Intravenous Immunoglobulin Doesn’t Decrease Mortality for Suspected or Proven Sepsis in the Neonate

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BACKGROUND

Neonates are at higher risk of infection due to immuno-incompetence. Maternal transport of immunoglobulins to the fetus mainly occurs after 32 weeks' gestation, and endogenous synthesis begins several months after birth. Administration of intravenous immunoglobulin (IVIG) provides immunoglobulin G (IgG) that can bind to cell surface receptors, provide opsonic activity, activate complement, promote antibody-dependent cytotoxicity and improve neutrophilic chemoluminescence. Theoretically, infectious morbidity and mortality could be reduced by the administration of IVIG.
Objectives

- To assess the effects of IVIG on mortality/morbidity caused by suspected infection.
- To assess the effects of IVIG on mortality/morbidity caused by proven infection.
- To assess the effects of IVIG on mortality/morbidity caused by suspected or proven infection at study entry in neonates.
- To assess in a subgroup analysis the effects of IgM-enriched IVIG on mortality from suspected infection.

Search methods

For this update, MEDLINE, EMBASE, The Cochrane Library, CINAHL, trial registries, Web of Science, reference lists of identified studies, meta-analyses, and personal files were searched in 2013.

Selection criteria

Randomized or quasi-randomized controlled trials; newborn infants; IVIG for treatment of suspected or proven bacterial/fungal infection compared with placebo or no intervention; one of the following outcomes was reported: Mortality, length of hospital stay, or psychomotor development at follow-up.

- Suspected infection was defined as clinical symptoms and signs consistent with infection without isolation of a causative organism.
- Proven infection was defined as clinical symptoms and signs consistent with infection in association with isolation at autopsy of a causative organism (bacteria or fungi) from blood culture, cerebrospinal fluid culture, urine culture or a normally sterile site (e.g. liver, spleen, meninges, and lung).

Types of interventions

IVIG (polyvalent or IgM enriched) to treat suspected or proven bacterial or fungal infection versus control (placebo or no treatment).

Primary outcome

- Mortality from any cause during initial hospital stay.

Secondary outcomes

- Length of hospital stay.
- Long-term psychomotor development at 18 months corrected age or at a later age.
- Growth at 18 months corrected age or at a later age.
- Death at 18 months corrected age or at a later age.
- Death or major disability at 18 months corrected age or later.
- Increased number of infections during childhood.
- Side effects.

Data collection and analysis

Statistical analyses included typical risk ratio (RR), risk difference (RD), weighted mean difference (WMD), number needed to treat for an additional beneficial outcome (NNTB), or an additional harmful outcome (NNTH) (all with 95% confidence intervals (CIs) and the I-squared (I²) statistic to examine for statistical heterogeneity).

MAIN RESULTS

A total of eight studies evaluating 3,871 infants are included in this review. Mortality during hospital stay in infants with clinically suspected infection at trial entry was not significantly different after IVIG treatment (eight studies ($n=2,425$); typical RR 0.94, 95% CI 0.80-1.12; typical RD - 0.01, 95% CI 0.04-0.02, $I^2 = 28\%$ for RR and 32% for RD) [Figure 1]. Death or major disability at 2 years corrected age was not significantly different in infants with suspected infection after IVIG treatment (one study ($n=1,985$); RR 0.98, 95% CI 0.88-1.09, RD - 0.01, 95% CI - 0.05 to 0.03). Mortality during hospital stay was not significantly different after IVIG treatment in infants with proven infection at trial entry (RR 0.95, 95% CI 0.74-1.21, RD - 0.01, 95% CI - 0.04 to 0.03). Death or major disability at 2 years corrected age was not significantly different after IVIG treatment in infants with proven infection at trial entry (one study ($n=3,493$); RR 1.00, 95% CI 0.91-1.18, RD 0.01, 95% CI - 0.04 to 0.06). Mortality during hospital stay in infants with clinically suspected or proven infection at trial entry was not significantly different after IVIG treatment (one study ($n=3,493$); RR 1.00, 95% CI 0.86-1.16; RD 0.00, 95% CI - 0.02-0.03). Death or major disability at 2 years corrected age was not significantly different after IVIG treatment in infants with suspected or proven infection at trial entry (one study ($n=3,493$); RR 1.00, 95% CI 0.92-1.09; RD - 0.00, 95% CI - 0.03 to 0.03). Length of hospital stay was not reduced for infants with suspected/proven infection at trial entry (one study ($n=3,493$); mean difference (MD) 0.00 days, 95% CI - 0.61 to 0.61). No significant difference in mortality during hospital stay after IgM-enriched IVIG treatment for suspected infection was reported at trial entry (three studies ($n=164$); typical RR 0.57, 95% CI 0.31-1.04; RD - 0.12, 95% CI - 0.24 to 0.00; $P = 0.06$; $I^2 = 2\%$ for RR and 0% for RD).

AUTHORS’ CONCLUSIONS

Results show no reduction in death or major disability at 2 years of age.

- Routine administration of IVIG to prevent mortality in infants with suspected or proven neonatal infection is not recommended.
- No further research is recommended to test current IVIG preparations.
Comments
This large study included around 4,000 neonates have made a clear answer to the ever repeated logic question concerning the use of IVIG to prevent or treat suspected or proven sepsis in the immunocompromised newborn infants. The authors further recommended no further researches in this topic.

Citation
Ohlsson A, Lacy JB. Intravenous immunoglobulin for suspected or proven infection in neonates. Cochrane Database Syst Rev 2013:CD001239. DOI: 10.1002/14651858.CD001239.pub4.

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