RESEARCH BRIEF

SPOR Strategy for Patient-Oriented Research EVIDENCE ALLIANCE

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Antenatal and postpartum prevention of Rh alloimmunization: Findings from a systematic review and meta-analysis

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Summary

These systematic reviews provided all comparative evidence regarding the timing and dose of Rh immunoprophylaxis for Rh negative women at risk. Evidence was mainly from older publications (e.g., 1960s to 1980's), often resulting in limited reporting, as reporting guidelines were not yet introduced. This made it difficult to assess the risk of bias, resulting in many unclear ratings. There is evidence of a beneficial treatment effects for several comparisons, however, due to the very low and low certainty of the evidence, the magnitude of the treatment effects may be overestimated. Additionally, there were several subgroups of women (e.g., women undergoing amniocentesis) where there was no data.

Reference: *Antenatal and postpartum prevention of Rh alloimmunization: A systematic review and GRADE analysis. Hamel C, Esmaeilisaraji L, Thuku M, Michaud A, Sikora L, Fung-Kee-Fung K. PLoS One. 2020 Sep 10;15(9):e0238844.*

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What is the current situation?

Rh immunoprophylaxis (RhIg) was introduced into routine obstetrical care in the 1960s for Rh negative women at risk, leading to a dramatic fall in the number of Rh affected babies. To date, the published systematic review (SR) evidence supporting established protocols for prevention of Rh alloimmunization have been limited by methodological flaws, have been restricted to randomized controlled trials (RCTs), and have not all evaluated the certainty of the evidence. Our objective was to systematically review the evidence from RCT and comparative observational studies, for the effectiveness of RhIg in Rh-negative pregnant and postpartum women at risk of Rh alloimmunization.

What is the objective?

Research questions were as follows:

1. What is the optimal strategy to administer RhIg for immunoprophylaxis, what is the optimal dose of RhIg in Rh-negative pregnant and postpartum women at risk of Rh alloimmunization, and what is the certainty of the evidence?
2. For what obstetrical conditions is there evidence from RCTs and comparative observational studies to support antenatal immunoprophylaxis?

How was the review conducted?

- A systematic review was conducted to identify RCTs. This was later expanded to include comparative observational studies and a second SR was conducted.
- Several electronic databases were searched (eg., Medline, Embase, Cochrane Central Register of Controlled Trials) using study design filters, where applicable. Relevant websites and bibliographies of systematic reviews and guidelines were searched for studies published before 2000.
- Study selection was performed using the liberal accelerated method. Data collection, risk of bias assessments, and GRADE ratings were performed by one reviewer with verification done by a second reviewer, with discrepancies resolved through discussion.

What did the review find?

- **RCT SR**: From 467 citations identified (after deduplication and grey literature searching), 13 publications (11 unique studies) were included. Studies ranged in size from 14 to 4865 women (median: 740). Eight trials were published in the 1960's and 1970's. Studies reported on four different comparisons (e.g., postpartum RhIg, antenatal RhIg given either intramuscularly or intravenously). Risk of bias was moderate and high for all studies.
- **Observational SR**: From 572 citations identified (after deduplication and grey literature searching), 8 publications (representing 7 cohorts) were included. Studies were published between 1978 and 2013. Study sizes ranged from 117 to 27,926 participants. Studies reported on six different comparisons (e.g., postpartum RhIg to no treatment, treatment to no treatment after amniocentesis).
- There is some evidence of beneficial treatment effects (e.g., at 6-months postpartum, fewer women who received RhIg at delivery compared to no RhIg became sensitized [70 fewer sensitized women per 1,000 (95%CI: 67 to 71 fewer); I^2 =73%], however the certainty of the evidence is very low, which may result in an overestimation of the magnitude of the treatment effect.
- There is limited evidence on prophylaxis for invasive fetal procedures (e.g. amniocentesis) in the comparative literature, and few studies reported adverse events.

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