Maternal antibody against influenza neuraminidase in newborns: abridged secondary publication

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KEY MESSAGES

1. Infants whose mothers had a history of vaccination have a significantly higher maternal antibodies (MatNAb) titres to both group 1 and group 2 influenza viruses.
2. Infants whose mothers had a history of vaccination have significantly lower influenza infection than those whose mothers did not.
3. Lower birth weight is associated with lower MatNAb titres for N1 responses but not for N2 responses. When the birth weight is <2 kg, the MatNAb titres tend to be lower. Infected infants have significantly lower titres of N1 seasonal influenza.
4. The MatNAb titres can reduce the relative risk of influenza infection and is correlated with reduction in infection than haemagglutinin inhibition titres. When the MatNAb titre is ≥160, >50% relative risk reduction from infection is achieved.
5. Influenza vaccination in pregnant mothers can boost MatNAb titres in infants and reduce the risk of influenza infection. Therefore, inclusion of neuraminidase in influenza vaccines is beneficial.

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Influenza is a major public health concern worldwide, particularly in densely populated Hong Kong. In 2008, one million cases of influenza occurred in children aged <5 years.[1] Influenza immunity is acquired in an age- and exposure-related manners. Infants and young children are an important link in the transmission chain of influenza in communities and families. They are considered drivers of yearly epidemics. Infants aged <6 months do not possess an effective endogenous immune defence against influenza, and influenza vaccines are not recommended for infants aged <6 months.

Maternal antibodies (MatNAb) are mainly immunoglobulin (Ig) G, which is transferred through the placenta to protect newborns against influenza. The transfer of IgG is mediated by neonatal Fc receptor expressed on syncytiotrophoblast cells, depending on maternal titre of IgG, gestational age, placental integrity, IgG subclass, and nature of antigen.[2] Maternal immunisation can elevate the total IgG.

For infants, protection against influenza is provided by IgA from breast milk, but both IgA and IgG do not cross the intestinal epithelium in sufficient amounts. The major host protection in lung against influenza is IgG derived from serum. Thus, it is important to evaluate protection effects of serum antibodies transferred from placenta to infants.[3]

Antibodies to the influenza hemagglutinin play a role against specific strains. There is increasing evidence on the more important protective role of anti-neuraminidase antibodies.[4] The function of neuraminidase is to release budding virions from cells to facilitate spread to new cells. When neuraminidase is blocked by antibodies, the virions remain aggregated in a manner that hinder binding to cell receptors of new cells. Thus, virions are not able to spread and initiate subsequent rounds of infection. Consequently, the amplification and continuation of the infection process comes to a standstill. Therefore, antibodies against neuraminidase do not enable sterilising immunity but protection or resistance against infection and reduction of disease severity.[5] Thus, neuraminidase is a useful vaccine protective antigen. Moreover, the high conservation of viral neuraminidase makes the antibodies that bind to it largely cross-protective against novel strains. We aim to characterise the MatNAb and determine its correlation with protection against influenza in newborns.

Our results indicated that geometric mean titres for MatNAb responses against N1 and N2 seasonal influenza in infants were significantly higher when mothers had a history of vaccination, compared with those who did not. MatNAb responses were associated with seasonal MatNAb titre, infant birth weight, and mothers smoking status, but not with infant sex. There was a trend

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that birth weight of <2 kg was associated with lower neuraminidase responses for seasonal N1 but not for seasonal N2. MatNAb titres were significantly lower in infants infected by influenza within the first 2 months after birth. Most infections in infants were H3N2 infections. The cross-reactive MatNAb titres against unexposed highly pathogenic influenza viruses such as H5N1 were lower compared with seasonal MatNAb titres. The neuraminidase titre was not correlated with birth weight.

In conclusion, infants of vaccinated mothers have higher MatNAb titres to both group 1 and group 2 influenza viruses. Lower birth weight is associated with lower MatNAb titres for N1 responses but not for N2 responses. When the birth weight is <2 kg, the MatNAb titres tend to be lower. Infected infants have significantly lower titres of N1 seasonal influenza but not of N2 seasonal influenza. The MatNAb titres tend to reduce the relative risk of influenza infection and is correlated with reduction in infection than haemagglutinin inhibition titres. Influenza vaccination in pregnant mothers can help boost the MatNAb titres in infants and reduce the risk of influenza infection. Therefore, inclusion of neuraminidase in influenza vaccines is beneficial.

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