Safety of Immunization during Pregnancy

A review of the evidence

Global Advisory Committee
on Vaccine Safety

World Health Organization

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1. Introduction

Vaccine-preventable infectious diseases are responsible for significant maternal, neonatal, and young infant morbidity and mortality. Changes in the immune response in pregnant women – which are thought to occur in order to allow the woman to tolerate the semi-allogeneic foetus – may interfere with the development of the specific immune response to pathogens. These immunological changes may alter the susceptibility of the woman and the foetus to certain infectious diseases (1) and increase the risk of more serious outcomes. The immature adaptive immune systems of neonates and premature infants make them particularly vulnerable to morbidity and mortality due to infection.
Immunization of pregnant women can protect them directly against vaccine-preventable infections, and in so doing potentially protect the foetus. It can also directly protect the foetus and infant via specific antibodies transferred from the mother during the pregnancy.

At its meeting in November 2011, the Strategic Advisory Group of Experts (SAGE) of WHO asked the Global Advisory Committee on Vaccine Safety (GACVS) to provide support to a review of evidence on the safety of vaccinations in pregnant and lactating women. This request related to uncertainties about the safety of vaccination – whether intended or inadvertent – of pregnant women during mass vaccination campaigns. Such evidence would be particularly important in situations where manufacturers do not recommend the vaccination of pregnant women on solely precautionary grounds. However, evidence related to this issue is limited, as pre-licensing clinical trials of vaccines do not usually include pregnant and lactating women. Reports available also provide limited post-licensing data, as once again, pregnant women are usually not included in clinical trials. This in turn has limited the ability to make evidence-based decisions and provide optimal guidance on the use of vaccines in this population.

2. Methodology

This report presents an overview of the relevant literature on the safety of vaccination of pregnant women. In addition to reviewing the published literature, GACVS contacted regulatory authorities and pharmaceutical companies to obtain results of ongoing surveillance programmes for pertussis-containing and meningococcal vaccines in pregnant women. The cut-off point for the literature review was May 2013.

The availability and amount of data were assessed, as well as their overall quality in terms of consistency, strengths, and weaknesses. The conclusions are based on expert discussion and consensus rather than on a systematic review and grading system. This report focuses on vaccines that are currently available, with priority for review given to vaccines on the basis of two key criteria:

- their potential to reduce morbidity in the pregnant woman and/or her fetus; and
- their use (or anticipated use) in vaccination campaigns targeting pregnant women as well as vaccination campaigns where pregnant women may be inadvertently vaccinated.

Once the specific vaccines for review had been selected, a standard framework was developed which addressed the following issues:

- the demonstrated or potential benefit of vaccination during pregnancy; this included evidence of disease morbidity in pregnant women and foetuses, and of the efficacy or effectiveness of the vaccine in pregnant women;
- evidence of safety of vaccination or lack of evidence of adverse pregnancy outcomes; data from clinical trials, observational studies, published case reports, case series and passive surveillance systems were assessed, as were theoretical considerations and experimental data relating to potential harm to the fetus and the mother (e.g. type of vaccine, ability of the vaccine strain to cross the placenta, risk of infection related to gestational age)