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Vaccination of pregnant women

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Abstract

Vaccination of pregnant women for their protection and the protection of the fetus and the child is not common. Health professionals' prejudices about immunization of pregnant women increase the concerns of women and their families. Such behavior is not supported by scientific data. The literature describes the harmlessness of the vaccine for mother and child in the case of seasonal, pandemic or meningococcal flu, pneumococcus, tetanus, acellular pertussis, human papillomavirus, cholera, hepatitis A, Japanese encephalitis, rabies, anthrax, smallpox, yellow fever, mumps, measles and rubella, typhoid fever, inactivated or attenuated polio vaccines, and Bacillus Calmétte Guerin vaccines.

Many scientific studies show the beneficial effects of the flu vaccine for mother and baby and the pertussis vaccine for the baby. Staff of Obstetrics and Gynecology Departments, family doctors and midwives should include vaccinations in their standard clinical care.

Strategies are needed that are effective in reducing parents' reluctance to vaccinate. Every pregnant woman should be aware that the lack of vaccines before pregnancy does not preclude the use of some of them during pregnancy.

Key words: pregnancy; vaccine; immunization

Introduction

In connection to the Covid-19 pandemic, it is time to overcome the hesitation of many people, including health care workers, when it comes to proposing to vaccinate pregnant women [1]. Safety, effectiveness, or conflicting advice affect laymen. Inadequate training and increased workload affect healthcare professionals. The ancient distrust of any artificial interference with pregnancy, and the growing distrust of vaccines in the industrialized world today, may drive their use to a halt. On the contrary, we must now be convinced that the harmful attitudes that derive from them are based on low knowledge.

The protective effect in infants of maternal vaccinations during pregnancy was observed in 1879, when infants of mothers who received the Jennerian vaccine during pregnancy provided them with protection against smallpox [2]. Since 1879, a lot of evidence has been accumulated regarding the safety of vaccination in pregnancy with non-live vaccines [3,4]. Inactivated vaccine studies include inactivated seasonal or pandemic influenza, mono- or combination polysaccharides or conjugated meningococcus, tetanus toxoid, acellular pertussis, human papillomavirus, cholera, hepatitis A, Japanese encephalitis, rabies and anthrax vaccines [5, 6, 7].

Pregnant women are rightly excluded from live virus vaccine trials because of the theoretical risk of transmission of the vaccine virus to the fetus. Therefore, there are no data from prospective studies. Consequently, live virus vaccines are contraindicated in pregnant women. It is recommended to avoid vaccinations during pregnancy and avoiding pregnancy in the immediate period after administration of such vaccines [8, 9]. There is evidence from retrospective studies based on the results of studies in inadvertently vaccinated women that there is a complete absence of adverse effects affecting pregnancy, mother and child [9,10].

Safety has been demonstrated for smallpox, yellow fever (with the exception of a few reports of infection while breastfeeding), combined mumps, measles and rubella vaccine, quadrivalent influenza, typhoid fever, live attenuated oral poliomyelitis virus vaccines, and Bacillus Calmétte Guerin [11,12 , 13]. There are reports that yellow fever vaccination may cause infection with the vaccine strain through breast milk. In fact, the registry of pregnancies containing the varicella zoster vaccine was closed after approximately 920 reports of women who had inadvertently received the varicella vaccine in the three months prior to pregnancy or at any time during pregnancy were considered. There was no effect on pregnancy, mother or child [14].

Rubella

Tens of thousands of pregnant women have received the rubella vaccine in South America during massive campaigns to eradicate rubella and congenital rubella syndrome. No side effects have been observed in pregnant women, mothers and children. One child developed IgM antibodies to the vaccine virus at birth, but no evidence of congenital rubella was found. [15, 16, 17]. Similar reassuring results were found in the United States, West Germany, Sweden, and the United Kingdom. 680 pregnant women received the vaccine against rubella. No child with Congenital Rubella Syndrome was born [18]. Some babies were born with anti-rubella IgM, but no signs of congenital rubella virus.

Measles

Due to the worldwide presence of Odra, the Center for Disease Control and Prevention / CDC / and the American College of Obstetricians and Gynecologist / ACOG / recommend that, in addition to rubella resistance, measles immunity should be assessed. It is proposed that 2 doses of MMR vaccine should be given before planned pregnancy in high-risk women [15, 17]. However, when 1 dose is administered, serological tests to demonstrate immunity to measles are recommended. Demonstration of resistance to rubella is not an indicator of measles immunity. In the absence of measles IgG antibodies, a booster dose of MMR vaccines should be given and pregnancy should be waited 4 weeks as live vaccines may theoretically pose a risk to the fetus. The current immunity to rubella, thanks to the compulsory vaccination of girls who were not sick at the age of 13, is an important element of prenatal tests. Women who are immunocompromised should be vaccinated before they become pregnant. In the USA, taking into account their adverse impact on the developing intrauterine fetus, ACOG and CDC propose to determine the serological status of women in the pre-conception period. In the absence of immunity, she recommends MMR vaccination at least 4 weeks before the planned pregnancy. The use of live vaccines theoretically increases the risk of fetal infection. According to the literature data, the risk of transmission of the virus from the vaccine to the fetus is <0.2%, and at the same time, having any of these diseases is not a contraindication to vaccine administration [17,18].

The arrangements for the safety of live vaccines should not be considered as an incentive to the deliberate administration of these vaccines in pregnant women. We must advise women to avoid pregnancy for one month after receiving rubella vaccine. It is possible that this is an example of excessive caution, but in medical practice it is wise to primum non nocere - that is, first, do no harm [19]. These studies suggest that if a pregnant woman is inadvertently vaccinated, she should be made aware of the theoretical grounds for concern for the fetus, but vaccination during pregnancy should not inevitably be a reason to consider abortion.

Pertussis, tetanus, diphtheria

Several studies show that immunization during pregnancy with a vaccine against tetanus, diphtheria and pertussis is as immunogenic as in non-pregnant women [20]. Pregnant women show a humoral response to tetanus and diphtheria toxoids, as well as to Bordetella pertussis antigens (pertussis toxin, filamentous hemagglutinin and pertactin). In contrast, the proliferative response and interferon-γ (expression of cellular immunity) are transient and impaired [20]. The American Academy of Pediatrics recommends vaccinating pregnant women against tetanus, influenza and whooping cough [21]. Vaccinating pregnant women against tetanus is essential to avoid neonatal tetanus [22]. Despite pertussis vaccination, its morbidity and mortality remains high worldwide, especially among newborns and infants under three months of age [25,26,27]. 90% of deaths occur in this age group. At least two immunization strategies are conceivable to protect the infant. The first is a protection strategy that involves parents, caregivers and other people in close proximity to protect infants from transmitting the virus [28, 29]. This strategy may not prevent family colonization and neonatal transmission because Bordetella pertussis is transmitted to the infant by vaccinated but infected but asymptomatic family members [29,30]. The second strategy is to vaccinate pregnant women by passively transferring antibodies to whooping cough. This approach has been shown to be effective in preventing pertussis and placental transmission of maternal antibodies [31,32]. The interference manifests itself in all conditions and is related not to the amount of antibodies but to their quality and occurs when the same vaccine is used in the mother and infant. Thus, the solution is to immunize the mother and the infant with two

different vaccines. There is a second opposing theory that vaccination with the same vaccine for mother and newborn would be beneficial because immune memory would play a role in later antibody responses and antibody affinity (so-called genetic imprinting). In many countries, the use of acellular pertussis vaccine for adults in combination with tetanus toxoid and diphtheria toxoid (Tdap) is recommended in pregnant women to protect newborns in the first months of life when they are too young to be vaccinated. It is an effective protection for them, especially in the first 3 months of life, when they are exposed to pertussis complications and mortality. The resulting maternal antibodies are transferred to the fetus in the second trimester of pregnancy and provide passive immunity until the infant is immunized first.

Influenza

The influenza during pregnancy increases the risk of cleft palate, heart defects or neural tube defects [23]. Pregnant women show a reduced response of CD8 lymphocytes and dendritic cells to the influenza virus when physiological changes in hemodynamics and respiration occur [24]. The overlapping of these harmful mechanisms increases the risk of developing influenza [24]. Flu in pregnancy is dangerous for both mother and baby. A meta-analysis of 33 studies in which more than 1,600 children were exposed in utero to maternal flu, showed that approximately 3.5% of the children had neural tube, limb, heart or gastrointestinal defects, cleft palate or hydrocephalus. As there is a transplacental passage of antibodies to the influenza virus, 68% of the child is protected against the disease in the first six months of life [5]. This is the age range at which the vaccine is not recommended, but it is also the age range where the risk of death is higher compared to other age groups [5]. Therefore, it is recommended that a booster dose of seasonal influenza and whooping cough vaccines be given, especially during pregnancy. Influenza vaccines can be given at any time during pregnancy, and pertussis vaccines after the first trimester of pregnancy. Both require an interval of at least 14 days between immunization and delivery, and, especially in whooping cough, early immunization has been shown to increase antibody titer in neonates. [33].

Chickenpox and shingles

Chickenpox infection during pregnancy poses a high risk to the fetus and mother. A woman's immunity to VZV is assessed before she becomes pregnant on the basis of information about a history of varicella or receiving a vaccine against VZV, or a positive result of a serological test for VZV. VZV vaccine is a live attenuated vaccine, therefore vaccination should be done 4 weeks prior to conception as there is a theoretical risk of birth defects. If a pregnant woman comes into contact with a person suffering from chickenpox and the serological status is unknown or immunity is absent, specific immunoglobulin should be administered within 96 hours, because VZV infection can cause both chickenpox and shingles (HZ). The development of shingles rarely occurs during pregnancy. HZ in the mother does not increase fetal mortality, and VZV is rarely transmitted to the fetus. However, HZ increases maternal morbidity. Following infection with herpes zoster, patients usually develop viral prodrome preceding the appearance of the characteristic rash of herpes zoster. HZ is clinically diagnosed from rash but can be confirmed by polymerase chain reaction and enzyme immunoassay. Pregnant women with uncomplicated herpes zoster should be treated with oral acyclovir. In terms of prophylaxis, varicella and shingles vaccinations are not recommended for pregnant women and it is important that non-immunized pregnant women avoid exposure to VZV. Although a shingles infection has minimal impact on the fetus, maternal shingles and its complications place a significant burden. It is important to focus care on the mother (with appropriate treatment and management of complications as they develop). If a woman is

vaccinated with the VZV vaccine, the planned pregnancy should be postponed by at least 4 weeks [34].

Vaccination against HPV is widespread. Millions of doses have been administered worldwide. Inadvertent administration during pregnancy may occur because the main target audience is young fertile women of childbearing age who may not be aware of their pregnancy at the time of vaccination. To investigate the topic of HPV vaccine and pregnancy, the PubMed and Embase databases were searched for relevant literature published in English over the past 10 years. Most of the evidence of adverse events in the fetus following HPV vaccination relates to spontaneous abortion. None of the relevant studies showed a significantly increased rate of spontaneous abortions in the overall analyzes. There were no indications of other adverse events related to HPV vaccine during pregnancy or immediately after conception. The human papillomavirus (HPV) quadrivalent vaccine is recommended for all girls and women between 9 and 26 years of age. Some may have inadvertent exposure to vaccination in early pregnancy, but there is little data on the safety of the HPV quadrivalent vaccine in this context. A study funded by the Novo Nordisk Foundation and the Danish Medical Research Council with quadrivalent HPV vaccine during pregnancy did not show a significantly higher risk of adverse pregnancy outcomes than in the absence of such exposure.

Hepatitis A

Viral hepatitis, mainly caused by hepatitis A, B, C, D, and E viruses, is an inflammation of the liver and an important global health challenge. Hepatitis causes liver disease during pregnancy, so preventing and controlling mother-to-child transmission is an important concern for the pregnant population. ACIP recommends administration of inactivated HA vaccine during pregnancy only if the benefit outweighs the potential risk of HA and the inactive vaccine during pregnancy should be administered at 0 and 6 months of pregnancy [36,37]. The Food and Drug Administration (FDA) classifies inactive HA vaccines as class C drugs for use in pregnant women. In addition, there is a theory that immunoglobulin is important during pregnancy to prevent exposure. In the Vaccine Adverse Event Reporting System (VAERS), an undesirable result of vaccination in pregnancy was spontaneous miscarriage [37].

Hepatitis B

Vaccinations can be effective in preventing horizontal and vertical transmission of hepatitis B or C, which reduces the risk of this disease. While theoretically inactive vaccines given to pregnant women do not increase the risk of adverse maternal or fetal effects, it is currently accepted to only administer 2 vaccines (influenza and Tdap (tetanus, diphtheria and pertussis) during pregnancy. Vaccination against viral hepatitis during pregnancy is of benefit. not only to mothers, but also to the developing fetus thanks to passive maternal protection. Therefore, vaccination of susceptible or high-risk pregnant women should be considered. There are 2 types of hepatitis B (HB) vaccines: plasma-derived vaccines and recombinant HB vaccines however, only recombinant HB vaccines are used worldwide. Recombinant HB vaccines in a 3- or 4-dose schedule, such as Engerix-B, are effective and safe in adult infants, although data on the safety of HB vaccines during pregnancy are somewhat limited. , neither of them testifies to the existence of There will be more side effects in vaccinated pregnant women than in unvaccinated women. Moreover, the evidence shows that the main side effects of the injection are mild and are generally limited to a local reaction. Another study in the VAERS database described adverse effects of pregnancy, showing that approximately 50% of 88 women reported pregnancy complications, including spontaneous abortions, stillbirths, birth defects, and premature births, although the actual number may be understated. Overall, the

available data do not provide consistent data on the efficacy and safety of HB vaccines during pregnancy [37,38].

Hepatitis C

Hepatitis C virus (HCV) infection is also an important cause of chronic liver disease, cirrhosis, and liver cancer. Approximately 1-8% of pregnant women worldwide are positive for HCV infection, but the prevalence of infection in pregnancy is difficult to confirm due to the lack of representative large-scale studies. In the case of hepatitis C in children, vertical transmission plays an important role; It is estimated that the frequency of mother-to-child transmission from HCV non-HIV infected women is 2–8%. This situation occurs 2-3 times more often in mothers co-infected with HIV. Currently, there is no vaccine against hepatitis C, and immunoglobulin is not effective in preventing HCV infection before or after exposure [39,40].

Hepatitis D

Hepatitis D infection only occurs with HBV infection. Co-infection usually leads to acute HDV infection, while superinfection causes chronic infection in over 90% of cases. Acute HDV infection is not directly fatal in pregnancy, but infection can promote liver disease associated with HBV. Therefore, hepatitis D is considered to be one of the most severe forms of viral hepatitis in humans. There are no HD vaccines or immunoglobulins to prevent hepatitis D, but measures to prevent hepatitis B are also generally effective against HDV infection [40].

Hepatitis E

Hepatitis E virus (HEV) infection is a common cause of non-A, non-B, acute intestinal hepatitis transmitted through the gut. Compared to other types of viral hepatitis, pregnant women have an increased risk of getting HEV. Pregnant women infected with HEV are characterized by high morbidity and mortality from acute liver failure, and adverse maternal effects such as abortion, premature birth, stillbirth and intrauterine death are common in those infected. Moreover, some studies have observed vertical transmission among infected mothers [40,41]. In addition, immunoglobulin is not recommended for the prevention of hepatitis E; although limited, existing evidence suggests its protective effect on infection with this type of virus.

The efficacy and safety of HE vaccines

The inclusion of hepatitis B vaccination in national immunization programs has significantly reduced the transmission of hepatitis B virus (HBV). A key control strategy is the birth rate and immunization of the infants. Additional measures include the use of Hepatitis B Immunoglobulin (HBIG) and the diagnosis of mothers at high risk of HBV transmission and the use of medications. Vaccination against HBV and HAV is important in women planning pregnancy. HBV vaccine is administered in the form of 3 doses / 0-1-4 months /, HAV which is inactivated can be administered in the form of 2 doses / 6-18 months / before exposure, or as prophylaxis after exposure / 6-18 months / . These vaccines are recombinant, therefore there is no requirement to defer the concept after vaccination. If the vaccination series is not completed before pregnancy, vaccination may be administered during pregnancy because of the benefits that outweigh the potential risks. Whilst there are limited data from trials with limited number of samples that suggest efficacy or safety of hepatitis B and E vaccines in pregnant women, additional data are needed to provide evidence of vaccination during pregnancy [36, 37].

Pregnancy should not be a contraindication to vaccination with inactivated vaccines or immunoglobulin, as vaccination of pregnant women protects sensitive or high-risk mothers, fetuses and infants. There is no global policy regarding immunization during pregnancy. Although HBIG administered to pregnant women infected with HBV may reduce the incidence of intrauterine infections, it is not approved worldwide, possibly due to the potential risk or prohibitive cost of therapy. In addition, compared with hepatitis A, B, C and D viruses, cases of lightning hepatitis failure have been observed in pregnant women with HEV infection. The HEV vaccine currently available in China may be a candidate for preventing hepatitis E infection in pregnant women. Moreover, due to obstacles in clinical trials of vaccines in pregnant women, observational studies may be useful in assessing the efficacy and safety of vaccinations during pregnancy [41].

Summary

Vaccination of pregnant women to protect the pregnant woman, the fetus and the child has by no means become commonplace. The bias of health professionals increases the concerns of women and their families.

Obstetrician gynecologists, family doctors and midwives must incorporate vaccinations into standard clinical care. Strong communication strategies are needed to reduce parental reluctance to vaccinate and regulatory agencies approval to use vaccines during pregnancy. It must be clear that the lack of clinical trials in pregnant women, and hence the absence of a statement on the use of the vaccine in pregnant women, does not preclude its use during pregnancy. The reluctance to vaccination is associated with parents' concerns about the vaccination themselves or their children. There are a wide range of factors contributing to the decision not to vaccinate, including the compulsory nature of vaccines, their incidental temporal association with adverse health outcomes, ignorance of preventable diseases through vaccination, and distrust of health facilities. The percentage of parents applying for non-medical exemptions from school immunization requirements has increased over the past decade. Reluctance to vaccinate is an important issue that needs to be addressed because effective control of vaccine-preventable diseases generally requires extremely high vaccination timelines indefinitely. The multifactorial and complex causes of vaccine failure require a wide range of approaches at the individual, provider, health system and national levels. These include tailored messages for parents who have concerns about immunization, especially for women who are pregnant for the first time. The potential of vaccines to prevent disease and save lives has never been greater. However, this potential is directly dependent on parental acceptance of vaccines, which requires trust in vaccines, healthcare professionals who recommend and administer vaccines, and systems to ensure vaccine safety.

Conclusions

1. Obstetrician-gynecologists, family doctors and midwives, who already provide women with a large and valuable set of medical care, must incorporate vaccinations into standard clinical care. They must be convinced that vaccination of pregnant women has become an inevitable preventive measure that protects mother, fetus and child.
2. Doctors have a big impact on the parents' decision on vaccination. Physician-directed intervention does not reduce the mother's reluctance to vaccinate or improve the physician's effectiveness.
3. Challenges for healthcare professionals to inform and educate pregnant women include fear of needles, a lack of knowledge about the vaccine, a lack of perceived benefits, and a lack of knowledge about the serious consequences of preventable disease.

4. Research is needed to identify other communication strategies that are effective in reducing the reluctance of parents to vaccination in primary health care.
5. In many countries, the vaccine is not contraindicated for use in pregnant women, but no vaccine is approved for use specifically during pregnancy

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