Introduction

Maternal immunization – Promises and concerns

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ABSTRACT

In this issue of Vaccine, the maternal immunization platform as an approach to protect mothers and infants against diverse pathogens is presented. Potential vaccine targets and the safety, science, trial designs, ethical considerations, and international perspectives focusing on low and middle income countries (LMIC) are reviewed. This information provides a timely update because maternal immunization is increasingly being considered as a potential intervention to prevent maternal and/or neonatal disease. Simultaneously, lessons learned from both older clinical studies and recent immunization implementation programs in pregnant women must be appreciated. Immunization during pregnancy to protect both the woman and her infant is not new [1,2]; maternal immunization programs to protect against maternal and neonatal tetanus have been proven to be effective [3] and have been ongoing for decades. Although earlier studies were not always conducted with the rigor of current trials, lessons learned from both old and new studies conducted for pertussis [4,5] influenza [1,6], as well as Hemophilus influenza type b polysaccharide and conjugate vaccines [7] should be taken into account as the field moves forward.

Worldwide maternal immunization programs utilizing tetanus toxoid vaccines began in the 1980s based on high rates of mortality documented in many developing countries from tetanus disease in both mothers and infants following childbirth [3]. Maternal immunization remains an important tool – but not the only tool – for preventing both maternal and neonatal tetanus in developing countries where the risk of acquiring tetanus during childbirth is high [8]. Tetanus immunization during pregnancy is currently an important tool, particularly in countries where no tetanus vaccines after the infant series are administered. A marked decline in neonatal tetanus has been documented over the past decades, although the persistence of neonatal tetanus indicates the need to continue efforts to combat this preventable disease.

Increased rates of morbidity and mortality in pregnant women, particularly in the third trimester of pregnancy, were documented following infection with the 2009–2010 pandemic strains of influenza A/H1N1 and documented in many countries [9]. Disease in pregnant women in this century was reminiscent of descriptions of pandemic disease going back to 1918 [10]. Risks to the fetus due to preterm onset of labor, although not active infection, were also documented during this recent pandemic [11,12]. No evidence of fetal priming or sensitization following maternal influenza or tetanus vaccination has been documented. The public health response to this increased disease burden in pregnant women resulted in priority for immunization of pregnant women with inactivated influenza vaccines in many high-income countries. Subsequently, the safety and effectiveness of this approach has been reported and the analysis of this approach to prevent influenza-related morbidity and mortality in mothers and infants explored at nationally and internationally [11–13]. Recently, a study supported by the Bill and Melinda Gates Foundation in South Africa documented the safety and efficacy of maternal influenza vaccine during the post-pandemic period [14]. Descriptions of maternal influenza immunization from the perspective of tropical countries and the WHO will be presented in this issue.

Maternal immunization has also been advocated as an important strategy to prevent neonatal pertussis in the USA and United Kingdom due to increasing morbidity and mortality from neonatal pertussis disease [15,16]. Recommendations for the use of acellular pertussis vaccines and combination vaccines to pregnant women were based on the presence of fatal cases of pertussis in young infants. At the time these recommendations were made, little data was available on the safety and efficacy of maternal immunization on the subsequent immune response to vaccination in infants. After the implementation of this approach, the effectiveness as well as the safety, immunogenicity, antibody transfer, and impact on infant immunization was demonstrated [6,16]. The potential application of this approach in low and middle income countries will be explored in this issue.
The increased acceptance of immunization to prevent influenza in pregnant women represented a shift in the acceptance of maternal immunization in many countries. The use of maternal acellular pertussis vaccine to prevent severe neonatal disease represents another important paradigm shift because the rationale for maternal pertussis vaccination is chiefly to protect the infant, not the mother. However, both mothers and infants have potential benefit from influenza or pertussis vaccines, and both vaccines are known to be safe, well tolerated, and immunogenic in adults. For both pathogens, maternal immunization programs were instituted because of overwhelming epidemiological evidence of the burden of disease and public health and community acceptance that this risk was high. This increasing interest in and utilization of maternal vaccines demonstrates the potential benefit but also the new challenges to those involved in communication about research issues, as well as health care providers caring for pregnant women, public health agencies, regulatory authorities, and pharmaceutical companies.

New questions regarding maternal immunization are being raised. Obstetricians, midwives, and other healthcare workers caring for pregnant women are becoming more interested in maternal immunization but nonetheless want to know, how many vaccines can we give these women? How can future trials of new maternal vaccines be conducted when the standard of care is already to administer at least one vaccine? What new targets should receive priority? If multiple new maternal vaccines are developed and shown to be safe and effective, which vaccine(s) should have priority? The development of new maternal vaccines is dependent on the availability of a safe, immunogenic, and effective product but more importantly, the epidemiology of the target pathogen in representative countries or populations must be ascertained, and the true burden of disease in the mother and infant characterized. Lack of data characterizing the true risk of infections in the first month of life is profound, particularly in developing countries where hospital access may be limited and surveillance of disease is linked to those children surviving long enough to actually reach the hospital. The true burden of disease and mortality due to neonatal pertussis, respiratory syncytial virus (RSV), and Group B streptococcus (GBS) remain relatively poorly characterized in many parts of the world today. The potentially devastating impact and long term sequelae of infections with cytomegalovirus, herpes simplex virus, and toxoplasmosis are similarly not appreciated in many LMIC but argue for consideration of vaccination strategies including but not limited to maternal immunization.

Future maternal immunization targets, vaccines, and policies require an assessment of risks and potential benefits. The tempting application of maternal immunization platform as a panacea to all potential neonatal infections must be weighed in terms of the burden of disease, the work and time involved for those providing prenatal care, the cost-effectiveness of such interventions, and the safety, benefits, and risks of this approach. Safety considerations remain paramount although data remain reassuring to date [17]. Even the relatively limited epidemiological data from many developing countries might demonstrate the likelihood of moderate to marked potential benefit to infants if partial reduction in neonatal disease due to CMV, GBS, or RSV could be demonstrated; conversely, rates of neonatal disease may vary depending on the setting, the medical system available, or rates of coinfection with HIV or tuberculosis. Other potential targets for maternal immunization include malaria, meningococcus, pneumococcus, tuberculosis, or even rabies. The potential benefit to infants may be demonstrated even if pathogen-specific attack rates are relatively low because sequelae of these infections can be severe. Costs for procuring, storing, administering, and documenting vaccines for pregnant women may be considerable, with potentially lower direct maternal benefit. A relatively low burden of neonatal disease combined with an expensive vaccine or one not easily stored and administered may not be worthwhile.

Increasing rates of routine prenatal care for pregnant women is a world health goal being actively promoted; the workload of nurses and clinical staff already overworked in prenatal clinics in LMIC may be nearly maximized in some settings. Additional support for prenatal clinics in developing countries may require increased support for maternal health care overall. Nonetheless, the potential for maternal immunization to protect the mother and infant needs serious consideration. Prioritization of vaccine targets for maternal immunization by researchers, public health officials and health care workers needs to begin now.

References


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