



" Evaluation of rubella IgG avidity maturation over time in pregnant women"

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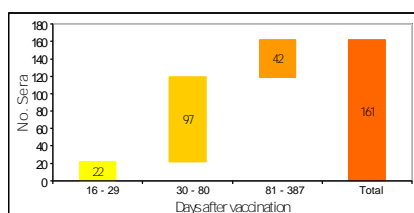
ABSTRACT

There is a significant risk of the development of congenital rubella syndrome in the baby of a woman having a primary rubella infection during her first trimester of pregnancy. Critical clinical management decisions with respect to termination of pregnancy are based in part on the laboratory confirmation of the rubella infection. Rubella IgG avidity is a very useful method for confirming rubella IgM positive results in pregnant women. In order to properly interpret rubella avidity results, it is imperative that we understand the timing of the avidity maturation of rubella-specific IgG. Our objective was to determine the optimal avidity index cutoff values and the timing of maturation of rubella-specific IgG avidity in pregnant women. Sera positive for rubella IgM from 161 pregnant women who were inadvertently vaccinated during a mass rubella immunization campaign in Brazil in 2001-2002 were collected from 16 to 387 days post-vaccination. Sera were tested using an in-house rubella IgG assay originally developed in the UK, and avidity indexes were calculated (OD of denaturant-washed wells / OD on non-denaturant washed wells). The optimal avidity index cutoffs for this in-house rubella IgG assay were determined to be <40% for low avidity, 40-60% for intermediate avidity, and >60% for high avidity. Maturation from low to high avidity begins around 30 days post-rubella immunization and 100% of sera are no longer considered low avidity by 80 days post-immunization. This study has allowed us to determine the optimal cutoff values for low and high rubella IgG avidity, and to characterize the maturation of avidity over time in the context of confirming suspected rubella in pregnant women.

MATERIAL AND METHODS

MATERIAL

Serum samples from 161 pregnant women inadvertently vaccinated were obtained during the vaccination program held in Brazil in 2001-2002. All sera had given positive results in both rubella IgM and IgG assays used. These serum samples were taken at different time intervals.



METHODS

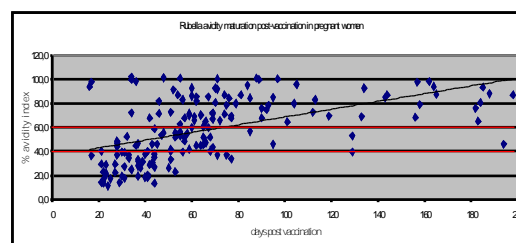
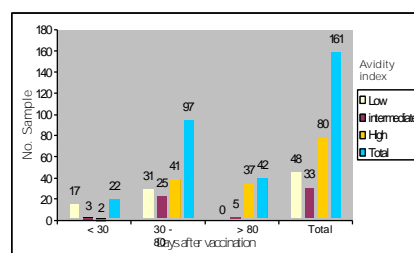
Rubella-specific IgM and IgG assay

Rubella IgM and IgG antibodies were determined by a commercially available ELISA Enzygnost Anti-Rubella Virus IgM and Enzygnost Anti-Rubella Virus IgG according to the instructions provided by the manufacturer (Dade-Behring, Marburg, Germany).

Rubella-specific IgG avidity

In-house method originally developed in the UK and adapted in NML, Winnipeg by Mubareka et al (to be published). Six control sera consisting of two high avidity, two low avidity, and two rubella IgG negative were included in each run. The avidity index (AI) was calculated for each specimen as follows: mean optical density (OD) assay with DEA / mean OD assay with NGS/PBST X 100.

RESULTS



CONCLUSIONS

The proportion of IgG that remains bound to antigen provides information related to the stage of infection (Enders & Knotek 1989, Korhonen et al 1999, Thomas et al 1992). Low-avidity IgG is indicative of a primary infection whereas high-avidity IgG is typical of a past infection or re-infection.

Our results from pregnant women positive for rubella IgM antibodies showed that maturation from low to high avidity begins around 30 days post-rubella immunization and 100% of sera are no longer considered low avidity by 80 days post-immunization.

Considering the similarity of the rate of low avidity IgG occurrence in avidity-ELISA after vaccination and after natural rubella, the result presented for low avidity was in agreement with Hedman et al (1989), who showed that after vaccination of previously non-immune subjects, IgG synthesized during the first 2 months exhibited low avidity indexes (<30%).

The avidity test can be incorporated in the routine diagnostic service in laboratory as a supplement to the rubella IgG and IgM antibody ELISA's when the results of both these tests are positive. Furthermore, it is important to take into account the period of rash onset, the date of sample collection, as well as clinical and epidemiological data.

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