost-effective than treatment for groups 1–10 and culture for groups 11 and 12, but this is uncertain and is based on expert opinion on vaccine efficacy. The expected value of perfect information (EVPI) results suggest that moderate investment in research would be worthwhile.

Implications for policy

Two limitations of the analysis are the exclusion of adverse effects of antibiotics and organisational costs to implement (or reverse) a new intervention. In outlining policy, we assume that limiting antibiotic exposure is worthwhile and that adding to current practice would be easier to implement than changing it.

Current best practice involves treating 7.4% of women. Extension of clinical recommendations to treat all preterm women, while continuing to give the same treatments to high-risk term women would gain an additional £14 million net benefit for the UK per year and increase the proportion of women exposed to antibiotics to 11%.

In the absence of vaccination, the cost-effective option is culture-based testing of women in groups 11 and 12, combined with treatment for the rest. An alternative strategy, in which women with elective Caesarean section at term (group 7) also undergo culture testing, would generate marginally less benefit, but reduce treatment to 21% (from 27%) of women.

If vaccination becomes available, the cost-effective strategy (net benefit £50.5 million) would be vaccination for all and treatment of risk groups 1–10 (19% of all women treated). Therefore, an advantage of vaccine is that strategies which provide more net benefit can be adopted without an increase in antibiotic exposure.

Conclusions

Based on our findings, immediate extension of current practice to treat all preterm and high-risk term deliveries would be beneficial.

Thereafter, it is not clear whether the optimal choice would be culture-based testing for low-risk women, or vaccination plus treatment of all preterm and high-risk term women. There are also important issues of timing. Vaccination is unlikely to be available for the next 5 years and could not be implemented without Phase III trials, which will substantially reduce uncertainty over vaccine efficacy. In the meantime, implementation of culture testing for low-risk women appears to be the most cost-effective option but implementation costs could be significant and not recouped if, subsequently, a vaccination strategy was adopted.

Recommendations for further research

The EVPI analyses indicated that spending on further research could be worthwhile and would provide maximum returns of between £29 million and £67 million. These results suggest that adoption of treatment for preterm and high-risk term women and research into vaccine efficacy may be beneficial before deciding whether to adopt culture-based screening for low-risk women, or vaccination for all without screening. Cost-effectiveness of vaccine compared with other interventions should be re-evaluated after Phase III trials, which are needed anyway to gain a licence.

Studies comparing culture with PCR testing or no intervention in the low-risk term groups (7, 11 and 12) might also be informative, but would need to be extremely large.

The proposed very large cluster randomised trial of culture-based testing versus no intervention for low-risk women, plus treatment for high-risk women in both arms, would base the primary results on aggregate rates of neonatal infection. The high-risk pregnancies would account for 41% of early-onset GBS, but would not be separately identifiable. This would complicate interpretation of the trial and the consequent dilution of the treatment effect would require a large increase in sample size compared with a trial in which risk groups were identifiable.

Comparison of oral and intravenous treatment could also be valuable, as this might better inform treatment in preterm groups 1, 5 and 6. Finally, study designs other than clinical trials could contribute important information. For example, more information on the consequences of infection outcomes for disability, quality of life, healthcare costs and life expectancy could be valuable. Further EVPI analysis aimed at specific sets of parameters could throw light on the research priorities.

Publication

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NIHR Health Technology Assessment Programme

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